



PGEU GPUE

*Pharmaceutical Group of European Union
Groupement Pharmaceutique de l'Union Européenne*

Position Paper on Medicine Shortages

The Pharmaceutical Group of the European Union (PGEU) is the association representing community pharmacists in 31 European countries. In Europe over 400.000 community pharmacists provide services throughout a network of more than 160.000 pharmacies, to an estimated 46 million European citizens daily.

PGEU's objective is to promote the role of pharmacists as key players in healthcare systems throughout Europe and to ensure that the views of the pharmacy profession are taken into account in the EU decision-making process.

Executive Summary

The unavailability of medicines is on the rise in Europe and it has a tremendous impact on patients. Medicine shortages occur across all healthcare settings and involve both essential life-saving medicines and very commonly used drugs.

Community pharmacists are very concerned about this phenomenon, which can compromise patients' health. Moreover, pharmacies and pharmacists invest a lot of resources dealing with shortages which constitutes not only a financial burden but also a loss of opportunity to spend time with other patient-centred tasks and to improve the quality of care.

Today, community pharmacists still manage to ensure continuity of care and minimise the impact on their patients' health status in most cases. However, several barriers should be removed to further support community pharmacists in this key role, considering that the impact on practice is increasing every day.

PGEU calls for a number of coordinated actions that should be taken at different policy levels to reduce the burden of medicine shortages on the public, healthcare professionals and supply chain actors:

1. **Ensure availability:** All stakeholders and governments must *put patients' needs first* when developing business policies, national laws and strategies that can affect the timely and adequate supply of medicines. Equally, effective compliance with EU & national laws related to the public service obligations of supply chain actors needs to be assured.
2. **Widen professional competence:** The scope of pharmacy practice should be extended when medicines are in short supply, so pharmacists can use their skills and knowledge to better manage patient care and ensure continuity of treatment. Shared electronic communication tools offer opportunities for an effective and close collaboration with prescribers in order to ensure continuity of care and patient safety.
3. **Improve communication:** Effective communication frameworks between all medicine supply chain actors and national competent authorities should be set up to ensure that community pharmacists have timely information on a (foreseen) medicine shortage.
4. **Compensate financial impact:** The negative financial impact of medicine shortages on patients should be compensated through appropriate reimbursement and remuneration provisions. The resource investment by pharmacists and pharmacies should equally be recognized and valued.
5. **Develop effective governance systems:** A close collaboration between EU Member States and the European Medicines Agency (EMA) is needed especially to improve reporting, monitoring and communication on medicine shortages. At national level, more structural, timely and transparent collaboration models between supply chain stakeholders and national competent authorities must be developed in order to increase the efficiency and effectiveness of joint notification and assessment practices, and to empower pharmacists in reducing the impact on their patients.

1. Introduction

Medicines shortages are today one of the biggest barriers towards patients' access to medicines in Europe. Over the past years, the situation has worsened significantly^{1,2,3,4}, leading to a high impact on patients.

Across countries and institutions, medicine shortages are defined through a range of diverging definitions⁵. Most of these definitions do not capture the full impact of the unavailability of medicines on patients, including the frequently occurring short-term unavailability of medicines, or are due to their specific purpose (such as harmonising reporting criteria for marketing authorisation holders) not applicable for both supply and demand side.

For the purposes of this paper, the term “medicine shortage” covers *every (temporally) inability for a community or hospital pharmacy to supply patients with the medicinal product requested as a result of factors beyond their control, requiring the dispensing of an alternative agent or even discontinuation of an ongoing medical therapy*. It should also be noted that equally for medical devices, shortages occur and can strongly impact patient care.

PGEU has conducted an annual survey for a number of consecutive years to evaluate the progression of medicine shortages in Europe and to understand their impact on the community pharmacy practice. In 2018, **all responding member countries (21) indicated they had experienced shortages in the previous 12 months**, and **38% of responding countries indicated that the situation had become worse compared to the previous year**. For instance, in Portugal, the National Association of Pharmacies (ANF) reported a 32.8% increase of medicines short in supply when compared to 2017.

These shortages occur across all healthcare settings and involve both essential life-saving medicines and very commonly used medicines such as ibuprofen⁶. The European Association of Hospital Pharmacists' 2018 Medicine Shortages Survey has highlighted that in the hospital setting, medicine shortages have become more problematic in recent years and offer a high burden on patients and pharmacy practice⁴. Ultimately, patients and consumers are the ones affected by medicine shortages. The unavailability of a medicine causes inconvenience and distress to the patient, but worse, may negatively affect health outcomes.

¹ <https://nos.nl/artikel/2267384-weer-meer-medicijnen-niet-leverbaar.html>

² https://www.rtf.be/info/societe/detail_les-pharmaciens-tirent-la-sonnette-d-alarme-une-grosse-penurie-de-medicaments?id=10062023

³ <https://www.bbc.com/news/health>

⁴ EAHP's 2018 Survey on Medicines Shortages to improve patient outcomes, available from: http://www.eahp.eu/sites/default/files/report_medicines_shortages2018.pdf

⁵ De Weerd, Elfi et al. “Toward a European definition for a drug shortage: a qualitative study.” *Frontiers in pharmacology* vol. 6 253. 30 Oct. 2015, available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4626567/>

⁶ <https://www.apotheke-adhoc.de/nachrichten/detail/markt/ibuprofen-jetzt-wird-kontingiert/?platform=hootsuite>

Results of a survey⁷ run by the French patient organisation France Assos Santé showed that 25% of respondents had already been denied supply to a medicine because of a shortage. 45% of these impacted respondents had to delay, change or stop treatment, which 21% found distressing. Consequences included aggravation of symptoms (14%), errors when taking an alternative medicine (4%) and even hospitalisation (4%).

If a prescribed medicine is not available, the patient may be given an alternative, which in some cases is not adequate and may be more expensive. Where there are no alternatives available, and the patient does not receive his/her treatment, the outcome may be fatal. Ultimately, patients may lose confidence in the health system. The root causes of the problem are diverse and complex, but **medicine shortages generally are the result of different economic, manufacturing or regulatory causes⁸**, such as:

- The increasingly globalised nature of pharmaceutical manufacturing, including Active Pharmaceutical Ingredients (API), with production concentrated in fewer sites distributed around the world;
- Shifts in demand, resulting from longer term factors such as demographic change, but also short-term factors such as tendering of medicines leading to difficulties in providing sufficient quantities of medicines for some markets;
- Pricing strategies, both low and high, and regulatory changes that in some cases may have an impact on supply;
- The imposition of fixed quotas of medicines by the pharmaceutical industry, often not sufficient in relation to patients' actual needs;
- The removal of the traditional role of the full line wholesalers as a result of Direct to Pharmacy (DTP) schemes in some markets;
- The abolition and ineffectiveness of public service obligation/minimum national stock keeping requirements in some countries;
- The lack of priority given to smaller markets;
- The effects of the European internal market dynamics (e.g. exports).

⁷ <http://www.france-assos-sante.org/sites/default/files/Penuries-medicaments-Resultats-BVA-dec2018.pdf>

⁸ Addressing medicine shortages in Europe, a report by The Economist Intelligence Unit. Available from : <http://graphics.eiu.com/upload/topic-pages/medicine-shortages/Addressing-medicine-shortages-in-Europe-EIU.pdf>

2. Impact on community pharmacy practice

In 2018, pharmacy organisations in several European countries have raised attention to the problem of unavailability of medicines. For instance, its increasing occurrence in Belgium², France⁹, the Netherlands¹, Portugal¹⁰ and the United Kingdom³ has been covered extensively in national media in 2018 and has triggered a public debate.

Our 2018 Survey on Medicine Shortages highlighted that **pharmacists in Europe spend on average 5.6 hours/week on mitigating shortages**. This time is invested by pharmacists to ensure patients can continue treatments where possible and such a task is done without receiving any type of financial compensation. Time solving problems caused by shortages is time that pharmacists could better spend advising and caring for patients.

Pharmacists try to reduce the inconvenience for patients and the impact on their care to the absolute minimum. Especially, for essential and life-saving medicines, community pharmacists often ensure a minimum stock of a number of highly expensive medicines for an individual patient, taking the risk of not being able to dispense them anymore when unforeseen therapy switches occur.

Additionally, in some countries **medicine shortages are even resulting in a direct loss to pharmacists** caused by increased sourcing prices as a reaction to low availability of a certain medicine^{3,11}.

⁹ <https://www.bfmtv.com/sante/penurie-de-medicaments-les-ruptures-de-stock-s-aggravent-1554956.html>

¹⁰ According to data of the National Association of Pharmacies (ANF), in 2018 64.1 million cases of packs on shortage were reported, 32.8% more than in the same period in 2017.

¹¹ <https://psnc.org.uk/funding-and-statistics/funding-distribution/dispensing-at-a-loss/>

3. Solutions offered by community pharmacy

As highlighted above, searching for solutions to ensure continuity of treatment due to medicine shortages has become a daily activity of community pharmacists in Europe. However, the type of solutions community pharmacists can offer to patients differ between European countries as a result of national legislation and regulation.

For the purposes of this paper, we adopt the following definitions related to the scope of pharmacy practice:

- Generic substitution: *The practice of exchanging at pharmacy level one medicine instead of another with the same active substance, strength and pharmaceutical from another manufacturer, without consulting the prescriber.*

In the context of medicine shortages, this covers both the substitution from a branded drug to a generic drug, substitution from one generic drug to another generic drug, and the substitution from a generic drug to a branded drug in exceptional circumstances (e.g. branded drug is the only available alternative).

- Therapeutic substitution: *The practice of exchanging at pharmacy level one medicine instead of another with a different active substance and with the same therapeutic intent, in consultation with the prescriber and patient or in accordance with national/local protocols.*

Currently¹², in most EU countries where therapeutic substitution is allowed in case of medicine shortages, it is done in consultation with the prescriber and patient. In early 2019, in the UK changes to legislation were started to permit the Government to use Serious Shortage Protocols (SSPs) in the event of a serious shortage of a medicine. These protocols would allow UK pharmacists to perform therapeutic substitution, amongst other options, as a solution to manage the medicine shortage¹³. Each protocol would set out precisely what action pharmacists can take, under what circumstances and for which patients.

- Therapeutic switching: *The decision by the prescriber to exchange one medicine for another with the same therapeutic intent.*

¹² May 2019

¹³ <https://psnc.org.uk/contract-it/brexit-and-community-pharmacy/serious-shortage-protocols-ssps/>

Depending on national rules, the most common solutions offered by community pharmacists are the following:

- Sourcing the same medicine from alternative authorised sources (e.g. other pharmacies where legally allowed or sourcing directly from manufacturers in case of contingency plans);
- Changing to the same medicine with a different strength when still available, and adjusting therapy posology accordingly;
- Generic substitution;
- Therapeutic substitution;
- Preparing a compounded formulation;
- Importing the medicine from a country where it is available and legally allowed.

According to recent data¹⁴ of the Royal Dutch Pharmacists Association (KNMP) Farmanco¹⁵ platform, **community pharmacists in the Netherlands were able to ensure continuity of treatment for their patients in 99% of medicine shortages cases:**

- 62%: solution possible with medicine containing the same active substance (through sourcing from other pharmacies, substituting brand, pack size and/or dosage);
- 25%: therapeutic substitution in consultation with the treating physician;
- 10%: import from another country;
- 2%: preparing a compounded medicine.

In several European countries, generic and/or therapeutic substitution by community pharmacists is still not legally allowed to assist the patients in need, even if they have the appropriate professional skills and knowledge. In case of prohibition of generic substitution, pharmacists must contact the prescriber or even have to send patients back to their doctor asking for a new prescription in order to dispense alternative medicines. Due to the high frequency of these requests, this offers an additional high burden on pharmacists and patients, and results in practical frustrations when, for instance, a prescriber cannot be reached immediately.

In countries where generic and/or therapeutic substitution is allowed, **it is crucial that pharmacists have access to sufficient information** (e.g. through shared electronic patient/medication records) to make well-informed decisions in case of medicine shortages. Vice versa, it is **equally important that pharmacists share any information on a therapeutic substitution/switch with the prescriber** so that **continuity of care** is ensured as part of a shared decision-making process. Systems should also be in place so that prescribers are better informed on existing medicine shortages and, consequently, can immediately prescribe an alternative medicine for their patients.

¹⁴ <https://farmanco.knmp.nl/tekorten-in-cijfers>

¹⁵ <https://farmanco.knmp.nl/>

4. Communication within the Supply Chain

An additional source of frustration among community pharmacists is the **lack of communication about the shortage, its severity, potential alternatives and how long it will take to be resolved**. This information, if provided in a timely and efficient manner, would allow pharmacists to serve their patients better and plan their practice and stock accordingly.

Together with the European associations representing manufacturers of medicinal products, parallel distributors, pharmaceutical wholesalers, industrial pharmacists and hospital pharmacists, PGEU has addressed the issue of communication in the **2017 Joint Supply Chain Actors Statement on Information and Medicinal Products Shortages**¹⁶. The recommendations call for greater transparency and availability of medicine shortage data, early detection and assessment of potential shortages, consistency of reporting, increased access to the information available across all parts of the supply chain, improved data infrastructure, and collaborative governance processes.

At the same time, pharmacists often experience or foresee supply difficulties before the industry or wholesalers are aware that there is, or will be, a problem. **Reporting systems should therefore be open to reports from all medicine supply chain stakeholders (including community pharmacists)**, with reference to the origin of reports of suspected shortages. 'Signals' of medicine shortages can then be periodically assessed by the national competent authority (NCA) to see if signals anticipate potential shortages or reflect actual shortages.

For example, in Ireland, the key stakeholders mentioned above have worked with the Health Products Regulatory Authority (HPRA) to produce a Medicine Shortages Framework¹⁷ and medicines shortages are notified to all stakeholders by e-mail weekly and through the HPRA website¹⁸.

In France, supply chain actors (manufacturers, wholesalers, community and hospital pharmacists) can notify shortages experienced at their respective level, both top-down and bottom-up through the electronic 'DP-Ruptures' system¹⁹. This automated system, developed by the French Chamber of Pharmacists, also connects the French Medicines Agency ANSM allowing for efficient exchange of information with supply chain stakeholders.

¹⁶ 2017 Joint Supply Chain Actors Statement on Information and Medicinal Products Shortages available from:

<https://pgeu.eu/en/component/attachments/attachments.html?task=attachment&id=4468>

¹⁷ HPRA Medicinal Product Shortages: a framework for a multi-stakeholder approach to handling shortages of human medicinal products. Available from: <https://www.hpra.ie/docs/default-source/publications-forms/guidance-documents/adv-g0020-medicines-shortages-framework-v2.pdf?sfvrsn=4>

¹⁸ <https://www.hpra.ie/homepage/medicines/medicines-information/medicines-shortages>

¹⁹ <http://www.ordre.pharmacien.fr/Le-Dossier-Pharmaceutique/Ruptures-d-approvisionnement-et-DP-Ruptures>

5. Role of public authorities

The European dimension to the issue of medicine shortages has been acknowledged by both national authorities and EU institutions. In 2016, the European Medicines Agency (EMA) and the Head of Medicines Agencies (HMA) created an **HMA/EMA Task Force on the Availability of Authorised Medicines for Human and Veterinary Use** to provide strategic support and advice to tackle disruptions in supply of human and veterinary medicines and ensure their continued availability. In August 2018, the new EMA/HMA Taskforce published its new work programme aiming to tackling the problem from three critical angles: marketing authorisation, supply chain disruptions and communication.

PGEU welcomes a **close collaboration between EU Member States and the EMA** and sees particularly opportunities in **improving reporting, monitoring and communication on medicine shortages**. A comprehensive EU communication strategy on shortages could ensure that information to healthcare professionals and the public on medicine shortages is universally accessible across Europe.

Today, across EU member states there are still too many differences in information provision on medicine shortages to key stakeholders such as pharmacists²⁰. Results of a 2018 European Commission survey^{21,22} have highlighted the **heterogeneous transposition by EU Member States of Article 23a of EU Directive 2001/83/EC**²³, which states that in case of foreseen disruption of a medicinal product's supply (temporarily or permanently), the marketing authorisation holder shall notify the competent authority of the respective Member State no less than two months prior to the supply interruption.

Additionally, the survey responses²⁰ have shown **varying practices in regards to sharing this obligatory notification information to pharmacists**, with some countries making this information accessible to pharmacies, others requiring MAH to communicate directly to pharmacies, and finally highlighting countries that have no clear communication strategy to pharmacists at all.

In response to this issue, in several European countries, pharmacy associations have pro-actively developed tools for pharmacists that provide timely and effective information to support them in mitigating shortages for their patients, often in close collaboration with their national competent authorities.

²⁰ Bochenek, Tomasz et al. "Systemic Measures and Legislative and Organizational Frameworks Aimed at Preventing or Mitigating Drug Shortages in 28 European and Western Asian Countries." *Frontiers in pharmacology* vol. 8 942. 18 Jan. 2018, doi:10.3389/fphar.2017.00942.

Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5779072/>

²¹ https://ec.europa.eu/health/sites/health/files/files/committee/ev_20180525_summary_en.pdf

²² https://ec.europa.eu/health/sites/health/files/files/committee/ev_20180525_rd03_en.pdf

²³ https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf

Examples are the Royal Dutch Pharmacists Association (KNMP) Farmanco Platform¹⁴, the French Chamber of Pharmacists (Ordre national des pharmaciens) Dossier Pharmaceutique Ruptures¹⁹, the Slovakian Chamber of Pharmacists (Slovenská Lekárnická Komora) drug shortages database²⁰, the Spanish General Pharmaceutical Council (Consejo General) CISMED platform¹⁶, and the Portuguese National Pharmacy Association (ANF) drug shortages database¹⁶.

National competent authorities and the European Medicines Agency should use these best practices as examples for developing **structural, timely and transparent collaboration models with supply chain actors** in order to increase the efficiency and effectiveness of joint notification and assessment practices, and to empower pharmacists in reducing the impact on European patients.

Member States also have a strong responsibility in taking appropriate measures in relation to the **obligation of continuous supply by marketing authorisations holders and wholesaler distributors** as laid down in article 81²⁴ of EU Directive 2001/83/EC. Depending on the national situation and public service obligations laid down in national legislation, Member States have several policy levers to ensure compliance by supply chain actors, taking into account the dynamics of the EU internal market²⁵.

Finally, as recommended by the European Parliament in its resolution on EU options for improving access to medicines²⁶, Member States must also assess the **impact of parallel trade and supply quotas** and address the **withdrawal of effective medicines** from the market for **economic reasons**.

²⁴ This article states that the holder of a marketing authorisation for a medicinal product and distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medicinal product to pharmacies and persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered

²⁵ Paper on the obligation of continuous supply to tackle the problem of shortages of medicines Agreed by the Ad-hoc technical meeting under the Pharmaceutical Committee on shortages of medicines on 25 May 2018. Available from: https://ec.europa.eu/health/sites/health/files/files/committee/ev_20180525_rd01_en.pdf

²⁶ European Parliament resolution of 2 March 2017 on EU options for improving access to medicines. Available from : <http://www.europarl.europa.eu/sides/getDoc.do?type=TA&reference=P8-TA-2017-0061&language=EN&ring=A8-2017-0040>

6. Recommendations

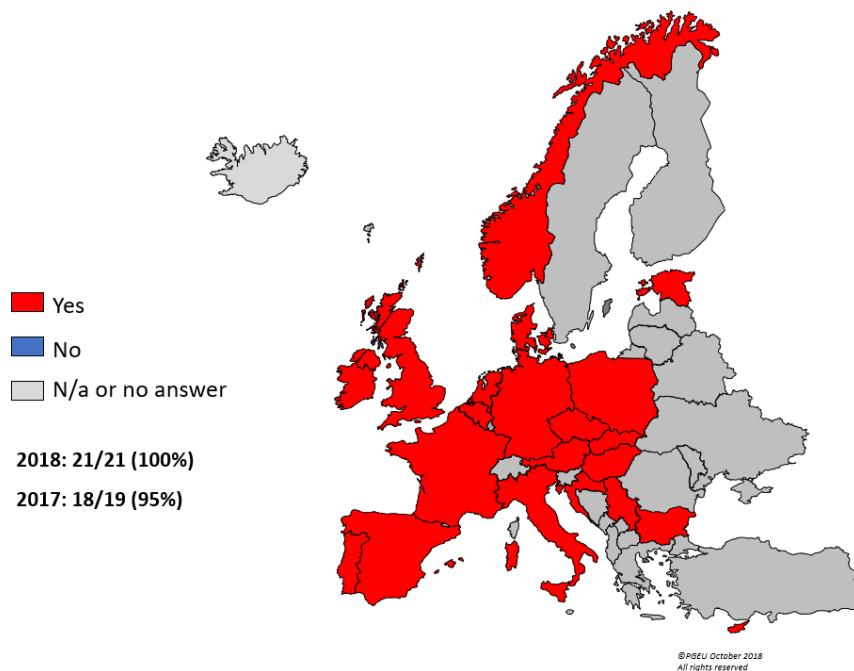
To effectively address the growing issue of medicine shortages in Europe, PGEU calls on the EU Institutions, Member States and supply chain actors to:

1. **Ensure availability:** In developing business policies and national laws and strategies all stakeholders and governments must *put patients' needs first*. These strategies should first and foremost aim to ensure timely and adequate supply of medicines to patients. The full impact of policies aimed at reducing medicine prices on the supply and availability of medicines needs therefore to be taken into account by policy makers. Equally, appropriate measures need to be taken to ensure compliance with EU & national law related to the public service obligations by marketing authorisation holders and wholesaler distributors, taking into account the dynamics of the EU internal market.
2. **Widen professional competence:** The scope of pharmacy practice should be extended when medicines are in short supply, so pharmacists can use their skills and knowledge to better manage patient care and ensure continuity of treatment. When a medicine is not available, pharmacists should be allowed to substitute with the most appropriate alternative as part of a shared decision-making process with prescribers and patients or in accordance with national protocols where appropriate. Shared electronic communication tools between pharmacists and prescribers (e.g. shared electronic health records) can enable this process effectively and safely.
3. **Improve communication:** The following principles should be adopted by national and European competent authorities, when developing policies and communication strategies on shortages:
 - a. Ensure greater transparency and availability of medicine shortages data;
 - b. Encourage early detection and central assessment of potential shortages by connecting all medicine supply chain actors and NCAs at national level in consistent reporting systems;
 - c. Increase access to the information available across all parts of the supply chain.
4. **Compensate financial impact:** The negative financial impact of medicine shortages on patients should be compensated through appropriate reimbursement and remuneration provisions. The resource investment by pharmacists and pharmacies should equally be recognized and valued.
5. **Develop effective governance systems:** A close collaboration between EU Member States and the European Medicines Agency (EMA) is needed especially to improve reporting, monitoring and communication on medicine shortages. At national level, more structural, timely and transparent collaboration models between supply chain stakeholders and national competent authorities must be developed in order to increase the efficiency and effectiveness of joint notification and assessment practices, and to empower pharmacists in reducing the impact on European patients.

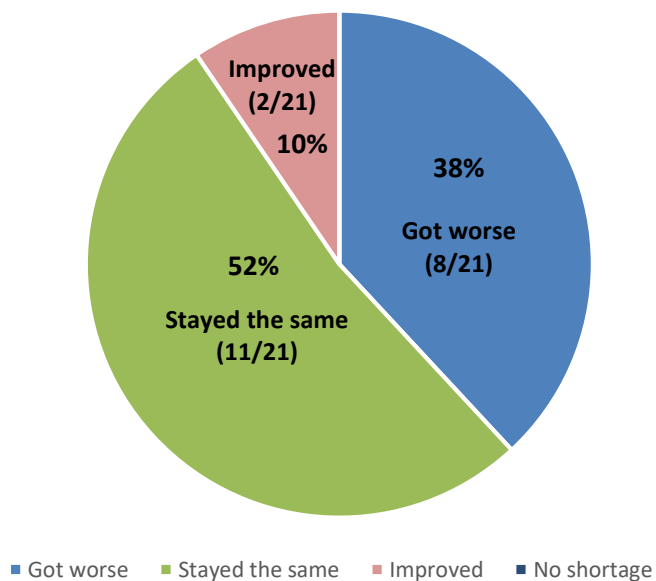


ANNEX: 2018 PGEU Medicine Shortages Survey Results (October 2018)

Q1: In the last 12 months have you experienced medicines shortages in your country?



Q2: In the last 12 months the shortages situation has:

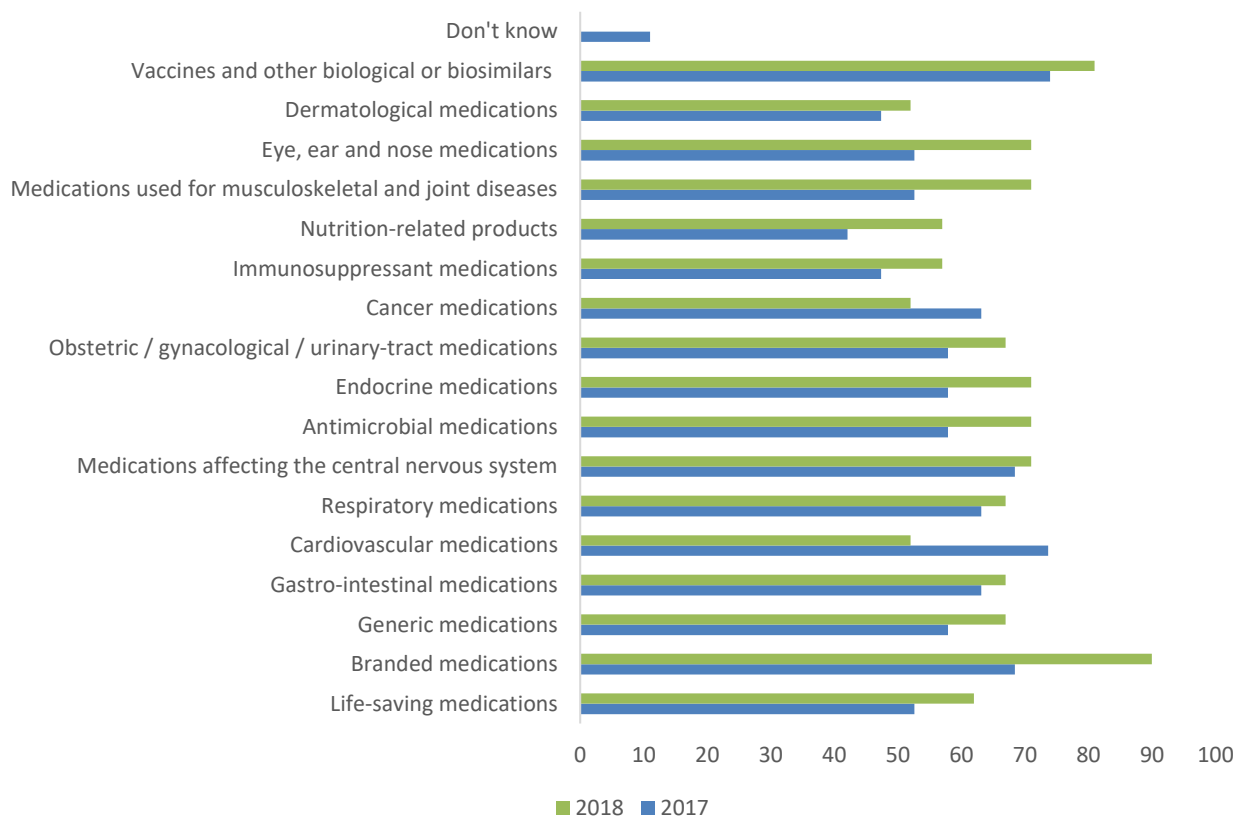




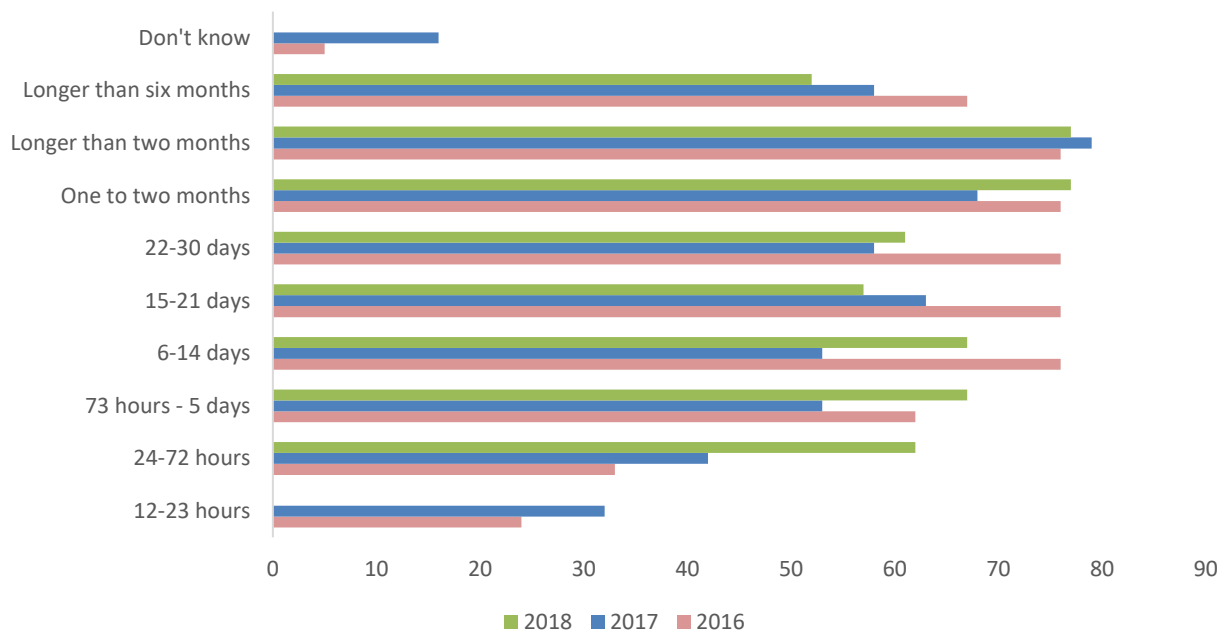
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Q3: Which medicines have been in short supply? (% of countries)



Q4: For which of the following time periods has a medicine been unavailable? (% of countries)





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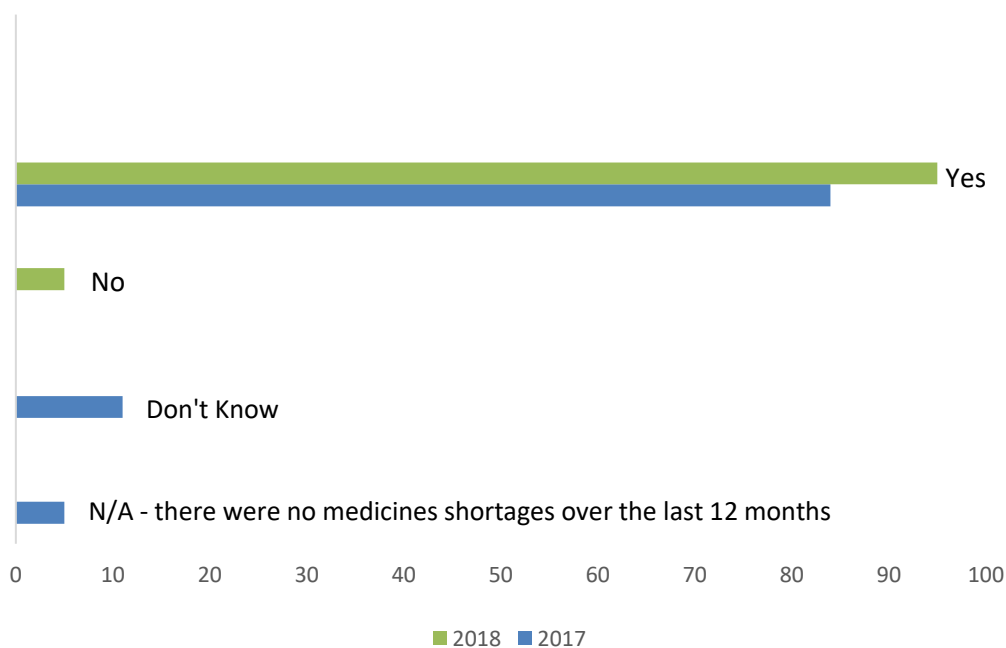
Q5: Average time spent per pharmacist per week (hours) dealing with shortages in Europe.



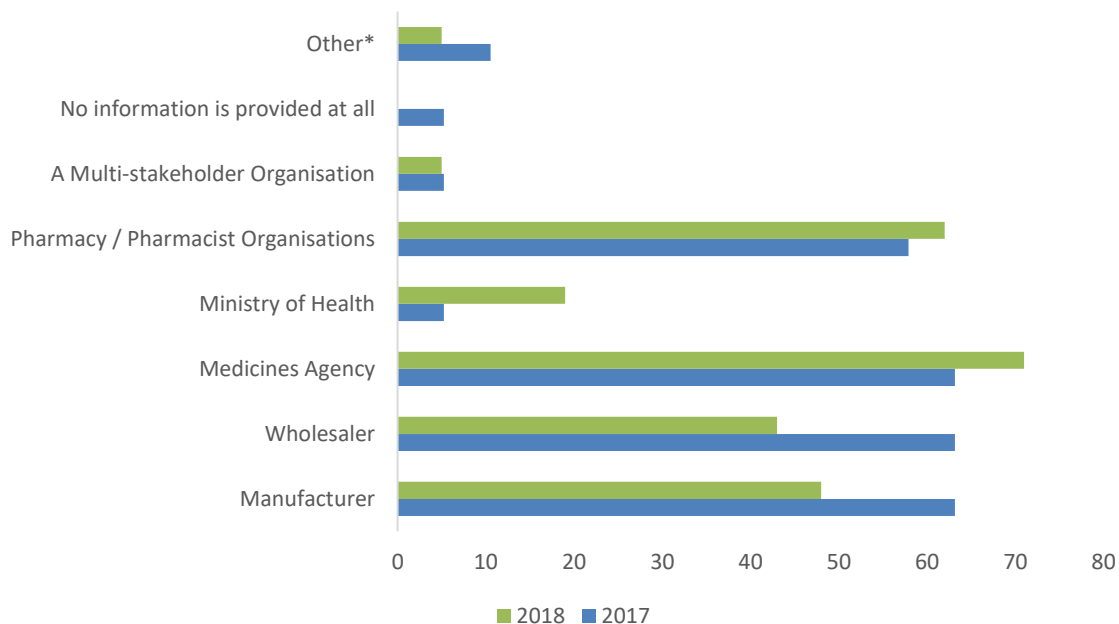
5,6 hours

(2017: 6,9 hours & 2016: 6,5 hours)

Q6: Have medicines shortages adversely affected patients? (% of countries)



Q7: Who provides information on shortages?



Summary of the main findings

- All responding countries have experienced shortages within the last 12 months, as was for 2017 and 2016.
- 38% of responding countries stated the situation had become worse over the last 12 months compared to 37% from 2017 and 48% in 2016. 52% stated the situation had stayed the same compared to 48% in 2017 and 43% in 2016, and only 10% stated the situation had improved (compared to 5% in 2017 and 2016)).
- There have been increases in shortages since 2017 in all classes of medication except for cancer medications and cardiovascular medications.
- There have been decreases of shortages that had lasted over 6 months (half of responding countries, compared to two-thirds in 2016 & 2017). Similar responses in countries reporting shortages of longer than 2 months compared to previous years have been obtained (77%, this year, 79%, in 2016 and 76% in 2015). Short-term shortages (up to 72 hours) have increased significantly for the third consecutive year whereas medium-term shortages (73 hours to up to two months) show comparable responses to 2017.
- On average, the amount of time that pharmacists spend on mitigating shortages each week is 5,6 hours/week.
- 95% of responding countries reported that these shortages have potentially harmed patients.
- In most countries, pharmacists receive information on medicines shortages mainly from medicines agencies and pharmacy/pharmacist organisations. There has been a decrease in provision of information on shortages by wholesalers and manufacturers.

EAHP Position Paper on Medicines Shortages

The problems caused by medicines shortages are serious, threaten the well-being of patients and have far reaching consequences for European health systems. Consequently, the European Association of Hospital Pharmacists (EAHP) started in 2013 to analyse in more detail the challenge posed by medicines shortages. Two pan-European surveys on medicines shortages in the hospital sector were conducted by the Association in 2014¹ and 2018² to investigate the prevalence and nature of shortages as well as direct impact on patient care. The percentage of hospital pharmacists reporting shortages to be an issue in particular in terms of delivering the best care to patients has seen a significant increase in 2018 with 91.8% respondents – compared to 86.2% in 2014 – stressing that medicines shortages constitute a problem in their hospital pharmacy.³ Such reports are alarming and demonstrate the urgent need to draft and implement corrective policies at all decision-making and professional levels across Europe. Multi-stakeholder action is urgently needed since only joint efforts can help diminish the impact of medicines shortages on patients. Consequently,

EAHP advises national governments to evaluate if their shortages measures and management systems are fit for purpose and to rectify shortcomings where and when needed.

EAHP urges national governments and healthcare organisations to evoke appropriate staffing levels in order to lower the impact that medicines shortages currently have on the overall patient services provided by hospital pharmacists.

EAHP calls on the European Commission to urgently commence an investigation of the medicines shortage problem looking at the causing factors and propose solutions that will help alleviate or solve shortages.

EAHP appeals for improved information exchange between authorities and supply chain actors as well as best practice sharing and implementation support on shortage management strategies between relevant national regulatory bodies to support patient safety.

EAHP urges the EMA and the HMA to consider the development of a comprehensive communication strategy on medicines shortages.

ACTION IN THE SUPPLY CHAIN

To minimise patient impact, all supply chain actors, including hospital pharmacists, wholesalers, manufactures and national competent authorities, have the obligation and responsibility to collaborate more closely in terms of resolving the shortages problem. When it comes to medicines availability, hospital pharmacists are the key information holder inside the hospital. They are responsible for sharing relevant notices on forthcoming shortages with colleagues, including the hospital management and prescribers. However, in order to fulfil this role, all supply chain actors, especially wholesalers and manufacturers, must communicate more effectively to hospital pharmacies about likely and current shortages. Such communication should be carried out in a timely manner and contain insights on how imminent the issue is, the expected duration of the shortage and whether alternatives are available. Communication between supply chain actors should be facilitated by national competent authorities to make sure that each entity works diligently and with urgency on bringing to an end the shortage difficulties that are currently experienced throughout Europe. The

overarching objective of these collaborative actions must be that the entire supply chain works together in minimising the detrimental effects on patients.

Managing medicines shortages and ensuring continuity of supply can cause the diversion of significant amounts of time⁴ and attention from other important tasks that a hospital pharmacist must perform in the provision of high quality, safe and efficacious care. It can also add to already high levels of stress experienced at the workplace. As shown in the results of the 2018 EAHP Medicines Shortages Survey, medicines shortages have the potential to result in increased medication error rates and lead to the delay or even the cancellation of therapies. Furthermore, efforts to reduce costs in health systems are very often undermined by having to opt for either a more costly or a less effective alternative that, in the long term, augments the use of financial resources by increasing the likelihood of hospital stay or readmission. Consequently, **EAHP urges** national governments and healthcare organisations to evoke appropriate staffing levels in order to lower the impact that medicines shortages currently have on the overall patient services provided by hospital pharmacists.

Hospital pharmacists in particular should remain vigilant and alert to the issue of medicines shortages as well as fully engage with prescribers and managers. To this end, they should raise awareness about the issue at local level and ensure the development and implementation of appropriate contingency plans. To better address the impact caused by shortages on patients and their therapy, hospital pharmacists should use and keep up to date their pharmacy skills in order to identify other solutions which can include small scale production of a medicine without a marketing authorisation.

ACTION AT NATIONAL LEVEL

The results of the 2018 EAHP Medicines Shortages Survey showed that many European countries have reporting systems in place. However, the views on their effectiveness were mixed with only 56% of participants judging their systems to be functional. Given the high degree of divergency throughout Europe, efforts should be made to strengthen the robustness and functionality of these reporting systems.⁵ Consequently, **EAHP appeals for** improved information exchange between authorities and supply chain actors as well as best practice sharing and implementation support on shortage management strategies between relevant national regulatory bodies to support patient safety. Ideally, it should be an expectation in each country that medicines are available to pharmacies within 24 hours of having ordered them.

The demand by hospital pharmacists for more timely and accurate information is increasing.⁶ To achieve higher quality of information, authorities and pharmacy practices should invest in combining their sourced shortages data. Such a measure would safeguard the timely detection of both temporary and permanent shortages since different signals on potential medicines shortages are being picked up by authorities and hospital pharmacists.⁷ In addition, national regulatory bodies should ensure action is taken against elements of the supply chain found to be in breach of legal and ethical obligations in relation to supply.⁸ Consideration should also be given to putting in place more rigorous rules on issuing timely alerts about shortage problems. **EAHP advises** national governments to evaluate if their shortages measures and management systems are fit for purpose and to rectify shortcomings where and when needed. This includes the removal of legal barriers that prevent compounding by hospital pharmacists in case of a medicine shortage.

ACTION AT PAN-EUROPEAN LEVEL

The problems created by medicines shortages have been widely reported by healthcare professionals^{9,10} as well as patients¹¹ and acknowledged at the European level by the European Medicines Agency (EMA), the European Commission and the Heads of Medicines Agencies (HMA). This

acknowledgement manifested itself on the one hand in the creation of a dedicated task force on the availability of authorised medicines for human and veterinary use¹² and on the other hand through dedicated research funding in the field of medicines shortages from the European Cooperation in Science and Technology (eCOST). Despite the efforts of the European Medicines Shortages Research Network¹³, funded by eCOST, the problem of medicines shortages continues to persist. The issues caused by medicines shortages are understood to be multifactorial. However, robust data on the causes are missing. To fill this information gap, **EAHP calls on** the European Commission to urgently commence an investigation on the medicines shortage problem by focusing on the causing factors and propose solutions that will help alleviate or solve shortages.

Closer collaboration between Member States is crucial for the pan-European solution finding process. The EMA and the European Commission are the most suitable actors to coordinate such action since they can build on their previous work, experience, expertise and involvement to date in this area. Further efforts should however be invested in the development of a comprehensive communication strategy, including the introduction of a unified European medicines identification system. Only a comprehensive communication strategy on shortages targeting all European states will ensure that all supply chain actors, including hospital pharmacists, receive adequate information on the shortage of medicines in their countries. National early reporting systems that exist in a number of countries should be complemented by a European-wide database that lists reasons and estimated durations of shortages. In addition, this system should include advice on alternatives which includes the expertise is provided by hospital pharmacists.

EAHP urges the EMA and the HMA to consider the development of a comprehensive communication strategy on medicines shortages.

¹ European Association of Hospital Pharmacists. Medicines shortages in European hospitals. The evidence and case for action. Brussels: European Association of Hospital Pharmacists (EAHP), 2014. Available from:

http://www.eahp.eu/sites/default/files/shortages_report05online.pdf.

² European Association of Hospital Pharmacists. EAHP's 2018 Survey on medicines shortages to improve patient outcomes. Brussels: European Association of Hospital Pharmacists (EAHP), 2018. Available from:

http://www.eahp.eu/sites/default/files/report_medicines_shortages2018.pdf.

³ Miljković N, Gibbons N, Batista A, et al Results of EAHP's 2018 Survey on Medicines Shortages Eur J Hosp Pharm 2019;26:60-65.

⁴ In some hospital pharmacies, many hundreds of hours. Drugs available in the EU – Future shortages? EJPB Practice. Volume 13. 2007/3.

⁵ Bochenek T et al (2018) Systemic Measures and Legislative and Organizational Frameworks Aimed at Preventing or Mitigating Drug Shortages in 28 European and Western Asian Countries. Front. Pharmacol. 8:942. Available from:

https://www.frontiersin.org/articles/10.3389/fphar.2017.00942/full?utm_source=Email_to_authors&utm_medium=Email&utm_content=T1_11.5e1_author&utm_campaign=Email_publication&field=journalName=Frontiers_in_Pharmacology&id=323253.

⁶ European Association of Hospital Pharmacists. EAHP's 2018 Survey on medicines shortages to improve patient outcomes. Brussels: European Association of Hospital Pharmacists (EAHP), 2018. Available from:

http://www.eahp.eu/sites/default/files/report_medicines_shortages2018.pdf.

⁷ Postma DJ, De Smet PAGM, Gispén-de Wied CC, Leufkens HGM and Mantel-Teeuwisse AK (2018) Drug Shortages From the Perspectives of Authorities and Pharmacy Practice in the Netherlands: An Observational Study. Front. Pharmacol. 9:1243. Available from:

<https://www.frontiersin.org/articles/10.3389/fphar.2018.01243/full>.

⁸ De Weerd E, Simoens S, Hombroeckx L, Casteels M, Huys I. Causes of drug shortages in the legal pharmaceutical framework. Regul Toxicol Pharmacol. Elsevier Inc.; 2015;71: 251–258.

⁹ The Economist Intelligence Unit. Cancer medicines shortages in Europe. Policy recommendations to prevent and manage shortages. London: the Economist Intelligence Unit Limited, 2017. Available from: <http://www.eiu.com/graphics/marketing/pdf/ESMO-Cancer-medicines-shortages.pdf>.

¹⁰ Postma DJ, De Smet PAGM, Gispén-de Wied CC, Leufkens HGM and Mantel-Teeuwisse AK (2018) Drug Shortages From the Perspectives of Authorities and Pharmacy Practice in the Netherlands: An Observational Study. Front. Pharmacol. 9:1243. Available from:

<https://www.frontiersin.org/articles/10.3389/fphar.2018.01243/full>.

¹¹ EURORDIS. Common position between patients', consumers, and healthcare professionals' organisations involved in the activities of the European Medicines Agency on Supply Shortages of Medicines. Paris: EURORDIS, 2014. Available from:

<http://download2.eurordis.org.s3.amazonaws.com/documents/pdf/common-position-supply-shortages-final-10-2013.pdf>.

¹² Heads of Medicines Agencies. European Medicines Agency EU regulatory network reflection paper on the availability of authorised medicinal products for human and veterinary use. 2018. Available from: [http://www.hma.eu/fileadmin/dateien/HMA_joint/00-About_HMA/03-](http://www.hma.eu/fileadmin/dateien/HMA_joint/00-About_HMA/03-Working_Groups/TF_Availability/2018_08_TF_AAM_Reflection_paper_on_the_availability_of_authorised_medicinal_products_for_human_and_veterinary_use.pdf)

[Working_Groups/TF_Availability/2018_08_TF_AAM_Reflection_paper_on_the_availability_of_authorised_medicinal_products_for_human_and_veterinary_use.pdf](http://www.hma.eu/fileadmin/dateien/HMA_joint/00-About_HMA/03-Working_Groups/TF_Availability/2018_08_TF_AAM_Reflection_paper_on_the_availability_of_authorised_medicinal_products_for_human_and_veterinary_use.pdf).

¹³ eCOST. European Medicines Shortages Research Network – addressing supply problems to patients (Medicines Shortages) CA15105. Brussels: European Cooperation in Science and Technology (eCOST). Available from: <http://www.medicinesshortages.eu/>.

MEDICINE SHORTAGES IN EUROPE AND THEIR IMPACT ON PATIENTS A Reflection Paper

Executive summary

Currently no agreed definition of shortages exists– and for the purpose of this paper, we mean that medicines are not available for a patient.

It is without question that the availability and continuous supply of medicines is the cornerstone of a healthy society and therefore a key priority for European healthcare systems.

GIRP welcomes the recent release of the [EU Commission's Communication on Shortages](#).

Despite increasing medicines shortages, there is still a fundamental lack of clarity on their actual causes and there is an urgent need for robust solutions to resolve the problem.

Numerous plausible explanations have been put forward as reasons for medicines shortages. It seems that the reasons differ from country to country and from product to product. However, on a closer look, it is clear that there are some common underlying causes which seem to influence medicines shortages.

Based on the views of (full-service) healthcare distributors, this paper aims to initiate a deeper discussion and to outline distributors' perspectives on the causes of shortages, the impact and some potential solutions.

Our initial reflection reveals the following to be among the key underlying root causes of shortages:

- The increasing risk of supply disruption is attributed to the globalisation of production chains which do not have enough alternative sources of supply. The complexity and globalisation of production, where APIs are sourced in one country, products are produced in another one and packaged in a third country leads to a high sensitivity for the slightest failure, which then can create a general shortage across Europe, as evidenced by the recent global Valsartan® shortage¹
- The Falsified Medicines Directive mandates that Active Pharmaceutical Ingredients (APIs) imported into the EU must comply with European Good Manufacturing Practice guidelines (GMP) which has a knock-on effect on the sourcing of 'approved' APIs for the production of medicines. The unavailability of APIs complying with the EU standards leads to production and supply disruptions.
- Lack of market attractiveness from an economic perspective for certain (older) medicines results in manufacturers stopping production of some low-income generating products. A similar effect is caused by comparisons to international reference pricing regimes (leading to a downward spiral of prices).
- Ongoing healthcare budget challenges are contributing to the problem. Member States are coming to terms with increasing healthcare costs associated with longevity which is resulting in reduced incentives such as price reductions and margin cuts for marketing products.
- Procurement policy failures such as the apparent race by payers to grant tenders based on the lowest price possible without due consideration to secondary impacts on market sustainability or to the supply chain operators.
- Unforeseen disruptions or extraordinary demand due to bad weather, force majeure or viral outbreaks can result in shortages of certain products which suddenly see a rapid increase in volume demand;
- Stringent supply quotas imposed by pharmaceutical manufacturers on pharmaceutical full-service healthcare distributors with the attempt to steer the supply of medicines on the national markets.

¹ <https://www.fda.gov/Drugs/DrugSafety/ucm613916.htm>

When supply quotas are imposed without flexibility and understanding of changes in the market they can be a reason for medicines shortages instead of avoiding them.

- Parallel trading (PT) by distributors is frequently cited by other stakeholders as a contributing factor to shortages. Our initial reflection has not uncovered any real-world evidence to support this, and it is notable that many academic studies on this subject recycle stakeholder claims rather than concrete facts and figures. We would caution others against forming conclusions without evidence to support this. To highlight this fact, medicine shortages are a common problem in USA, Australia and Switzerland yet parallel trade does not operate in these countries.

This paper also reflects on those impacted most by shortages and yields one clear conclusion – patients are the most affected by medicines shortages. Furthermore, pharmacists as healthcare professionals must spend valuable time sourcing medicines instead of caring for their patients.

Having considered some of the root cause of shortages and those impacted by them, the paper looks at some possible pragmatic solutions to addressing the following issues:

- Combating production-related shortages with the support of the European Medicines Agency (EMA) and the national Medicines Agencies is key to preventing, anticipating, mitigating and managing shortages of important medicines caused by manufacturing/GMP compliance problems to avoid competition for products in short supply. Anticipation is crucial to soften the impact of a shortages situation for patients allowing to swiftly implement alternative treatment measures.²
- The European Commission and national authorities should adopt actions to support the continuation of products through market attractiveness for older medicines.
- We would welcome measures to encourage API manufacturing back into the EU thereby reducing exposure to remote global API production problems.
- Disruptions of supplies and unexpected demand of medicines can be combated through closer cooperation with pharmaceutical full-service healthcare distributors and by using preparedness programmes and buffer stocks established at European and / or national level.
- Full Service Distributors can play an important role in the sourcing and importation of medicines in short supply.
- Shortages arising due to economic hardship are partially resolved by the significant contribution of pharmaceutical full-service healthcare distributors to the economics of the sector in terms of pre-financing (function of pharmaceutical manufacturers and pharmaceutical full-service healthcare distributors) medicines' stocks in retail pharmacies' and hospitals.
- System failures can be dealt with through the effective monitoring and enforcement of Article 81, paragraph 2 of the Directive 2001/83/EC which refers to a joint obligation of pharmaceutical manufacturers and wholesalers to *"ensure appropriate and continued supplies of medicinal products to pharmacies and other persons authorised to supply medicinal products to the public so that the needs of patients in the Member State in question are covered"*. The introduction of a Public Service Obligation (PSO) on wholesale distributors combined with the right of the pharmaceutical full-service healthcare distributors to be supplied by pharmaceutical manufacturers, including the enforcement of these obligations, could be an efficient way to mitigate supply related shortages in order to fulfil the demand of the national market.
- In order to combat unjustified supply quotas, stakeholders in the supply chain should aim for increased collaboration, responsibility and accountability.

² Dominique Martin, CEO of ANSM in Sciences et Avenir, 28 February 2018

https://www.sciencesetavenir.fr/sante/530-sigalements-de-medicaments-en-rupture-de-stock-en-2017-une-augmentation-de-30_121655

Introduction

The continuity of supply and availability of medicines are key priorities of the European healthcare systems. Ensuring the availability of medicines for patients is therefore reflected in the EU legal framework governing the pharmaceutical sector, requiring supply chain partners to comply with it in accordance with Article 81 of Directive 2001/83³. However, medicine shortages have become an increasing problem in recent years. Due to the lack of availability of medicines, full-service healthcare distributors encounter difficulties ensuring the continuous supply of the full range of medicines. Recent studies have shown that medicine shortages not only adversely affect therapy and cause poorer treatment outcomes, but also compromise or delay medical procedures, lead to medication errors and to the use of less desirable, often more expensive, alternative medicinal products⁴.

Healthcare professionals are increasingly alarmed about the effects that unavailability of medicines has on patients and the significantly increased resources required for sourcing the medicines for their patients⁵. Shortages have seen a growth in number (1483 products in Italy in May 2018⁶, 530 products in France in 2017⁷) and complexity across Europe. Supply chain partners along with national and European authorities seek ways to prevent and solve this issue. Still, the measures adopted so far have not proved to be very effective at eliminating shortages of medicines.

Today, more and more Member States are facing shortages and discussions have been taken up not only at national level, but also on European level however, solutions are not easily found. The issue is as complex as the reasons for shortages of medicines are manifold and there is no quick fix available by implementing a single measure.

Medicines shortages are not only a European, but also an international problem. In the US, the Food and Drug Administration (FDA) has been working on reducing medicines shortages for over 12 years. In the past, the number of medicine shortages has annually tripled from 2005 to 2010.⁸ More recently the US shortages overall seem to have decreased from 251 products in 2011 to 23 products in 2016. According to the FDA 66% refer to quality and manufacturing related issues and 27% to problems with raw materials.⁹ While progress has been made, a high percentage of shortages are sterile injectables, including chemotherapy, anaesthesia and other acute medicines.

When considering medicines shortages in comparative terms between the US and Europe, it is worth noting that in Europe, parallel trade is among the most frequently cited reason for shortages, whereas in the US where shortages have been and continue to be a problem, no parallel trade activities occur.

Why do medicines shortages occur?

Until now, no clear answers could be given as to what triggers medicine shortages. Numerous reasons have been put forward, but they differ from country to country and from product to product. However, several dynamic forces appear to influence the lack of medicines such as the globalisation of manufacturing and subsequently their supply chains.

³ Directive 2001/83, Article 81, par 2: "The holder of a marketing authorisation for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medicinal product to pharmacies and persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered."

⁴ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113.pdf

⁵ http://www.ashp.org/DocLibrary/Policy/DrugShortages/ASHP_shortage_guide09.pdf

⁶ http://www.agenziafarmaco.gov.it/sites/default/files/elenco-medicinali-carenti_09.05.2018.pdf

⁷ <http://www.leparisien.fr/societe/penurie-inedite-de-medicaments-vitaux-en-france-27-02-2018-7582320.php>

⁸ <http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/ucm277755.pdf>

⁹ <https://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm441585.htm>

New provisions for Active Pharmaceutical Ingredients (APIs) and production related shortages

Pharmaceutical manufacturers increasingly encounter problems accessing active or key ingredients for the medicines they produce, due to the fact that many sources of active substances for life-saving medicines such as antibiotics are located outside the EU, including in countries with uncertain political and regulatory systems¹⁰. In addition, fewer medicines production sites, often scattered geographically, lead to supply shortages at a regional or even global level.

The European Union has increased quality assurance through new mandatory regulations for APIs imported from third countries with the adoption of the Falsified Medicines Directive. Under regulations in the Directive, which came into effect on 2nd July 2013, it is mandated that APIs imported into the EU must comply with European Good Manufacturing Practice (GMP) with written confirmation of compliance with EU standards. This increased API regulatory burden for manufacturers can also affect the certainty of medicines supply within the EU.

Lack of economic market attractiveness and policy failures

Reasons that may drive manufacturers to cease the production of specific medicines include the diminishing demand for products, lower profitability or the intention to move resources elsewhere. The lack of attractiveness of markets from an economic perspective is thus an important motive for unavailability of medicines. If medicines are to be made available on a national market, it is important that all operators, not only pharmaceutical manufacturers, but also pharmaceutical full-service healthcare distributors and pharmacies, can undertake their activities in a sustainable way. Especially in times of economic hardship it is crucial to consider the economic viability. Measures like international reference pricing lead to a downwards spiral of prices and the marketing of products in countries with the lowest reference prices becomes increasingly unattractive. The spill over effect of low prices therefore undermines the willingness for solidarity with countries, which are facing economic problems.

Shortages can also be a mirror of policy failures, caused by the constant aim of payers for the lowest price possible, often without considering the far-reaching consequences of the different measures used to bringing prices down. An increasing number of countries have introduced tendering procedures, creating in many cases shortages of products from the successful pharmaceutical manufacturer at least in the short term.

Disruptions of supplies and unexpected demand of medicines

Unforeseen medicine shortages may be caused by various interruptions in the normal delivery of medicines through the pharmaceutical supply chain and distribution network. Bad weather conditions, natural disasters, failed inspections or damage to production and storage facilities may result in a shortage of either raw materials or finished medicinal products. Furthermore, sudden outbreaks of viral diseases and a surge in demand for specific products can cause sudden shortages of specific medicines. Vaccines manufacturers in Europe are highly concerned about the continuous availability of vaccines and call for a multi stakeholder platform in order to improve the sustainable supply of vaccines¹¹.

Budgetary pressure and economic constraints

Due to constant budget pressure and economic constraints, the medicines supply chain is encountering an unprecedented economic burden. Supply chain partners and specifically pharmaceutical full-service healthcare distributors are often put in the position of having to pre-finance the healthcare system due to delayed

¹⁰ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113Al.pdf

¹¹ http://www.vaccines europe.eu/wp-content/uploads/2016/06/VE-Paper_shortagesFIN-2.pdf

payments. In some country's payment delays escalated to a worrisome level, causing supply chain partners to withdraw credit lines and to ask for pre-payment of medicine deliveries.

The tense economic climate also had a negative impact on wholesale remuneration, shrinking them to a level at which pharmaceutical full-service healthcare distributors are just about covering their costs. Current cost pressures on pharmaceutical full-service healthcare distributors might also lead to a reduction in the number of deliveries, which on the other hand would force pharmacies to increase their medicines stock.

Supply quotas

Supply quotas unilaterally imposed by pharmaceutical manufacturers can have a potential boomerang effect and cause supply shortages instead of avoiding them. Pharmaceutical manufacturers impose supply quotas on pharmaceutical full-service healthcare distributors to try to control and steer the supply of medicines on national markets. In practice, however, quotas when imposed without any flexibility have proven to aggravate the underlying problem rather than address it, causing major problems on a daily basis for pharmaceutical full-service healthcare distributors, who face significant challenges to obtain the needed stock of medication for the patients¹². Pharmaceutical full-service healthcare distributors struggle on a daily basis with the reality of supply quotas which when applied with view to impeding parallel trade they constitute an abuse of a dominant market position under the anti-trust provisions of the Treaty of the European Union unless it provides objective justifications. The challenge for pharmaceutical full-service healthcare distributors lies in the fact that it is left to the competency of the national court to determine what constitutes an ordinary order which is a burdensome / disproportionate process for a pharmaceutical full-service healthcare distributor to pursue in the course of daily business transactions.¹³.

The core problem is that in the case of quota restrictions full service healthcare distributors are supplied with only certain pre-set quantities of medicines, within defined time periods. The quantities are defined and allocated by pharmaceutical manufacturers and are often insufficient to meet the demands of full-service healthcare distributors, as usually quotas are based on historic data. If quotas are exhausted, full service healthcare distributors are not supplied with additional stocks of the respective products, even in circumstances where there is an obviously higher demand for these products from their usual customers and where pharmaceutical manufacturers clearly have the quantities available to meet the demand. Therefore, full service healthcare distributors are obliged to pass on quota restrictions, equally limiting their possibility to meet additional demand from pharmacies and patients, leading to shortages.

The way quota systems are imposed on pharmaceutical full-service healthcare distributors significantly differ between pharmaceutical manufacturers and Member States. Some pharmaceutical manufacturers do not communicate the volume of products comprised in their quota and only inform pharmaceutical full-service healthcare distributors once their quota is exhausted. This seriously affects the full-service healthcare distributor 's ability to plan the supply of the product for the national market. Quotas therefore can create tensions in the supply chain and sometimes hinder patients' access to their required medicines rather than facilitating it. Furthermore, the pharmaceutical full-service healthcare distributors are only able to deliver

¹² <http://www.appg.org.uk/APPG%20Pharmacy%20-%20Report%20of%20Inquiry%20Into%20NHS%20Medicines%20Shortages.pdf>

¹³ In September 2008, the ECJ gave a preliminary ruling based on national proceedings between the pharmaceutical company GlaxoSmithKline and Greek wholesalers exporting pharmaceutical products to countries where prices for medicines are higher, following referral from the Athens Court of Appeal (Joined Cases C-468/06 to C-478/06 Sot. Lelos & Sia E.E). The ECJ ruled that a dominant company's refusal to supply wholesalers with a view to impeding parallel trade constitutes an abuse of a dominant market position under Article 82 of the EC Treaty unless it provides objective justifications. While differences in national price regulations and Member States' control over pharmaceutical prices are in themselves not sufficient justifications, the court found that a producer of pharmaceutical products must be in a position to protect its own commercial interests if it is confronted with orders that are out of the ordinary in terms of quantity. Whether such orders are out of the ordinary is an issue for national courts to decide, taking into account the needs of the particular national market and previous trading relations between the parties.

medicines that they have on stock. Even in countries such as Switzerland¹⁴, where no medicines exports are allowed, it has been reported that pharmaceutical full-service healthcare distributors do not have sufficient supplies to satisfy the demand of the market¹⁵ due to quotas.

Who is affected by medicines shortages?

Medicines shortages have far-reaching effects throughout the healthcare sector, but above all patients are the ones suffering the most from the lack of medication.

Due to supply shortages, pharmacists need to dedicate more and more time sourcing medicines instead of dedicating this time advising and consulting with patients. Pharmacists are healthcare professionals and their time is too valuable to chase up medicines instead of caring for their patients. In this context it should also be noted that pharmaceutical full-service healthcare distributors are bound to respect the orders made by the pharmacists and cannot substitute products out of stock with alternative ones (they are legally not allowed to deliver alternative or substitute products). Therefore, in case of shortages pharmaceutical full-service healthcare distributors cannot fulfil their public service obligation to provide pharmacies with all products needed by their patients. Medicines shortages have negative effects on pharmaceutical full-service healthcare distributors ability to distribute medicines whenever and wherever needed.

How can medicines shortages be overcome?

The solutions listed hereafter represent the pharmaceutical full-service healthcare distributors' views on how medicines shortages can be combated. Pharmaceutical full-service healthcare distributors firmly believe that any sustainable solution to resolve the problem of medicines shortages has to take into account all manifold reasons of their cause. Fostering a closer and more transparent discussion and collaboration between political decision makers, health authorities, the pharmaceutical industry, pharmaceutical full-service healthcare distributors, parallel-traders, pharmacists, healthcare providers, payers and patients at national and European level are a pre-requisite to address shortages of medicines.

Combating production related shortages

Although most shortages are dealt with by National competent authorities, the European Medicines Agency (EMA) is involved when a medicine shortage is linked to a safety concern or affects several Member States. The shortages catalogue of EMA therefore contains information on medicine shortages that affect more than one European Union (EU) Member State. For the substances on the list, EMA has assessed the shortage and provided recommendations to patients and healthcare professionals across the EU¹⁶.

In November 2012 EMA published a reflection paper¹⁷ concerning public health incidents that can arise due to manufacturing disruptions linked to problems such as quality defects or Good-manufacturing-practice (GMP) compliance issues, which was followed by an implementation plan (2012-2015)¹⁸ defining actions to co-ordinate the assessment of shortages, develop risk-minimisation measures, alleviate the impact on patients and communicate within the EU regulatory network.

¹⁴ <https://www.watson.ch/schweiz/wirtschaft/866351797-schweizer-spitaeler>

¹⁵ <http://drugshortage.ch/index.php/uebersicht-2/>

¹⁶

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000376.jsp&mid=WC0b01ac058074f178

¹⁷ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113.pdf

¹⁸ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135114.pdf

Furthermore, EMA organised a workshop on product shortages due to manufacturing and quality problems in October 2013, which led to the creation of an inter-industry association taskforce with the objective of proposing solutions to prevent the root causes of shortages due to manufacturing and quality problems. A stakeholder meeting on 9 October 2015 reviewed the progress made since the previous workshop and for the first time involved all supply chain actors.

Also, the Heads of Medicines Agencies Network (HMA) has teamed up with EMA in a Task Force on the Availability of Authorised Medicines for Human and Veterinary Use¹⁹ to provide strategic support and advice to tackle disruptions in supply of human and veterinary medicines and ensure their continued availability. Its key priorities include: minimising supply disruptions and avoiding shortages by facilitating approval and marketing of medicines, strategies to improve prevention and management of shortages, encouraging best practices, improving information sharing and fostering collaboration with stakeholders.

Combating shortages due to a lack of economic market attractiveness

In the past, under the framework of the Corporate Social Responsibility initiative of DG ENTR – now DG GROWTH - a project group on facilitating supply in small markets carried out a survey on shortages of medicines in small countries. The surprising result of this survey showed that there is a significant shortage of products containing old molecules for which there is no economic incentive to bring to the market due to the very limited number of patients. The recommendations put forward, included a set of measures improving cross-border collaboration as well as the economies of scale²⁰.

National competent authorities should consider installing a monitoring system of the impact of their desire to constantly decrease medicines prices through various mechanisms (international reference pricing, tendering) as well as of specific national requirements to bring products to the market of their country on medicines availability.

Combating disruptions of supplies and unexpected demand of medicines

In October 2013 the European Parliament and the Council adopted a decision to better protect European citizens from a wide range of serious cross-border health threats²¹. Health threats can be biological, chemical or environmental in nature. Existing rules on preparing for and managing health emergencies were strengthened and the Health Security Committee was given a stronger mandate to react in a crisis.

The European Commission is currently tackling the problem of medicines shortages and plans, as one of the measures, to create a public portal of vaccine safety evidence and an EU-wide data warehouse to prevent shortages are currently on their way. The Commission envisions the system holding information on vaccine stocks, enabling details of an impending shortage in one country to quickly spread. Forewarning regulators could enable mitigating actions²².

Whereas GIRP and its members warmly welcome this proposal, the role of the supply chain and its potential to mitigate availability problems of essential medicines in case of health threats has been underestimated. Practical examples in this respect can be found on national level such as consignment stock held in the premises of pharmaceutical full-service healthcare distributors. We believe that it is essential that all partners

¹⁹ <http://www.hma.eu/522.html>

²⁰ <https://ec.europa.eu/docsroom/documents/7625?locale=en>

²¹

https://ec.europa.eu/health/sites/health/files/preparedness_response/docs/decision_serious_crossborder_threats_22102013_en.pdf

²² <https://www.raps.org/news-and-articles/news-articles/2018/5/eu-regulatory-roundup-ema-proposes-changes-to-vac>

in the supply chain, together with national and European competent authorities, collaborate on crisis preparedness and jointly elaborate emergency plans.

It is a joint responsibility that in cases of sudden disease outbreaks, bioterrorism, other cross-border health crisis, or in case of problems related to the production, storage or distribution of medicines, patients in Europe should be able to have access to the required medicines without delay.

Combating medicines shortages due to economic hardships

GIRP would like to raise the awareness of European and national decision makers as well as of our European and national supply chain partners about the significant pre-financing function of pharmaceutical full-service healthcare distributors, which in most cases is largely underestimated. According to a study published by IPF, pharmaceutical full-service healthcare distributors pre-finance 11.8 billion Euro in the 6 largest European countries alone²³.

It is out of the question that in the current economic climate pre-financing is further extended. Demands by the pharmaceutical industry for earlier or immediate settlement of invoices cannot be met without passing on a part of this demand to pharmacists who are also in a difficult position to request timely payments from governments or social security systems. Delayed payments, the withdrawal of credit lines and the demand for pre-payments of medicine deliveries aggravate the situation of medicines availability in cash-stripped economies.

GIRP therefore appeals to national competent authorities and to payers on national level to take note of the pre-financing function of pharmaceutical full-service healthcare distributors as well as of the savings they bring to healthcare systems through the bundling of orders from manufacturers to pharmacies. Further pressure on pharmaceutical full-service healthcare distributors' mark-ups would lead to a reduction of service levels and to higher capital demands on pharmacies to increase their stock without bringing any savings to the healthcare sector of a country.

Combating policy failures

In 2016, the Dutch Presidency invited the Commission to assess the impact of protection mechanisms and incentives on shortages of medicines and the Slovakian Presidency made "shortages of medicines" a priority for its Presidency. During the Working Party on Public Health on 15 July 2016 and the informal Health Council on 3-4 October, all Member States agreed that the topic deserves action at EU level. During the informal Health Council, many Member States supported the proposal to examine Article 81²⁴ of the pharmaceutical legislation which is difficult to implement and enforce and called for the Commission to better clarify the obligations of the marketing authorisation holders and full-service healthcare distributors (pharmaceutical full-line wholesalers) and what the limits of their responsibilities are.

²³ IPF study February 2017, Fig. 32, p. 46 <http://www.girp.eu/files/GIRP-IPF%20Study%202016.pdf>

²⁴ "the holder of a marketing authorisation for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medicinal product to pharmacies and persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered"

In February 2017 also, the European Parliament also adopted recommendations on shortages of medicines in the context of the report on access to medicines in Europe²⁵. This report calls on the Commission and the Council to formulate a better definition of the concept and analyse the causes of shortages of medicines²⁶.

Linked to the call of the Council and the European Parliament, the European Commission has asked Member States on their views on the implementation of Article 81 on the obligation of continuous supply with the objective to help Member States to exchange information and good practices to address more efficiently the problem of shortage of medicines.

Article 81, paragraph 2 of the Directive 2001/83/EC refers to a joint obligation of pharmaceutical manufacturers and pharmaceutical full-service healthcare distributors to *"ensure appropriate and continued supplies of medicinal product to pharmacies and other persons authorised to supply medicinal products to the public so that the needs of patients in the Member State in question are covered"*. Public service obligations in place in several Member States oblige pharmaceutical full-service healthcare distributors to *"guarantee an adequate range of medicinal products to meet the requirements of a specific geographical area and to deliver the supplies requested within a very short time over the entire area in question"*.

The final assessment of responses received by the Member States was published by the European Commission on 25 June 2018.²⁷

Several Member States have included additional provisions on both Marketing Authorisation Holders and wholesale distributors. 4 Member States (BE, DE, FR and SI) make a distinction between full service healthcare distributors, which are bound to Public Service Obligations and other distributors for whom such obligations do not apply.

The document maps current measures in place, however, does not provide guidance on best practices to follow.

Medicine shortages caused by policy failures could be addressed by the implementation and enforcement of public service obligations on pharmaceutical full-service healthcare distributors, which are carefully tailored to local market conditions and drafted in collaboration with national regulators. GIRP members already abide in several European countries by public service obligations and in the other EU countries voluntarily fulfil a public service function. In order for public service obligations to work effectively they need to be equally backed-up by the obligation of the pharmaceutical industry to provide adequate and continuous supplies to pharmaceutical full-service healthcare distributors, who - without this obligation of the industry - would not be in a position to fulfil their PSO obligations. Also, it is essential that these obligations are adequately controlled and enforced by public authorities and also enforceable between private parties i.e. by pharmaceutical full-service healthcare distributors without relying on public authorities.

GIRP firmly believes that all stakeholders should strongly collaborate in order to ensure the continuous supply of medicines to patients. Therefore, pharmaceutical full-service healthcare distributors stand ready to closely work together with all supply chain partners, national and European authorities as well as payers and other healthcare providers in order to combat medicine shortages. GIRP has already collaborated with the other EU level supply chain stakeholder associations to adopt a Joint Statement on Information and Medicinal Products Shortages.²⁸ All supply chain stakeholders strongly believe that the input, perspectives and experience of the variety of stakeholders affected by the issue of shortages needs to be sought and taken on board to reach

²⁵ <http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+REPORT+A8-2017-0040+0+DOC+XML+V0//EN>

²⁶ <http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+REPORT+A8-2017-0040+0+DOC+XML+V0//EN>

²⁷ https://ec.europa.eu/health/sites/health/files/files/committee/ev_20180525_summary_en.pdf

²⁸ http://www.girp.eu/sites/default/files/documents/supply_chain_statement_on_information_on_medicine_shortages.pdf

best-informed conclusions. We strongly encourage further efforts in this direction together with National and European Authorities.

Combating negative impacts of supply quotas

From the pharmaceutical full-service healthcare distributors' perspective, a viable solution for the hurdle imposed by supply quotas on the continuous availability of medicines would be to ask pharmaceutical manufacturers to make the process of the allocation of supply quotas less burdensome for pharmaceutical full-service healthcare distributors, taking into account the variations of medicines demand and supply patterns in their country. As also stated by the Matrix Insight report, drafted for the European Commission "...companies impose quotas and supply caps, which in turn lead to availability problems... If the quotas are exhausted, the wholesalers will not be supplied with further stocks of the product. The level of quotas differs between producers and Member States and in some cases may not be communicated to the wholesaler, affecting the wholesaler's ability to plan the supply of the product in advance"²⁹.

In this respect GIRP once again appeals to the stakeholders in the supply chain for an increased collaboration, responsibility and accountability.

It is evident that the reasons for shortages differ from country to country, and product to product, so solutions should be sought ultimately at national level and implemented on the single product basis. However, the cross-border effects of various political and economic measures are not negligible and therefore an in-depth discussion at European level is indispensable to avoid negative impact on other countries' healthcare systems and find a sustainable way forward.

Full service healthcare distributors call for and embrace opportunities for increased collaboration and cooperation with the supply chain partners and governments as well as payers in order to find feasible solutions to ensure patients in Europe have continued access to the medicines they require. We invite all parties to come together and move forward with a future vision for the adequate and continuous supply of medicines in a spirit of flexibility, trust and partnership. Our priority as well as our core role and function as pharmaceutical full-service healthcare distributors is to make sure that pharmacies receive the ordered medicines and patients can access them in a safe and efficient manner.

GIRP

European Healthcare Distribution Association
Brussels, October 2018

²⁹ http://ehpta.eu/pdf/Matrix_report.pdf

On 3 April 2020, the CPME Executive Committee adopted the 'CPME Policy on Medicine Shortages' (CPME 2020/005 FINAL).

CPME Policy on Medicine Shortages

The Standing Committee of European Doctors (CPME) represents national medical associations across Europe. We are committed to contributing the medical profession's point of view to EU and European policy-making through pro-active cooperation on a wide range of health and healthcare related issues¹.

Policy Summary

For a number of reasons medicine shortages and/or interruption in the supply chain have increasingly become an issue for Member States over the last years. Medicine shortages negatively impact public health contributing to increased costs for health systems and patients². Moreover, unavailability of medicines can significantly limit doctors' ability to provide appropriate treatment. Therefore, there is a need to prevent shortages, tackle those already existing and increase the transparency of the supply chain. The current crisis concerns all Member States and demands a common European response³.

The proposed measures include communicative, organisational and legislative solutions.

They comprise monitoring of medicine shortages at the EU level and establishing tools for information exchange among Member States, adopting widely agreed definitions of medicine shortages and essential medicines, and influencing distribution of medicines by stockpiling and parallel trade.

The EU should become more independent in supplying medicines to European citizens and diversify providers in the European market. Moreover, there is also a need to enhance and enforce current obligations of the pharmaceutical industry, including a clarification of the Directive 2001/83/EC on the Community code relating to medicinal products for human use.

¹CPME is registered in the Transparency Register with the ID number 9276943405-41.

More information about CPME's activities can be found under www.cpme.eu

²T. Bochenek, V. Abilova, et al., *Systemic Measures and Legislative and Organizational Frameworks Aimed at Preventing or Mitigating Medicine Shortages in 28 European and Western Asian Countries*, Front. Pharmacol. 8:942., January 2018, doi: 10.3389/fphar.2017.00942

³A. Acosta, E. P. Vanegas, et al., *Medicine Shortages: Gaps Between Countries and Global Perspectives*, Front. Pharmacol. 10:763., July 2019, doi: 10.3389/fphar.2019.00763

A. Shortages in the EU

Although medicine shortages are not a new phenomenon, there is a clear increase in Europe over the last years. The current crisis concerns the entire EU across all health care settings affecting supply of day-to-day and essential medicines⁴. Medicine shortages are a daily experience of doctors, and hospital and community pharmacists. Significant unavailability of medicines has been reported by most EU Member States.

A pan-European survey among hospital pharmacists has identified shortages as a major problem in the hospital sector, with an overwhelming majority of respondents stressing that shortages have become more troublesome during the last years⁵. A similar increase is reported by community pharmacists⁶.

To prevent supply problems, several Member States have already undertaken actions at national level addressing the export of certain medicines, stockpiling or the reinforcement of legal obligations of pharmaceutical companies and wholesalers⁷.

B. Impact of shortages on patients, doctors and health systems

Medicine shortages are a growing public health threat with a serious impact on health care systems and public health. They can severely limit doctors' ability to provide appropriate treatment.

Medicine shortages have an unquestionable impact on public health.

They contribute to increased costs for health systems (e.g. purchasing more expensive medicines, increasing inventory levels or additional workforce spending) and patients (e.g. paying for more expensive or non-refundable alternative medicines).

A medicine shortage means in practice that doctors cannot give the necessary medicines to patients. That can lead to possible delays in patients' treatment, to the need to switch to alternative therapies

⁴The Pharmaceutical Group of the European Union (PGEU), [Position Paper on Medicine Shortages](#), Brussels, 2019, p.2.

⁵The European Association of Hospital Pharmacists (EAHP), [2018 Medicines Shortage Survey](#), Brussels, 2019, p.6.

⁶According to a study by the Pharmaceutical Group of the European Union (PGEU) all responding countries experienced medicine shortages in community pharmacies over the previous year, and most of them indicated that the situation worsened compared to 2018. See: The Pharmaceutical Group of the European Union (PGEU), [2019 PGEU Medicine Shortages Survey](#), Brussels, 2020, p. 3.

⁷Head of Medicines Agencies (HMA), [Availability of medicinal products for human use](#), October 2019, see also: Heads of Medicines Agencies (HMA) / European Medicines Agency (EMA), [Good practice guidance for communication...](#), EMA/632473/2018, July 2019 and HMA/EMA, [Guidance on detection and notification of shortages of medicinal products...](#), EMA/674304/2018, July 2019.

that could be less effective, to adverse effects and adherence problems or even life threat when a shortage concerns essential medicines⁸.

Medicine shortages result in additional workload for doctors and pharmacists as they must spend time managing the unavailability, tracking inventory, identifying alternatives and making decisions about rationing scarce supplies.

Scarcity or unavailability of medicines can create situations in which physicians have to make a choice of providing a certain treatment to one patient while denying it to another. The decision whether to deny a treatment or to change a medication plan raises serious ethical questions as regards equality and can affect the relationship of trust between a physician and the disadvantaged patient.

C. Addressing shortages at EU level

1. Identifying root causes

Medicine shortages are a multi-factorial problem that can stem from unpredictable and predictable causes. They can result from different economic, manufacturing or regulatory reasons⁹.

Currently, the majority of Active Pharmaceutical Ingredients (API) and medicines are produced outside of Europe in limited number of manufacturing sites. Distant location of factories makes it more difficult to inspect them and results in longer, less transparent and fragile supply chains¹⁰. Unforeseen disruptions or quality and production problems have far-reaching consequences. Moreover, at the production sites, delays in supply can also result from the shortages of raw materials¹¹.

Besides, the shortages can be also caused by the pharmaceutical industry's pricing strategies, products discontinuations from unprofitable markets or imposing supply quotas¹².

Other potential root causes include national tendering procedures focused solely on the price criteria, parallel trade, stockpiling on national level that can endanger situation in other Member States or increased demand.

⁸Medicine shortages jeopardize rational pharmacotherapy and patient safety, especially if essential medicines are not available. There are several reasons of that e.g., as the medicines recommended on the basis of solid evidence in Clinical Practice Guidelines cannot be prescribed, necessary changes in treatment regimens in response to medicine shortages (e.g. psychotropic, anti-epileptic and oncology medicines) alter the efficacy and tolerability of the treatment and – of crucial importance – this often leads to medication errors.

⁹The Economist Intelligence Unit, [Addressing medicine shortages in Europe...](#), The Economist Intelligence Unit Limited, 2017, pp. 10-14. For the root causes identified on the US market see also: Food and Drug Administration (FDA), [Drug Shortages: Root Causes and Potential Solutions](#), 2019, pp. 21-31.

¹⁰R.E. Ferner, J. K. Aronson, et al., [Crisis in the supply of medicines](#), BMJ 2019;367:l5841, October 2019, doi: <https://doi.org/10.1136/bmj.l5841>

¹¹World Health Organization (WHO), [Medicines shortages](#), WHO Drug Information Vol. 30, No. 2, 2016, pp. 180-181.

¹²M. Beck, J. Buckley, [Managing pharmaceutical shortages: an overview and classification of policy responses in Europe and the USA](#) SAGE journals, March 2019, <https://doi.org/10.1177/0020852318815330>

As these potential causes are interlinked a comprehensive response is needed.

However, dedicated research on medicine shortages in Europe is scarce¹³. The particular root causes affecting EU Member States need to be identified and concrete solutions defined. An independent study led by the European Commission is a prerequisite to undertaking effective actions.

2. The role of EU institutions

CPME recognises various recent and current initiatives in the EU institutions¹⁴. However, EU action should take a more coherent approach. CPME strongly advises to establish a European action plan on access to medicines that would include the measures proposed in this policy and take into consideration solutions suggested in other papers¹⁵.

In December 2019, the Finnish Presidency of the EU emphasised a need to take concrete measures by Member States and the European Commission to ensure medicines availability¹⁶. Subsequently, the Croatian EU Presidency and the German EU Presidency have committed to address pharmaceutical policy with a focus on availability of medicines.

Likewise, Member States have proposed to set up an EU agenda on pharmaceutical policy 2020-2024 with the focus on identifying the root causes of current shortages and means to tackle them¹⁷.

The European Commission has a strong political mandate to address medicine shortages¹⁸. The Commissioner for Health, Stella Kyriakides, has committed to tackle the crisis and to submit a communication on pharmaceutical policy in late 2020¹⁹.

Given supervision of medicines, input from national registries, and information from all agencies in Europe, CPME recognises EMA the body best suited to take the responsibility of the European response

¹³T. Bochenek, V. Abilova, et al., *Systemic Measures and Legislative and Organizational Frameworks...*, Op.cit, p.2; European Healthcare Distribution Association (GIRP), *Medicine Shortages in Europe and Their Impact on Patients*, October 2018, p.3.

¹⁴Council of the European Union, *Council conclusions on strengthening the balance in the pharmaceutical systems...*, 2016/C 269/06. July 2016; European Parliament, *European Parliament resolution on EU options for improving access to medicines*, P8_TA(2017)0061, March 2017.

¹⁵World Health Organisation (WHO), *Addressing the global shortage of, and access to, medicines and vaccines*, EB142/13, January 2018; EAHP, *EAHP Position Paper on Medicines*, Revised version adopted in June 2019; HMA/EMA, Heads of Medicines Agencies (HMA) / European Medicines Agency (EMA), *Good practice guidance for communication...*, Op. cit.; HMA/EMA, *Guidance on detection and notification...*, Op. Cit.

¹⁶Council of the European Union, *European pharmaceutical policy - strengthened cooperation and coordination with the aim to improve access to medicines*, Brussels, November 2019.

¹⁷Council of the European Union, *Meeting of the Employment, Social Policy, Health and Consumer Affairs Council*, December 2019.

¹⁸European Commission, *Mission letter to Stella Kyriakides, Commissioner for Health and Food Safety*, Brussels, 1 December 2019, p.4.

¹⁹Council of the European Union, *Meeting of the...*, Op Cit., December 2019.

to medicine shortages. EMA published guidelines in 2019²⁰, created a catalogue on medicine shortages²¹ and established a task force on the availability of authorised medicines for human and veterinary use, along with the Heads of Medicines Agencies (HMA)²². Moreover, the second phase of a pilot project of the EU Single Point of Contact network is ongoing²³.

Nevertheless, CPME observes that EMA's capacity and role in addressing medicine shortages is insufficient. EMA should be provided with a better mandate and better infrastructure. Moreover, EMA should be entirely publicly funded as a prerequisite to its independence.

D. Strengthened cooperation, centralised actions and dedicated leadership

To eliminate and prevent shortages, significant measures must be taken by all Member States and their national competent authorities coordinated by the EU.

These should refer to a package of measures targeted on communication, organisation and legislation level.

1. Steering distribution of medicines

Medicine shortages can be addressed by measures related to their distribution that include stockpiling or restricting parallel trade.

When needed, stockpiling of medicines should take place at EU level. National stockpiling should only be introduced when not endangering neighbouring countries, regions or health care facilities with patients in need of the stockpiled medication. To prevent a shortage, stockpiling for essential medicines should be introduced lasting at least four weeks in hospitals and two to three months in wholesalers' inventories.

Moreover, Member States should be allowed to temporarily ban parallel export. By parallel trade, medicines can be exported from Member States where they are relatively cheaper to the markets where their prices are higher. Temporal ban of parallel export of medicines in or at risk of shortage may help to avoid arise or aggravation of medicines' unavailability in countries at risk. Importantly,

²⁰Heads of Medicines Agencies (HMA), European Medicines Agency (EMA), [Guidance on detection and notification of shortages of medicinal products for Marketing Authorization Holders \(MAHs\) in the Union \(EEA\)](#), July 2019; Heads of Medicines Agencies (HMA), European Medicines Agency (EMA), [Good practice guidance for communication to the public on medicines' availability issues](#), July 2019.

²¹European Medicines Agency (EMA), *Shortages catalogue*, accessible at: the EMA's [website](#).

²²Heads of Medicines Agencies (HMA) / European Medicines Agency (EMA), *Task force on the availability of authorised medicines for human and veterinary use*, accessible at: the HMA's [website](#).

²³European Medicines Agency (EMA), [Highlights of the EMA Management Board meeting](#), December 2019.

applying such a measure must be justified, reasonable and proportionate to ensure a legitimate public interest²⁴, not to infringe the principles of free trade and movement of goods within the EU²⁵.

While addressing the distribution of medicines in shortage, the EU and Member States should be very cautious about online sales of medicines. The safety of medicines sold online must be guaranteed. Still, too many illegal online practices can be found. Illegal online pharmacies can sell prescription medicines without medical prescriptions and professional supervision (often at a higher price), taking advantage of traditional supply disruptions.

Moreover, it should be explored whether to establish a central European database on medicines supply to the EU market which could include information on: which country authorised the medicine, under which trademark, whether it was resupplied to or withdrawn from the market and its supply status.

2. Monitoring, communication and common terminology

Communication is crucial in preventing shortages. Doctors must have access to up-to-date information to be able to adequately respond to arising and existing shortages. Early awareness of a supply problem and early identification of potential therapeutic alternatives may mitigate the possibility for adverse reactions endangering patient safety.

Moreover, it is critical to establish a standardised reporting system giving guidance as to what, when and how to report. Producers and importers should be obliged to report existing or arising shortages to the national competent authorities and the EMA. However, the reporting system will not properly function unless common definitions of a medicine shortage and clinically essential pharmaceuticals are agreed. The WHO, EMA and other stakeholders should join forces to work on a common terminology applicable at EU level and globally.

An EU-wide reporting system requires an agreed electronic template to be used. The EMA should propose such standard in consultation with the users (i.e. producers, physicians, pharmacists, hospitals etc.) and competent authorities. This could follow the example of the Commission's IMI (Internal Market Information System) communication tool.

Information reported to the EMA should be made accessible to all competent authorities in Member States who should decide whether the information should be published or made available to the other supply chain actors (physicians, pharmacists and hospitals) in a user-friendly format.

²⁴European Commission, [Infringement: Parallel trade of medicines](#), Press Release, May 2018.

²⁵Art 26 and Art 28-37 in: [Consolidated versions of the Treaty on European Union and the Treaty on the Functioning of the European Union](#), Official Journal C 326, 26/10/2012 P. 0001 - 0390, October, 2012, Art 26 and Art 28-37.

E. Increasing diversification of supply sources and reducing Europe's reliance on external manufacturing

Member States should adopt policies to increase diversification of supply sources and become more independent from production sites outside Europe, most importantly in case of essential medicines.

The current overreliance on manufacturing sites located in third and remote countries for the production of active pharmaceutical ingredients and medicines constitutes a real threat to the secure and stable supply in the EU. As an example, production sites could be affected by export restrictions in the countries of production. Clearly, Europe (as all other parts of the world) need to be able to steer production depending on its own needs. Bringing the production of essential medicines back into the EU could make the supply chain more transparent and would allow for an easier and more effective monitoring of manufacturing sites.

In view of the above, the EU should explore regulatory measures or financial incentives to shift the production of essential medicines back to Europe. This however should not compromise on quality, environmental or work safety standards in Europe.

Secondly, it should be examined how to diversify supply sources to ensure a better presence of providers on the European market. Dependence on a small number of drugs' suppliers can lead to shortages in case of the shutdowns of their facilities, regardless of the reasons. The ultimate goal of all providers should be to have at least two or three manufacturing sites as they can be subject to accidents and disruptions.

Moreover, the European Commission should engage with the Member States in a structured exchange of best practices on procurement procedures for medicines, issuing recommendations. Member States should be encouraged to apply other criteria than price in national tendering procedures such as reliability of supply and the number and location of production sites. One solution could be the creation of a label "medicine made in Europe" which national health systems can use as a requirement in tendering procedures.

F. Enhancement and enforcement of current obligations of pharmaceutical companies

1. Clarification and enforcement of the Community Code Directive

Current legislation does not ensure the stable supply of medicines. Clear regulatory guidance at EU level will help to avoid a heterogeneous transposition by Member States and will enable a better response to shortages²⁶.

The Directive 2001/83/EC²⁷ (the Community Code Directive) as the centrepiece of EU pharmaceutical legislation stipulates the obligations of market authorisation holders (MAH) entering the EU market. The Community Code directive obligates MAHs— “within the limits of their responsibilities – to ensure appropriate and continued supplies of medicinal products to cover the needs of patients” (Art 81). Moreover, in case of problems with such supply, either temporal or permanent, “MAHs are obliged to notify competent authorities at least two months before the interruption of the product placing on the market” (Art 23a).

The Community Code Directive requires clarification. The “limits of their responsibilities” must be specified. In fact, do current cases of shortages violate Art 81? And if so, what are the consequences? Obviously, the Directive cannot be enforced as it doesn’t provide for sanctions. The Community Code Directive must be strengthened to hold companies accountable.

Moreover, the Community Code Directive requires the introduction of an early warning system allowing for efficient communication on medicines supply status, see D.2.

2. Public service obligation to supply essential medicines

Essential medicines are not simple items of commerce²⁸.

As they are a critical component of patient care, appropriate access to essential medicines and prevention of their shortage cannot be addressed by “normal” market mechanisms. Essential medicines are a public good and should be always available and accessible. Therefore, to assure their stable supply, a public service obligation (PSO) should be imposed on their providers that should fulfil their duty of care. Moreover, it should be also explored whether the use of PSO could be justified in any other situation in that a medicine shortage might pose a risk to patient health²⁹.

²⁶European Commission, [Summary of Responses to the Questionnaire on the Measures implemented in the Member States territories in the context of Article 81 of Directive 2001/83/EC](#), May 2018.

²⁷Directive 2001/83/EC, [Community code relating to medicinal products for human use](#), OJ L 311, 28.11.2001, p. 67, November 2001.

²⁸The European Association of Hospital Pharmacists (EAHP), [Medicines shortages in European hospitals](#), Brussels, 2013, p. 2.

²⁹P.H. Truong, C.C. Rothe, T. Bochenek, *Medicine Shortages and Their Impact on Patients and Health Care Systems...*, [in:] A. P. Barbosa-Povoa et al. (eds.), *Pharmaceutical Supply Chains—Medicines Shortages*, Springer Nature Switzerland AG 2019, p. 67, https://doi.org/10.1007/978-3-030-15398-4_3.



Recommendations

- CPME calls on EU Member States to strengthen their collaboration and focus on common European solutions to medicine shortages.
- CPME calls on DG SANTE to better engage in addressing the problem benefiting from its strong mandate. DG SANTE should identify the root causes of the medicine shortages in the EU and establish a European action plan to tackle them.
- CPME calls on the European Commission to empower EMA by ensuring its independence and providing it with the required infrastructure and mandate.
- CPME calls on the European Parliament to address the problem in the ENVI Committee and make its own initiative report.
- CPME calls for monitoring of shortages at EU level and for the development of information sharing tools between EU Member States, including a common reporting template.
- CPME calls for the development of an agreed terminology and uniform definitions of what is a medicine shortage as well as clinically essential and non-essential pharmaceuticals that can be adopted on EU level and globally. The developed European list of essential medicines should serve as a basis for any measures against shortages at EU level.
- CPME argues that when needed, medicines' stockpiling should take place on EU level, and in case of ineffectiveness of other solutions, EU Member State should be allowed to temporarily ban parallel export.
- CPME calls on the European Commission to explore regulatory or financial incentives to shift the production of most important active pharmaceutical ingredients and medicines back to Europe and diversify supply sources on the EU market.
- CPME calls on the European Commission to propose legislation to clarify the Market Authorisation Holder's obligations under the Directive 2001/83/EC and develop an enforcement mechanism including penalties.
- CPME calls on the European Commission to encourage Member States to revise their national tendering procedures with a view to including other criteria than price, e.g. by creating a label "medicine made in Europe".
- CPME calls for considering essential medicines as a public good and for imposing a public service obligation on MAHs to assure their stable supply.

Common position between patients', consumers, and healthcare professionals' organisations involved in the activities of the European Medicines Agency on:

Supply Shortages of Medicines

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1. Introduction

A supply shortage of medicine may be defined as a situation in which the total supply of an authorised medicine or of a medicine used on a compassionate basis is inadequate to meet the current or projected demand at the patient level. The shortage may be local, national, European or international.

This common position prioritises supply shortages that affect medically necessary medicines (also called essential medicines). It proposes solutions on many aspects, acknowledging other issues exist that need further discussions.

W.H.O defines essential medicines as medicines that satisfy the priority health care needs of the population. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality (and at a price the individual and the community can afford).

Regardless of the cause of a medicine shortage, the public health consequences can be severe and cause a ripple effect that disregards national boundaries. The trend is particularly alarming as shortages affect the entire healthcare system, industry, healthcare professionals, and uppermost, the patients.

1.1. Extent of the problem

The number of reports of medicine shortages in the EU is increasing. According to these reports all classes of medicines are affected (see annexe 1 for shortages listed by some Member States).

In response to the problem national authorities in a number of EU Member States have started monitoring the situation and have set up websites for the public where information about current shortages is available.

In the UK, the Pharmaceutical Services Negotiating Committee (PSNC) maintains a list of branded

medicines in shortage¹ since 2012. This list is derived from information reported by pharmacies to PSNC and contains between 30 and 40 products at any given time, and they vary over time. The 30 to 40 products reported to be in shortage at any given time compares with circa 16,000 licensed preparations of medicines in the UK. However it would be wrong to conclude that the small percentage reported equates to a minor problem. The small proportion of medicines in shortage causes acute and disproportionate problems and difficulties for pharmacies and for patients.

In France, the National Academy of Pharmacy organised a conference² on medicines supply shortages on 20 March 2013. Pharmacists explained that everyday 5% of supply they ordered to wholesalers was out of stock in 2012, and for half of cases the shortage lasted for more than four days.

The evidence of a growing problem of medicine supply shortage in Europe has grown starker in recent years: in a European survey³ to which over 300 hospital pharmacists from 27 countries responded in 2012, 99% of pharmacists reported that they have been experiencing problems with medicines shortages, 63% reported the problem to be a weekly or daily occurrence and 73% said the problem has grown worse in the past year.

Annexe 1 lists some recent examples of supply shortages notified to national authorities in Europe in 2012 or 2013: epinephrine (anaphylactic shock syndrome), encapsulated potassium chloride (hypokalaemia), vecuronium bromide (general anaesthesia), rasagiline (Parkinson disease)...

In the US, 178 shortages were notified in 2010, of which 132 (74%) involved sterile injectable medicines. This represented an increase of 192% since 2005.

1.2. Consequences for patients

Patients are at risk of suffering deterioration in their health status if they do not receive the medicine they

are prescribed in a timely manner, and can ultimately suffer from serious harm that is avoidable.

For patients, shortages often translate into lower quality and safety of care, and unnecessary distress. They also reduce the amount of time various categories of healthcare professionals are able to spend with patients as they are being redeployed out of necessity to manage the shortage. Medicine shortages can trigger delays or discontinuation of both essential and recommended medical procedures and treatments, encourage the omission of medicine doses, increase the risk of surgical interventions and/or operating times and negatively impact on patient recovery periods (shortages of anaesthetics). Moreover, medicines that have become unavailable are often substituted with less effective, inferior or more expensive alternatives (which, depending on the nature of the health system in question, may sometimes not qualify for reimbursement). Unfamiliarity with alternative products can lead to an increased incidence of medication errors and/or adverse reactions, potentially causing fatalities, or worsening patient outcomes. When the replacement product is imported from another country, a package leaflet in another language has sometimes to be used.

In the UK, patients' associations and other patients representatives, reported a number of incidents where patients diagnosed with schizophrenia, and other mental health conditions, have not been able to access medication they need in order to stabilise their condition because it has been unavailable. Incidents have also been reported where diabetic patients have suffered hypoglycaemic attacks and have been hospitalised as a result of not being able to obtain the medicines they needed due to shortage¹. The 2012/13 survey of European hospital pharmacists also reported examples of chemotherapy treatments being interrupted or delayed due to medicines shortages⁴.

Among medicines that were recently in short supply in the EU (see a more comprehensive list in annexe 1), there are indubitable examples that illustrate the harm to patients:

¹ Report of the All Party Pharmaceutical Group, Rt Hon Kevin Barron Member of parliament, England and Wales. Inquiry into Medicines Shortages. [Here. http://www.webcitation.org/6Hz6BmqPR](http://www.webcitation.org/6Hz6BmqPR)

² Médicaments : Ruptures de stocks, ruptures d'approvisionnement, Académie Nationale de Pharmacie, *Séance thématique*, 20 March 2013. <http://www.webcitation.org/6HzB9Ly7T>

³ <http://www.eahp.eu/practice-and-policy/medicines-shortages>

⁴

<http://www.eahp.eu/sites/default/files/files/EAHpdeplMedicineHR2f.pdf>

- Supply shortages of antiretroviral treatments in France in 2011⁵: patients had to interrupt treatment for up to 3 weeks. The control of HIV virus replication was therefore lifted, with the risk of selecting treatment resistant strains, with dramatic consequences;
- Fabrazyme® shortage⁶: Fabrazyme® is an enzyme replacement therapy to treat Fabry disease, a rare and severe disease. A shortage lasted from 2009 to the end of 2012 and was worldwide. Patients were obliged to reduce the dose, or to switch to an alternative orphan medicine which in turn was not available in sufficient quantities. Although adverse reactions were sometimes difficult to objectify, 12% of patients on a reduced dose had a worsening of the disease, with occurrence of strokes, unbearable pain, weekly Fabry crisis, episodes of collapse, of lost consciousness, or were hospitalised for other reasons;
- Cerezyme® shortage: Cerezyme® is an enzyme replacement therapy for the treatment of the visceral symptoms of type 1 and type 3 Gaucher disease. This rare disease presents with hepatosplenomegaly, cytopenia and bone disease. Children can be severely affected. A worldwide shortage lasted from 2009 to the end of 2012, leading to interruptions of treatment and recurrence of disease manifestations in many patients⁷;
- Caelyx® shortage⁸: Caelyx® is indicated for severe diseases such as breast neoplasms, multiple myeloma, ovarian neoplasms or Kaposi sarcoma. Due to shortcomings in quality assurance at the manufacturing site in November 2011, the production of 12 products was interrupted, and

as there was no alternative treatment for Caelyx®, the EMA recommended maintaining the product on the market, after assessing the risks. This resulted in shortages in several EU countries from August 2011. The transfer to alternative manufacturing sites has been completed in April 2013.

1.3. Consequences for healthcare professionals (treating physicians, pharmacists, nurses)

Healthcare professionals have been confronted with several situations of medicine shortages in the past. Their responsibility is to inform patients on an individual basis about the situation and possible solutions. For instance, alternative treatments can be sought. If these are not available, supportive measures may need to be taken, sometimes with extreme consequences, e.g. splenectomy for a patient with Gaucher disease who cannot be treated with enzyme replacement therapy anymore. The frustration of healthcare professionals can be immense when they see their patients deteriorating in the absence of treatments. This frustration is enhanced when information is lacking and/or there is no transparency about how available inventory can and will be distributed. Of crucial importance to healthcare professionals is adequate and immediate information about the cause and duration of the shortage. Their input should be immediately sought when national or international guidelines for patient management are issued.

For health professionals, concerned about direct impact to their patients, shortages also pose particular capacity and communication challenges. Often staff needs to be reallocated and retrained to engage in crisis management activities. According to the PGEU survey on medicine shortages in 2013⁹, community pharmacists spend 2.5 - 5 hours each week processing information, sourcing medicines which they are not able to order from their usual wholesaler, informing patients and looking for an alternative treatment. This equates to 120-240 hours per pharmacy per year. Time solving problems caused by shortages is time that could be better spent advising and caring for patients.

⁵ TRT5 observations: <http://www.trt-5.org/article334.html>
TF1, 27 March 2011: <http://videos.tf1.fr/it-we/penurie-de-tritherapie-les-malades-lancent-un-cri-d-alarme-6330845.html>
L'Humanité Dimanche, 6 October 2011: http://www.trt-5.org/IMG/pdf/Humanite_dimanche_06_102011.pdf
Le Quotidien du Médecin, 31 October 2011: http://www.trt-5.org/IMG/pdf/31102011_ruptures_d_ARV_quotidien_du_pharmacien.pdf

⁶ EMA recommendations:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2010/07/news_detail_001046.jsp&mid=WC0b01ac058004d5c1
Eurordis Q&A on Fabrazyme® and Replagal® shortages :
http://www.eurordis.org/sites/default/files/Q&A_cross_border_care_final.pdf

⁷ C.E.M. Hollak, et al., Force Majeure: Therapeutic measures in response to restricted supply of imiglucerase (Cerezyme) for patients with Gaucher disease, Blood Cells Mol. Diseases (2009),

⁸ EMA recommendations :
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/public_health_alerts/2012/03/human_pharm_detail_000058.jsp&mid=WC0b01ac058001d126

⁹ <http://www.pgeu.eu/en/library/2-position-papers/154-pgeu-statement-on-medicine-shortages-in-european-community-pharmacies.html>

The lack of information about why a shortage has occurred, and when the situation might be expected to improve, leaves community or hospital pharmacists and other healthcare professionals unable to provide reliable assurance of future supply to a patient or healthcare team members, creating unwelcome uncertainty and anxiety for patients.

The increased number of medicine shortage becomes a real challenge for all healthcare professionals including nurses. For example no supply for an anticancer agent may lead to adverse outcomes in cancer patient¹⁰.

If a medicine in short supply is replaced with an alternative one, the risk of error increases. An American survey on the effect of oncology medicine shortages in cancer care shows that changes in therapy leading to near-miss errors were reported by 16% of participants, with 6% reporting one or more actual medication errors attributable to a medicine shortage¹¹. To avoid potential adverse effects due to medication error, it is important to ensure that necessary information about the reasons, the extent of shortage, the remaining stock and alternative treatment is available to all healthcare professionals.

1.4. Consequences for health care providers

Health system managers are faced with increased costs not only as a result of the diversion of resources in order to manage all aspects of the shortage (including identifying its causes and possible solutions, sourcing alternatives, etc.), but also because certain medicines may need to be purchased at much higher prices from so-called "grey market" sources, which also potentially compromise product quality (e.g., counterfeits). In the EU, medicine shortages might also stimulate an increase in cross-border treatments, which poses further challenges for continuity of care and information sharing.

¹⁰ J Pharm Pract. 2013 Jun;26(3):183-91. Clinical dilemmas and a review of strategies to manage drug shortages. Rider AE, Templet DJ, Daley MJ, Shuman C, Smith LV.

¹¹ Am J Health Syst Pharm. 2013 Apr 1;70(7):609-17. National survey on the effect of oncology drug shortages on cancer care. McBride A, Holle LM, Westendorf C, Sidebottom M, Griffith N, Muller RJ, Hoffman JM.

2. Possible causes of shortages

There are a number of reasons why some medicines are sometimes unavailable. The medicines supply chain is highly complex and its efficiency relies on performance of each individual actor of the supply chain including manufacturers of raw material (including active and non-active ingredients, containers and finished products), wholesalers, community pharmacies and intermediaries. If there is a disruption at any point of the supply chain shortages can occur.

Such disruptions can be caused by:

2.1. Medical or regulatory causes

- Shifts in demand, resulting from an actual use of the medicine which differs from the company's own estimates (e.g. a paediatric medicine also used in adults);
- In some cases, regulatory changes may impact on supply. For example the Heads of Medicines Agencies has warned that the implementation of the Falsified Medicines Directive may negatively impact the medicines shortage problem by restricting the availability of imported active pharmaceutical ingredients¹².

2.2. Economic causes

- The increasingly globalised nature of pharmaceutical manufacturing, with production concentrated in fewer sites distributed around the world. This tendency can have a severe impact on production capacity when for example, quality issues arise, or where there is difficulty in sourcing raw materials, transport hazards, natural hazards;
- In some cases, pricing strategies may impact on supply by reducing sustainability of supply;
- The lack of priority given to smaller markets by the pharmaceutical industry;
- Economic crisis and health budget control, where speculation encourages wholesalers and importers to purchase a medicine in EU countries where the price is lower and sell in countries where the catalogue price is higher. This then limits the supply in the country the medicine is imported from;

¹² <http://www.raps.org/focus-online/news/news-article-view/article/2638/eu-falsified-medicines-directive-could-result-in-drug-shortages.aspx>

- Decision of the marketing authorisation holder to withdraw the product from the market, for economic reasons or for switching the demand to a new, patented medicine with same or similar active ingredient;
- Financial pressure on the pharmaceutical industry: cost-containment measures limit their profits and the demand of their share-holders for dividends pressures management to reduce production costs, often to the detriment of quality and quality control.

2.3.Manufacturing causes

- Technical issues during the manufacturing process: for example 80% of antibiotics used in the EU are manufactured outside the EU, often in emerging countries (India, China, Brazil, Mexico) – only the final assembling is done in Europe;
- Contaminations or impurities due to inadequate quality assurance of raw materials and containers;
- Contaminations or impurities despite adequate quality assurance. Some medicinal products are very complex molecules or sophisticated biotech products that are more exposed to such risks;
- A monopoly on raw materials. If there is only one manufacturer, and the quality and/or volume is compromised, the situation becomes really critical.

2.4.Causes in relation to the organisation of the pharmaceutical market

- Increase in demand due to another shortage;
- The abolition of public service obligation / minimum national stock keeping requirements in some countries;
- The imposition of fixed quotas of medicines by the pharmaceutical industry, often inaccurately judging the true level of patient needs as well as removal of the traditional role of the full line wholesalers as a result of Direct-To-Patient schemes in some markets;
- Good Manufacturing Practices (GMP) in a global world: increasing issue reports by GMP inspectors, difficulties in ensuring / controlling GMP throughout the world;
- Tendering and procurement (e.g. Lithuania and procurement for antiretrovirals: a wholesaler submitted a very low bid but the company could not find a supplier that could deliver at that price).

3. Possible measures to prevent and manage supply shortages of medicines in the current regulatory framework

A fundamental principle: in developing policies and national laws and strategies, all stakeholders and governments must put patient needs first. These strategies should first and foremost aim to ensure timely and adequate supply of medicines to patients.

3.1.EMA reflection on supply shortages

At the European Medicines Agency since 2011, the Committee for Human Medicinal Products (CHMP) has repeatedly discussed problems of continuity of supply caused by manufacturing problems in relation to certain medicinal products¹³.

In November 2012, the EMA released a Reflection Paper on Supply Shortages of Medicines caused by manufacturing / Good Manufacturing Practice Compliance problems. This Reflection Paper summarises the lessons learned from previous crises where “the EMA had a supporting or co-ordinating role, and presents short and mid-term actions that may allow the Network to prevent, mitigate, and manage shortages of important medicinal products”. It discusses the regulators’ dilemma, the impact of globalisation, the industry approach, and presents the current regulatory framework.

Furthermore it proposes short and medium term actions, of which many correspond to recommendations patients’, consumers’ and healthcare professionals’ organisations are proposing here.

3.2.Recommendations to EMA

- There should be a European office/unit with dedicated staff to facilitate prevention, resolution of and communication on shortages, informing the public and providing outreach to healthcare professionals, patients’ organisations and other stakeholders (this office could be supervised by the EMA, for centrally authorised medicines and for other medicines based on certain criteria to be

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http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113.pdf

defined. It would operate in close collaboration with national competent authorities);

- EMA should collect and publish data on supply shortages in a public catalogue. We urge European authorities to undertake market research to improve their understanding of the scale of shortages, the causes (parallel trade, quotas and other supply chain responses, or other factors), duration of shortages, regional variations, what make a particular medicine attractive to exporters at a particular time, and impact on patients, pharmacists and others. The requirements of the 2012 FDASIA regulation in the USA, with its provision for mandatory annual reporting by the medicines regulator on the state of the shortages problem and actions necessary to address, might be a useful example to follow in this regard¹⁴;
- EMA should work with the companies to avoid or minimise the effect of a shortage (e.g. contact other manufacturers to increase production, validate the use of a filter when particles in injecting medicines...);
- Good Manufacturing Practices (GMP) inspections by the EMA and national agencies are already conducted on a large scale, however more resources may be needed to conduct inspections worldwide as needed;
- Transparency on inspection reports and instances of non-compliance should be improved (measures decided, timetables, and follow-up). All information on the causes of a shortage should be verifiable by regulatory inspectors, be they the result of a defect, a contamination, delays in the construction of a manufacturing site, difficulties in finding raw materials, consequences of a natural catastrophe, etc. EMA should also monitor the end of the shortage: the plan for managing growth in product demand going forward post-launch, where applicable, should be discussed with all stakeholders. This plan should be validated by authorities, and supervised by inspectors. This will help ensure that patients are not subject to aggressive competition between different pharmaceutical companies for example, where an alternative regimen has been proposed to replace that affected by the shortage. Here again, the interests of the patient should prevail.

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<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticAct/FDCA/SignificantAmendments/totheFDCA/FDASIA/ucm313121.htm>

3.3. Recommendations to public authorities

- To explore establishment of buffer stocks to be held by wholesalers to give greater flexibility to the supply chain (htt);
- To ensure fair and adequate distribution of the remaining supply: European and, in some cases, international coordination is needed to ensure fair and adequate distribution of remaining supply. In Europe, the allocation of supply to countries should be decided upon and agreed at the European level by the EMA and its scientific committees, with consultation of healthcare professionals and patients. The decisions made should be legally binding, and the European authority should have a clear legal mandate to decide and to enforce its decisions in Member States. When a Member State decides to stockpile enough supply for their needs, via a “safety supply”, this should be done in coordination with other Member States, to avoid pre-emption by some to the detriment of others;
- To establish a reporting mechanism to allow health care professionals and patients to actively report evidence of a product shortage to the authorities;
- To examine the causes of medicine shortages and formulate recommendations to prevent or alleviate shortages. There appears to be a responsibility gap between regulatory and public authorities in Europe in relation to fully examining causation of shortage and required solutions. The seriousness of the matter must be grasped and acted upon by those whom the public look to to address matters of public health concern.

3.4. Recommendations to industry

Before shortage

- Companies holding authorisations for medically necessary medicines should present a supply shortage risk assessment plan to European /National competent authorities, prior to marketing authorisation. The applicant would explain how the production capacity is planned in order to satisfy the demand (both for pre-marketing authorisation i.e. compassionate use and after marketing authorisation), and what measures the company could take if there is an issue (higher demand than expected, manufacturing defect...);
- This supply shortage risk assessment (SSRAP) plan should be agreed upon with EMA/national

authority before MA. Although small starting companies cannot be obliged to have different manufacturing sites, EMA should think of basic requirements to minimise a risk for shortage, including regular inspections and realistic calculations based upon assessment of population, production capacity etc.;

- The SSRAP should contain the following elements:
 - Information about production and distribution should be shared: confidentiality because of business sensitive information should not be accepted. In all cases, the interest of the patient should be prioritised;
 - When planning communication on products in development, anticipate the potential consequences on pre-market authorisation demand (compassionate use);
 - When planning a compassionate use programme, ensure inclusion criteria strictly match the definition in Regulation (EC) 726/2004 Title V, article 83.2, for a “group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorised medicinal product”. Else, the demand may oversize the manufacturing capacities at a stage when the manufacturer is still preparing the large scale production for future commercial use;
- The gap that exists between the marketing authorisation date and the amount of product available upstream of the authorisation is often shocking in the context of critical illness and major therapeutic hopes. Industry should adapt its production capacity to the planned dates of marketing authorisation in the US, EU, and Japan, and should master the adjustment of supply according to the patients who need the product the most in an ethical way.
- Description of supply chain management system in order to make it a subject of inspections (Best practices may need to be developed).

During shortage

- The manufacturer/MAA/MAH should inform the EMA and relevant HCP and patients’ organisations as soon as a shortage becomes possible (even if this may create false alerts), in particular for products when a shortage can provoke severe

damage to public health, as anticipation is key to prevent damage to the patients;

- When a shortage occurs, the marketing authorisation applicant (MAA) or holder (MAH) should always communicate the exact figures on manufacturing capacities and provide a calendar of production for the weeks/months to come, until the expected end of the shortage. In addition, the MAA/MAH should provide precise figures on how the product is currently used (which quantities are allocated to clinical trials in progress/to start, compassionate use, validation batches, stock for future market launch etc.). This information should be regularly updated and provided to all parties;
- HCP and patients’ organisations should be involved from the beginning and their expertise used to issue guidelines with the aim to protect the most vulnerable patients throughout the EU;
- Transparency is needed with respect to available inventory and a distribution plan should be made in line with recommendations, again involving HCP’s and patients.

3.5. Other recommendations

- Alternative unlicensed treatments should be made available through compassionate use programmes if considered sufficiently safe;
- General guidelines might be helpful, and should be developed with support of ethicists and legal advisors on how to distribute a small inventory of medicine when prioritisation is impossible (i.e. all patients are in equal need of treatment). Who is responsible to make a choice? How can a choice be made?
- The scope of pharmacy practice should be extended when medicines are in short supply, so pharmacists can use their skills to better manage patient care. Where a medicine is not available, an alternative medicine could be supplied following local guidelines and in consultation with a treating physician.
- Management of shortage in situations of extreme shortage: as a last resort, when it is clear that only very limited supply is available, and no clear biomedical criteria for allocation can be defined by consensus, the opinions of ethics committees already published as well as standard practice are in favour of random allocation (drawing lots). This may well be the only non-arbitrary, rational and fair way to allocate a very limited supply when demand largely exceeds supply. There are

successful examples of consensus medical criteria (e.g. for Gaucher disease: the Emergency Treatment Program, set up by EWGGD in collaboration with, but independent from, the marketing authorisation holder, was successful in prioritising patients). But when no consensus can be obtained, drawing lots may well be the only rational way to proceed.

4. Changes to the regulatory framework that are needed to better prevent and monitor supply shortages

- Legislation should require companies to notify the EMA of shortages even when the shortage is still uncertain, and not wait for it to be confirmed. False warnings will occur which should be handled with care to avoid unnecessary anxiety;
- Involvement of relevant patients' and healthcare professionals' organisations from the drafting of the SSRAP to until the end of a shortage should be systematic;
- Article 81 of the EU Directive on Medicines for Human Use¹¹ was intended to ensure adequate supply of any given product to the market. However, there is extensive evidence of situations where pharmacies can't obtain the medicines that they need for their patients. Consideration should be given to strengthening the provisions of Article 81;
- GMP Inspections should be more frequent for all medicines that are placed on the European market;
- For medicines that are life-saving, or to treat severe conditions, with no substitution product, the marketing authorisation applicant should take measures to minimise the risks (no single manufacturing chain, documenting the capacity to satisfy the potential demand for compassionate use and at the time of marketing authorisation...);
- Proposals for the organisation of the European medicine market, pricing policy, differential pricing, parallel import, to prevent "siphoning" supply from one Member State to others. The Commission and Council of Ministers should engage in a full review of the operation of the pricing system in Europe and whether it is best ensuring access to medicines for European patients in the overall sense, including, but not restricted to, its impact on medicine shortages.

However, nothing in the recommendations on supply shortages prevents a Member State from authorising the export of medicines to other Member States to the detriment of patients living on its territory, for instance by siphoning the medicine supply available for treatment of its patients. Export of medicine supply may create a shortage in a Member State for a given treatment. In such exceptional cases, the Member State should retain the right to remedy the situation on the grounds of public health, in accordance with Articles 52 and 62 TFEU. However, this limitation should be without prejudice to Member States' obligations under Regulation (EC) No 883/2004 of the European Parliament and of the Council of 29 April 2004 on the coordination of social security systems¹⁵;

- Regulatory impact assessments for pharmaceutical related legislation should explicitly give consideration to any potential unintended impacts of a proposed regulation on the medicines shortage problem. For example, the envisaged difficulties in relation to medicines shortages and the Falsified Medicines Directives provisions on third country API import might have been picked up and managed at an early stage in this case.

¹⁵ OJ L 166, 30.4.2004, p. 1.

5. Signatories of the position

As of 4 June 2014, the following organisations have signed this Common Position:

- AGE Platform Europe (AGE)
- Alzheimer Europe
- Asociación de Addison y Otras Enfermedades Endocrinas-Adisen (Spain)
- Association Surrénales (France)
- Behcet Syndrome Society UK
- DEBRA International
- European Association of Hospital Pharmacists (EAHP)
- European Aids Treatment Group (EATG)
- European Association of Urology (EAU)
- European Federation of Allergy and Airways Diseases Patients associations (EFA)
- European Federation of Neurological Associations (EFNA)
- European Federation of Internal Medicine (EFIM)
- European Institute of Women Health (EIWH)
- European Multiple Sclerosis Platform (EMSP)
- European Organisation for Rare Diseases (EURORDIS)
- European Public Health Alliance (EPHA)
- European Specialist Nurses Organisations (ESNO)
- European Union of Geriatric Medicine Society (EUGMS)
- International Patient Organisation for Primary Immuno-deficiencies (IPOPI)
- Patients Network for Medical Research and Health (EGAN)
- The European Consumers' Organisation (BEUC)
- The European Society of Oncology Pharmacy (ESOP)
- European Patients Forum (EPF)
- Spinal Muscular Atrophy Europe (SMAE)
- European Heart Network (EHN)
- European Haematology Association (EHA)
- European Working Group on Gaucher Disease (EWGGD)
- European Gaucher Alliance (EGA)
- European AIDS Clinical Society (EACS)
- European Liver Patient Association (ELPA)
- Pulmonary Hypertension Association Europe (PHA Europe)
- Standing Committee of European Doctors (CPME)
- European Academy of Paediatrics (EAP)
- Rett Syndrome Europe (RSE)
- European Foundation for the Care of Newborn Infants (EFCNI)
- European Federation of Neurological Societies (EFNS)
- European Society for Medical Oncology (ESMO)
- International Diabetes Federation European Region (IDF Europe)
- European Cancer Patient Coalition (ECPC)
- Thalassaemia International Federation (TIF)

- European Haemophilia Consortium (EHC)
- Myeloma UK
- European Association for Clinical Pharmacology and Therapeutics (EACPT)
- Myeloma Patients Europe (MPE)

And also

Rare Voices Australia Ltd.

POLICY PROPOSALS TO MINIMISE MEDICINE SUPPLY SHORTAGES IN EUROPE

Medicine shortages may negatively impact patient care and the patient experience. Shortages should be a priority of industry, supply chain stakeholders and national competent authorities, and deserve more than empathy or 'lip-service' but serious engagement and action.

EFPIA welcomes initiatives to address genuine shortages of medicinal products. The industry shares a common goal with all partners in healthcare - that is to ensure that all patients around the world have timely access to high quality medicines and vaccines. In Europe, the industry is committed to working closely with competent authorities to help ensure that medicines are accessible to all people, wherever they live, and to make healthcare more sustainable whilst securing future medical innovation.

Pharmaceutical companies should address issues relating to the manufacturing and supply of medicines and vaccines within their control to ensure the continuity of supply to people who need them. This is however a complex issue involving multiple stakeholders, and we need the active engagement and support of all of them to address this and minimise any negative impact on patient access.

Measures considered to address this issue should be proportionate and provide efficient, workable solutions that serve public health needs. It is also key to provide the right conditions and business environment to support the long-term sustainability of supply. This includes predictable and fair pricing and market access systems that reflect the various economic and healthcare needs across Europe.

EFPIA calls for:

1. Better understanding of the root causes and drivers of shortages. This should include identification of bottlenecks in the supply chain (the European Medicines Verification System set up in the context of Falsified Medicines Directive could readily be used for this purpose);
2. Better reporting of shortages through enhanced cooperation between supply chain stakeholders and the European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA) Task Force. Standardised reporting requirements for information on clearly defined shortages should be agreed, giving priority to critical products with high potential impact. The information should be uploaded onto a common portal to ensure a streamlined and effective alert system;
3. Effective enforcement of existing regulatory requirements on all actors in the supply chain at national level, coupled by measures to enhance transparency within the supply chain and support further dialogue across key stakeholders facilitating sharing of best practices;
4. Emergency intervention as the last resort, with greater solidarity among Member States to reduce disruptions in the supply chain by abolishing the distortive effects of national schemes incentivizing imports from lower income to higher income Member States (e.g. dispensing quotas for parallel imported products in Germany) or imposing significant national stockpiling obligations limiting supply for other EU markets;
5. Where needed, appropriate and proportionate temporary emergency measures enacted at national level to prevent shortages due to exports, to follow the good practice guidelines set out in this paper.

Drug shortages may negatively impact patient care and the patient experience. Over the recent past all of us have been confronted with specific examples or stories of patients who cannot get access to their treatment and these examples are difficult to bear when shortages relate to medication for life-threatening diseases or involving children and where there are no therapeutic alternatives. For these reasons drug shortages should be a priority of industry, supply chain stakeholders and national competent authorities, and deserve more than empathy or ‘lip-service’ but serious engagement and action.

The causes of unavailability of medicines in EU Member State markets are broadly threefold: i) products not being authorized; ii) products being authorized but not marketed; iii) products being authorized and marketed but unavailable due to shortages. This policy paper focuses on the last of these. Unequal availability and patient access to centrally approved medicines within the EU requires a separate in-depth discussion¹.

Shortages are defined in various ways by different competent authorities (including EMA) and stakeholders. In line with manufacturers’ public service obligation defined by Article 81 of Directive 2001/83/EU industry stakeholders have agreed to define a shortage of a medicinal product for human use as arising in the situation "when supply does not meet patient need at a national level for a period of more than two weeks".²

1. Better understanding of the root causes of drug shortages

The causes of shortages are multifactorial and include production disruptions, limited resilience of certain supply chains, unintended impact of pricing, reimbursement and procurement policies, stronger and/or unexpected demand due to public health emergencies or poor public forecasting, as well as supply chain problems and bottlenecks. The report on Drug Shortages ‘[Root causes and potential solutions](#)’ recently released by the US Food and Drug Administration (FDA)³ sheds additional light on drivers of shortages and observes that the root causes of shortages involve economic factors that are driven by both private and public sector decision-making. FDA lists three main root causes: i) Lack of incentives to produce less profitable medicines, ii) Market does not recognize and reward manufacturers for mature quality management systems and iii) Logistical and regulatory challenges make it difficult for the market to recover after a disruption. The FDA report also showcases the interdependencies of global manufacturing chains, including for Active Pharmaceutical Ingredients (APIs), exemplifying that the European Union is the second source of manufacturing of APIs (31%), behind Asia (45%).

¹ EFPIA – together with other EU Health stakeholders – have called upon the Commission to set up a High-Level Forum on Better Access to Healthcare Innovation involving Member States, Commission and stakeholders to discuss drivers leading to unequal availability across Europe. Decisions by economic operators to bring a medicinal product on to the market are always driven and influenced by a combination of factors (regulatory, legal and commercial). Thus, a holistic approach must be used to find solutions aimed at increasing availability. Eliminating one barrier will not significantly change the situation or lead to any satisfactory improvements in availability.

² See comments by EFPIA, Medicines for Europe and EASGP on EMA/HMA Guidance on detection and notification of shortages of medicinal products for Marketing Authorisation Holders in the Union: the definition included in the EMA/HMA Guidance refers to national demand rather than patients needs and therefore implies that it is the supply chain (e.g. wholesalers) that defines the existence of manufacturers’ shortages irrespective of patient needs. The EMA/HMA definition goes beyond the responsibilities of a marketing authorisation holder and the scope as identified in Article 81 of Directive 2001/83/EU.

³ Drug Shortages, Root Causes and Potential Solutions, US Food & Drug Administration (FDA), October 2019

Any work aimed at better understanding the causes of shortage in the supply chain and aspiring to propose meaningful solutions should start from the premises of the most correct measurement of the phenomena. Supply chains nowadays (including pharmaceuticals) rely on increasingly global and digitalised networks.⁴ This evolution has driven increased attention in the last forty years, both by the industry and by academic research, on defining and developing the right performance measures and metrics⁵ and equips us with a multitude of empirically tested supply chain measures and systems (Mishra et al., 2018), under the overarching principle that without correct measurements in place there cannot be any improvement in overall performance.⁶ EFPIA, therefore, highlights the need to enrich the current count of individual shortage events with a more comprehensive set of supply chain performance measures.

Causes and main drivers of shortages

The following table⁷ provides a visual representation of the majority of root causes of shortages. While the table aims to provide an easy-to-use overview, it has to be understood that shortages sometimes have multiple root causes which are intertwined and compound and exacerbate their cumulative effect. An in-depth analysis can only be carried out on a product (SKU) basis.

		Regulatory	Manufacturing	Quality	Economic	Supply chain
Products not authorized		Regulatory time lag	NA	NA	NA	NA
Products authorized but not launched		National requirements	Manufacturing capacity Natural disasters	NA	Market attractiveness Company size	NA
Products authorized and marketed but unavailable due to shortages	Temporary	NA	Manufacturing lag times GMP issues Surges in demand	API and excipient supply	Pricing mechanisms Tender practices Cost-containment measures	Supply quotas and parallel export Logistical inefficiency
	Permanent	NA	Manufacturing capacity	NA	Commercial withdrawals	NA

⁴ Mishra, D., Gunasekaran, A., Papadopoulos, T. & Dubey, R. 2018, "Supply chain performance measures and metrics: a bibliometric study", *Benchmarking*, vol. 25, no. 3, pp. 932-967.

⁵ Gunasekaran, A. & Kobu, B. 2007, "Performance measures and metrics in logistics and supply chain management: A review of recent literature (1995-2004) for research and applications", *International Journal of Production Research*, vol. 45, no. 12, pp. 2819-2840.

⁶ Kaplan, R.S. (ed) 1990, *Measures for Manufacturing Excellence*, 1st ed, Harvard Business School Press, Boston.

⁷ Supply chain stakeholders' perspectives on medicines shortages, presentation by AESGP, EAEPC, EAHP, EFPIA, EIPG, GIRP, Medicines for Europe & PGEU at the 8 November 2018 Multi-stakeholder workshop organized by HMA/EMA task force on availability of authorised medicines for human and veterinary use

In recent years, the industry has engaged with all relevant industry⁸ and supply-chain stakeholders^{9,10}, to address medicinal product shortages and seek solutions in partnership.

Despite multiple country reports, there is a lack of sound evidence and knowledge about the key drivers and extent of drug shortages. Most country information systems are based on different/diverging definitions of shortage, without any agreed view of what would be a meaningful disruption in the supply of medicines¹¹. Furthermore, most country information systems and most do not make any distinction between ‘suspected medicine shortage’ and ‘actual medicine shortage’. If the problem is to be effectively tackled, there needs to be a commonly agreed definition of what constitutes a genuine material disruption in the supply of medicines.

EFPIA calls for all relevant sources of information to be used in order to provide additional intelligence about the root causes and drivers of shortages, including the identification of bottlenecks in the supply chain. There are relevant sources of valuable data that are under-used or not used at all today. In particular, EFPIA recommends that the data stored in the interoperable network of national repositories being set up in the context of the Falsified Medicines Directive (Directive 2011/62/EU) and its Delegated Regulation 2016/161/EU on safety features be used for the monitoring of shortages.

The data stored in the National Medicines Verification Systems could provide useful intelligence regarding the number of packs for all prescription products being supplied by manufacturers on the various EU markets, number of packs dispensed in national pharmacies, number of packs exported (and/or imported), as well as on the level of stocks present in the supply chain at country level. The real time information in the repositories can be analysed according to very granular time frames (per day, per week, per month etc.) as well as per region (postal codes). That wealth of data would supplement information already provided by Marketing Authorisation Holders on manufacturing and quality related supply disruption to National Competent Authorities and, in providing information on causes and extent of shortages beyond manufacturing related issues, would greatly facilitate the detection and mitigation of genuine shortages.

The use of the repositories systems for the monitoring of shortages would benefit from further discussion between National Competent Authorities and relevant supply chain stakeholders with the goal of using every tool available to protect patient safety and public health¹².

⁸ Quality and Manufacturing Driven Supply Disruptions: Industry Communication Principles to Authorities, AESGP-EFPIA-EGA-PPTA, December 2014

⁹ Joint Supply Chain Actors Statement on Information and Medicinal Products Shortages, AESGP, EAHP, EAEP, EFPIA, EIPG, GIRP, Medicines for Europe, PGEU, January 2017

¹⁰ Joint Supply Chain Actors Statement on ‘Addressing the root causes of medicines shortages, AESGP, EAEP, EFPIA, EIPG, GIRP, Medicines for Europe, Vaccines Europe, 6 December 2019

¹¹ Not all products have the same criticality and impact with regards to patient needs and supply. The fact that a medicine is not available in a specific presentation but is available in other presentations cannot be put on the same footing with a shortage of a life supporting or life sustaining medicine.

¹² No less than 9 countries have already stated that they plan to use the repository systems developed in the scope of the Falsified Medicines Directive to monitor shortages whilst 8 other countries consider doing it. See response to Question 10.b in the [Summary of Responses](#) to the Questionnaire on the Measures implemented in the Member States territories in the context of Article 81 of Directive 2001/83/EC.

2. Better Reporting of Shortages

EFPIA is broadly supportive of existing mechanisms at national and at EU level to require the reporting of anticipated supply interruptions, but it is important to take into account product criticality and availability of alternative medicines. Regulatory obligations applicable to Marketing Authorisation holders (MAHs) are embodied in two main provisions of the EU legislation relating to the monitoring of supply and reporting of shortages:

- MAHs' obligation, in case a *"product ceases to be placed on the market of a Member State, either temporarily or permanently"* to *"notify the competent authority of that Member State ... no less than two months before the interruption in the placing on the market of the product,"*¹³ and
- MAHs' and distributors' public service obligations to ensure *"within the limits of their responsibilities, appropriate and continued supplies of medicinal product[s] to pharmacies and persons authorised to supply medicinal products so that the **needs of patients** in the Member State in question are covered."*¹⁴

Today, in Europe, there are different requirements for shortages notification in different Member States and the industry is complying with these requirements within the limits of their responsibilities as defined by the abovementioned provisions of EU law. When an interruption in the ability of the manufacturer to maintain the same cadence/volume of manufacturing and/or supply (due, for example, to manufacturing issues, quality related aspects, challenges with sourcing the sufficient amount of API etc.), the national competent authority is made aware in due time and specific mitigation solutions are discussed with the manufacturer so that the interruption does not lead to a shortage. Despite these best efforts, unforeseen circumstances (e.g. natural disasters, quality deviations, unexpected increase in demand, etc.) can hinder the ability of the manufacturer to notify the national competent authority two months in advance.

The pharmaceutical industry continues to establish increasingly robust quality and business management practices including holistic quality management systems, market forecasting methods and inventory management techniques. The successful implementation of these practices, in an integrated manner, is critical to ensuring that patients can rely on a continued supply of quality medicines. A proactive management system that actively assures and monitors quality standards, inventory levels and market signals is recommended for successful supply management to be achieved.

EFPIA member companies do recognise the importance of working towards preventing drug shortages and effectively managing supply before a shortage actually occurs. A management system itself can minimise the risks of drug product supply disruptions from arising. The [EFPIA 'Good Practice' Guide](#) describes in more details such management system that actively assures and monitors quality standards, inventory levels and market signals. These principles can either be

¹³ Article 23a of Directive 2001/83/EC. See also Article 123 for MAHs' notification obligations in case of suspension or withdrawal of the marketing of products, or the withdrawal or failure to renew the marketing authorisation for products.

¹⁴ Directive 2001/83/EC on the Community Code relating to medical products for human use provides that a public service obligation must be warranted on grounds of public health protection, and proportionate in relation to the objective of such protection, [2001] O.J. L311/67, Article 81, Recital 38.

employed proactively when the risk of drug shortage results from a situation internal to the company as well as reactively when it results from a market situation which was not foreseeable based on the company's internal indicators results and trends.

In this context, the industry welcomes the July 2019 Guidance on detection and notification of shortages of medicinal products for MAHs in the Union endorsed by EMA and Heads of Medicines Agencies¹⁵, which aims at providing a harmonized approach to the definition, detection and notification of shortages of medicinal products in the EEA. The definition of shortage (and demand) included in the Guidance will need to be interpreted in line with Article 81 of Directive 2001/83/EU focussing on patients' needs.¹⁶ Although the Guidance proposes a general reporting of any early detection of potential shortages, it should be understood that not all products have the same criticality and impact in terms of patient needs and supply. Priority must be given to critical products with a high impact rather than products with a moderate or low patient need where, for instance, there are alternative medications readily available. While aiming for a harmonised approach, the Guidance seems to exempt current/existing national reporting practices and tools which counters harmonisation efforts, adds further complexity and prevents a full standardization of the information to be reported in terms of content and format.

The industry is currently working with EMA and Heads of Medicines Agencies in order to ensure the effective implementation of the Guidance on detection and notification of shortages. The aim is to enable all EU competent authorities to receive more harmonised information about any potential disruption or interruption of supply at a very early stage, in order to be able to anticipate when a potential disruption is likely to turn into a shortage with an actual impact on patients. Getting to a common understanding that the best way to organise such a system is through a common portal with standardised reporting information format is in everyone's interests.

3. Effective Enforcement of Existing Regulatory Obligations

Better monitoring and rigorous enforcement of existing regulatory obligations on all actors in the supply chain, coupled with further measures to enhance transparency within the supply chain, would considerably improve the status quo. Such improvements can be done at a national level and can be facilitated by the sharing of best practices and closer consultation with stakeholders.

EU law requires each supply chain actor to qualify their suppliers and customers. This ensures, at each stage of the supply chain, that medicines are received from and supplied to duly authorised economic operators that fulfil their respective regulatory obligations.

Marketing authorisation holders ("MAHs") as well as wholesalers have a fundamental "public service" obligation to ensure *"within the limits of their responsibilities, appropriate and continued supplies of medicinal product[s] to pharmacies and persons authorised to supply medicinal products"*

¹⁵ https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-detection-notification-shortages-medicinal-products-marketing-authorisation-holders-mahs_en.pdf

¹⁶ Although the EMA/HMA Guidance states that 'Manufacturing Authorisation Holders have oversight of the supply of their medicines both nationally and globally' it should be stressed that MAHs do know how much product they are supplying to distributors in a country, however, they are not in a position to know how much of that volume is ultimately made available to patients in that country. MAHs may also not track or control in any way how product is disposed of by the distribution channel where such activities would amount to an infringement of Article 101 (1) or 102 of the TFEU.

*so that the needs of patients in the Member State in question are covered.*¹⁷ **Member States should evaluate the limits of the responsibilities of MAHs and wholesale distributors on a product-by-product basis.** There are scenarios where the MAH is not responsible for the shortage. For example, when the MAH's supply meets ordinary orders, in real-time, in relation to demand from patients of the Member State concerned, but a shortage is caused by a distributor's export/supply of medicines to another customer in a different Member State, without the MAH being aware. Another example is shortages caused by increased demand due to a shortage in the Member State of an alternative medicinal product produced by another company.¹⁸

Public service obligations imposed on MAHs should not lead to an obligation to sell to all entities with a wholesale licence in a market nor to an obligation to fulfil orders in full on a first-come, first-served basis. This would result in competitive distortions in the wholesaler market and increase the risk of the MAH being unable to supply other wholesalers in accordance with their usual orders, hence jeopardising that all pharmacies/patients' demand is met. The MAH should at all times be allowed to manage its supply chain in a way that best ensures that **patient** needs are met which is the fundamental obligation of the authorisation holder (see Art. 81 Directive 2001/83). The public service obligations of other actors in the supply chain should be enforced by national authorities and should not be the responsibility of MAHs.

Wholesalers, brokers and pharmacies are subject to separate licensing regimes. While in principle free to carry out multiple activities, they must have the appropriate licence for each. Distributors are required to have sufficient quality control and emergency plans in place.¹⁹ Requirements have also been imposed on those engaged in brokering medicinal products.²⁰

Strict adherence to these separate regulatory obligations is essential to the integrity and reliability of the overall supply chain. These public service obligations should be interpreted and enforced in a proactive manner which prioritises patient safety. The short-term commercial objectives of different actors in the supply chain should not play a role. Pharmacists should not be allowed to engage in wholesale activities without securing the appropriate licence in those countries where wholesale activities are open to them. They must demonstrate that in meeting the wholesaler obligations, their primary obligation to satisfy local patient demand at the retail level will not in any way be compromised. Non-compliance should result in the application of dissuasive penalties.

Increased transparency would also align with the policy objectives of the Falsified Medicines Directive and Delegated Regulation,²¹ which impose identification, reporting and quality control

¹⁷ Directive 2001/83/EC on the Community Code relating to medical products for human use provides that a public service obligation must be warranted on grounds of public health protection, and proportionate in relation to the objective of such protection, [2001] O.J. L311/67, Article 81, Recital 38.

¹⁸ [Paper](#) on the obligation of continuous supply to tackle the problem of shortages of medicines agreed by the ad-hoc technical meeting under the Pharmaceutical Committee on shortages of medicines on 25 May 2018, European Commission

¹⁹ Articles 78-79 and 84 Directive 2001/82/2001 and Commission Guidelines on Good Distribution Practice of Medicinal Products for Human Use, [2013] O.J. C.68/1.

²⁰ These amendments were introduced by Directive 2011/62/EU of the European Parliament and of the Council, amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products [2011] O.J. 174/74.

²¹ Directive 2011/62/EU of the European Parliament and of the Council, amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry

obligations on stakeholders to minimise the risk of counterfeit medicines penetrating the supply chain.²² The Directive also encourages greater transparency and cooperation across borders by obliging national authorities to submit certain information (e.g., compliance records of wholesalers who have passed inspections, and evidence of appropriate authorisations and certificates of good practice) to a centralised, publicly accessible database managed by the EMA. Greater transparency across the supply chain would make it easier for national authorities to:

- identify enforcement gaps,
- predict when and where shortages are likely to occur,
- focus their limited resources on the areas which pose the greatest risk to supply security, and
- devise suitable regulatory responses before patient access is affected.

4. Emergency Intervention as Last Resort to Ensure Security of Supply

National price controls condition and limit the single market in pharmaceuticals. Although superficially attractive, increased levels of parallel trade are unsustainable economically and politically to the extent they result in shortages of the lower priced medicine in any EU country. Due to mandatory price controls and resulting price differentials between Member States, arbitrage opportunities exist between any two EU countries, however lower income markets are a more attractive source of medicines' supply for parallel trade to the detriment of patients in those lower income countries.²³

Member States may take measures to prevent or address shortages of medicines by restricting the free movement of goods within the EU.²⁴ Member States are able - as a matter of EU law - to take measures to ensure security of supply where there is a genuine risk of shortages. Such measures include mandatory pre-export notification, consent requirements imposed on wholesalers, and restrictions on pharmacist wholesale activities. In exceptional circumstances, the imposition of limited export bans may be justified in respect of those medicines where there is a demonstrated supply shortage and consequent risk to patient safety. Even without such drastic measures, rigorous enforcement of public service obligations not only of MAHs but also of other actors in the distribution chain could help to reduce shortages especially in lower income Member States (see, for example, the measures introduced into the Polish Pharmaceutical Law in 2015 and 2019).

Such measures are lawful under EU law free movement principles provided they are taken in response to a genuine public health risk and are proportionate in that they are appropriate to

into the legal supply chain of falsified medicinal products [2011] O.J. 174/74 ("Falsified Medicines Directive").

²² See Article 1(17) Falsified Medicine Directive amending Article 80 of the Directive 2001/83/EC to require wholesalers to (i) keep records of all transactions, (ii) maintain a quality control system, and (iii) inform the relevant authority and the MAH in the event a falsified medicine is discovered.

²³ Research shows that the profits enjoyed by parallel traders can be as much as 20 times the net savings to the national healthcare system. See Kanavos and Kowal, Does pharmaceutical parallel trade serve the objectives of cost control?; *Eurohealth Vol 14 No 2, page 25*; see also Kanavos P, Costa-Font J. Pharmaceutical, Parallel Trade in Europe: stakeholder and competition effects. *Economic Policy* 2005;20(44):751–98.

²⁴ [Paper](#) on the obligation of continuous supply to tackle the problem of shortages of medicines agreed by the ad-hoc technical meeting under the Pharmaceutical Committee on shortages of medicines on 25 May 2018, European Commission

achieve the stated public health objective, and are not more restrictive than is necessary to achieve their legitimate objective.²⁵

EFPIA considers that when, despite best efforts, shortages do occur, national legislation designed to achieve security of supply should address the following six areas, further elaborated on in Annex I, to ensure compliance with EU law:

- i. A clear definition of the notion of shortage linked to patient demand and patient needs (actual and potential) and the scope of application of any emergency legislation;
- ii. A data driven methodology to identify actual and potential shortages;
- iii. A mechanism that allows a swift response to actual or potential shortages to minimise any negative impact on patients - enforcement should remain the responsibility of national competent authorities, and not be delegated to MAHs in order to avoid competition law compliance risks;
- iv. An appeals process allowing supply chain stakeholders to promptly challenge decisions adopted by the authorities to address shortages and obtain short-term relief as appropriate;
- v. A regular review mechanism to ensure that emergency measures continue to be in place or are rescinded as appropriate to accurately reflect market reality in line with the principle of proportionality - measures should not go beyond what is strictly necessary to achieve the underlying public health objective and the return to the normal situation after the lift of the emergency measure should be gradually introduced in order to avoid a ‘bullwhip’ effect in supply; and
- vi. Sufficiently deterrent but proportionate penalties for violations of the obligations imposed on supply chain actors to combat shortages.

Temporary emergency measures can act as an important safety valve, but they do little to alleviate the underlying problems/root causes that give rise to shortages and do not address the fundamental malaise of today's inequality of access to innovative medicines.

Call for Action

Member States should resist placing the entirety of the burden on manufacturers by imposing disproportionate requirements in terms of prevention plans, stock piling, reporting and/or penalties, without considering the potential effect of such country requirements on the continued supply of other EU markets. Industry is currently working with EMA and Heads of Medicines Agencies in order to ensure effective implementation of the July 2019 EMA/HMA guidance on detection and notification of shortages, which should enable all EU competent authorities to receive harmonised information about any potential disruption or interruption of supply at very early stage, from a common reporting portal. In most countries manufacturers are currently liaising with all supply chain stakeholders in order to fix short-term issues within the limits of their responsibilities.

²⁵ See for example Case C-169/07 *Hartlauer v Wiener Landesregierung*, ECLI:EU:C:2009:141, para. 55.

The challenges linked to shortages are complex and policy solutions require a holistic, comprehensive approach that reflects the multiple root causes, different stages in the production and supply and different stakeholders involved. Policy solutions need to address the different root causes of shortages. Furthermore, addressing the root causes of shortages is a marathon, not a sprint. Authorities and stakeholders need not get discouraged by the apparent lack of immediate effect singular actions to mitigate shortages. Action is needed on multiple fronts to achieve sustainable results. EFPIA calls for:

1. Better understanding of the root causes and drivers of shortages. This should include identification of bottlenecks in the supply chain (the European Medicines Verification System set up in the context of Falsified Medicines Directive could readily be used for this purpose);
2. Better reporting of shortages through enhanced cooperation between supply chain stakeholders and the European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA) Task Force. Standardised reporting requirements for information on clearly defined shortages should be agreed, giving priority to critical products with high potential impact. The information should be uploaded onto a common portal to ensure a streamlined and effective alert system;
3. Effective enforcement of existing regulatory requirements on all actors in the supply chain at national level, coupled by measures to enhance transparency within the supply chain and support further dialogue across key stakeholders facilitating sharing of best practices;
4. Emergency intervention as the last resort, with greater solidarity among Member States to reduce disruptions in the supply chain by abolishing the distortive effects of national schemes incentivizing imports from lower income to higher income Member States (e.g. dispensing quotas for parallel imported products in Germany) or imposing significant national stockpiling obligations limiting supply for other EU markets;
5. Where needed, appropriate and proportionate temporary emergency measures enacted at national level to prevent shortages due to exports, to follow the good practice guidelines set out in this paper.

ANNEX I

BEST PRACTICES FOR NATIONAL LAW MEASURES DESIGNED TO REDUCE THE RISK OF SUPPLY SHORTAGES

To be effective and compliant with EU free movement principles, shortages legislation should satisfy the following criteria:

1. Clear definition of the legislation's scope of application and of the notion of shortage linked to patient demand and patient needs (actual and potential)

Legislation should contain a clear definition of “shortage” as a trigger event.²⁶ By way of illustration, Romanian²⁷ measures define a shortage as a decrease of stocks below the national monthly average for 7 consecutive days.

Emergency measures should be limited to those medicines prone to actual or potential shortages that are considered essential for serious medical conditions. They should address whether there can be a shortage where alternative products are still available in the national market, drawing a distinction between patients to whom alternative treatments are available and those for whom alternative treatments are not available.

Similarly clear criteria should establish when a shortage ceases to exist and when any preventive measures should cease to apply. Stock levels should be continuously monitored so that any such measures are suspended once stocks have returned to normal levels for a defined set minimum period.

2. Systems to identify actual and potential shortages

Reliable, up-to-date and comprehensive information systems are essential not only in identifying, but also in communicating and resolving actual and potential shortages. They help to:

- Ensure that assessment of likely shortages is based on actual data;
- Implement contingency plans to minimise any adverse impact on patients;
- Implement a rapid alert and resolution process between different supply chain actors in urgent cases to avoid severe adverse impacts on patients;
- Provide patients with appropriate information (for example why their treatment needs to be disrupted, delayed or changed);
- Ensure the optimal management and distribution of remaining stock; and
- Facilitate substitution and/or provide therapeutic alternatives.

²⁶ In 2015, the Bulgarian Constitutional Court declared a legislative measure in Bulgaria unlawful due to, among other things, its vague definition of shortages.

²⁷ In early 2017, a number of legislative amendments aimed at reducing the shortage of medicines in Romania by limiting parallel exports entered into force. Shortage was defined as: the decrease of stocks below the national monthly average for 7 consecutive days. This stock decrease triggers an alert in the system and the export of the relevant medicine will be temporarily banned. Also, the medicine will be included on the Ministry of Health's special list of medicines under surveillance.

For any information system to be effective, it is important to specify:

- Which stakeholders (manufacturers/MAHs, distributors, pharmacies, prescribing physicians and maybe even patients?) are subject to reporting obligations;
- What information should be included in the system, for example, the products/dosages subject to a shortage or risk thereof, the cause of the shortage and the anticipated duration of the shortage;
- Who should have access to which information recorded in the system:
 - Competent authorities must have access to the information system for multiple purposes: to allow them to investigate whether a shortage is due to a distributor's failure to comply with its public service obligations or for another reason, for ongoing monitoring purposes, and to be able to take proportionate corrective measures where required;
 - Patients might have limited access to the information system, for example to alert authorities when certain medicines are unavailable at their local pharmacy, or to help them locate a pharmacy with their medicine in stock;²⁸
 - Other stakeholders, manufacturers/MAHs, distributors etc., may also be permitted to have limited access to the information system (for example, if it serves as a repository for their own sales and supply data) without, however, accessing any competitively sensitive information of other operators.

3. Swift response in case of risks of shortages and actual shortages

Where there is a genuine risk of shortages, corrective emergency measures may take various forms, including, mandatory pre-export notifications to the relevant authorities and a temporary refusal of exports.

Any process for mandatory pre-export notifications should provide for short review periods (15-30 days seems appropriate, a period of 6 months would likely be excessive) with approval being assumed where the authorities fail to respond within the deadline. Administrative delays or lack of resources should not prevent legitimate exports.

Responsibility should remain with the competent authorities to ensure the effectiveness of the emergency measures. Requirements on distributors to obtain pre-export written authorisations from manufacturers/MAHs (and prohibition of exports by distributors who do not possess such written authorisation) should be avoided including because they expose the stakeholders to competition compliance issues²⁹.

Where export bans are imposed as a result of shortages, they should not constitute blanket, indiscriminate bans. Authorities should review each export request individually and carefully assess whether there is an actual or potential shortage and whether the relevant medicine is essential for the treatment of certain serious medical conditions.

²⁸ Health authorities should provide information on alternative treatments available from other suppliers, and national reimbursement rules should not impede the provision of alternative treatments to patients in case of shortages.

²⁹ In 2017, amendments to Slovakia's Act on Medicinal Products entered into force, which significantly limit the possibility of exporting medicines reimbursed by the Slovak sick fund. The amendments included provisions that require distributors to obtain prior written authorisation from the manufacturer/MAH for the export of reimbursed medicines.

In sum, any response to the risk of shortages or actual shortages should be proportionate,³⁰ based on objective and transparent criteria, and should not allow relevant authorities to discriminate between different stakeholders.

4. Review mechanism

Mechanisms must be built into any emergency measures to ensure they are regularly reviewed, continue to reflect market reality, and are lifted as soon as the relevant shortage has ended.

5. Appeal process

Shortages legislation should provide for an effective and timely appeal process which allows affected stakeholders to challenge decisions imposed by the authorities to address shortages. For example, the adopted legislation in Poland³¹ in 2015 allows distributors to appeal against an export refusal decision within 7 days of receipt of the decision.

6. Penalties

Shortages legislation will not be effective unless strictly enforced. Legislation should therefore foresee penalties for violations that are sufficiently deterrent, but proportionate.

³⁰ In July 2019, the Belgian Constitutional Court suspended a measure prohibiting sales of medicines regarding which a shortage has been determined by wholesalers who are subject to public service obligations to normal wholesalers who are not subject to such an obligation. The Court found that this restriction was not proportionate because as it had not been shown that exports of normal wholesalers had an effect on the availability of medicines affected by shortages. Also, wholesalers subject to public service obligations are already restricted to supplying normal wholesalers only provided they still meet their public service obligations.

³¹ The European Commission did not raise any objections against a number of amendments to the Polish Pharmaceutical Law aimed at limiting shortages of medicines in Poland which were notified to the Commission under the procedure of Directive 2015/1535. This procedure prevents the creation of new technical barriers to trade by ensuring the compatibility of national legislation with EU law. The 2015 amendments i) require all participants active in the supply of medicines subject to reimbursement to inform the competent authority about their stock levels on a regular basis; ii) require distributors to notify the relevant authority in advance of any intention to export medicines outside Poland (including specifying the relevant volumes); iii) require the relevant authority to decide within 30 days whether to refuse to permit such export. For this decision, the authority considers such factors as: (i) whether there is a risk that the medicines are not available in Poland; and (ii) the importance of the medicines to public health; iii) require distributors to sell the relevant medicines within the territory of Poland where the relevant authority refuses to request to export, as any refusal decision is immediately enforceable; v) allow distributors to export without further delay if the authority does not respond within the 30 day time-limit (but distributors must nonetheless inform the relevant authority within seven days of the export). Distributors have the right to challenge each decision refusing export and so can properly defend their commercial interests in the event of a refusal decision by the authority. The Polish Pharmaceutical Law was updated in 2019 and provides for inter alia stricter penalties for unlawful exports.

Position Paper

Medicines shortages

Date of release: 27 September 2017

- Medicines for Europe aims at ensuring a **patient-centric proactive dialogue** on the availability and access of medicines involving all the stakeholders: payers, regulators and supply chain actors.
- Medicines shortages can be addressed when **multisource alternatives are available**.
- In order to tackle medicines shortages in a multi-source context, Medicines for Europe believes in an approach that **addresses both the root causes of medicines shortages (preventing medicines shortages)** and mitigates them once they occur (**mitigating medicines shortages**).

Executive summary

Causes of generic medicine shortages

- **Pressure of costly regulatory/quality procedures and cost-containment measures on generic medicines industry:**

Members of Medicines for Europe are highly committed to quality. To achieve this quality, manufacturers comply with important and stringent regulatory/quality procedures. These procedures are costly and experience has proven that there is an inability of the market to reward the investment on these procedures.

Additionally, the extreme pressure on prices due to **short-term cost containment measures such as tendering**, external reference pricing and payback mechanisms challenge the sustainability of our industry forcing the withdrawal of generic medicines from the market and increasing the risk of medicines shortages.

In order to tackle medicines shortages in a multi-source context, Medicines for Europe believes in an approach that **addresses both the root causes** of medicines shortages (**preventing medicines shortages**) and **mitigates** medicine shortages once they occur.

Recommendations to prevent medicine shortages (addressing the root causes)

- **Ensure market predictability:**
 - A predictable and sustainable pricing and reimbursement environment will increase the number of manufacturers in the market guaranteeing that in case one of the manufacturers cannot supply other manufacturers in the market are able to supply the medicine:
 - Revision and prevention of the application of short-term cost containment measures (e.g. mandated price reductions, internal and external reference pricing, tendering and payback mechanisms) to generic medicines that are undermining the long-term sustainability of manufacturers while increasing the risk of medicines shortages which ultimately affects patient health
 - Prevent disproportionate sanctions that can increase the risk of medicine shortages
- **Improve regulatory efficiency to reduce administrative and cost burden of keeping medicines in the market:**

- Implement flat fee structure for variations
 - Optimise the use of Centralised and Decentralised procedures for generic medicines
 - Increase flexibility to accept different pack sizes or multi-country packs to address market needs
 - Increase use of telematics tool (e.g. FMD, ISO-IDMP, Art. 57, etc.) for communication of changes currently requiring variation submission in large portfolios
 - Lower fees/costs for older molecules that still serve a healthcare need
- **Manage available market stock information with non-coercive systems:**
 - Use systems such as European Medicines Verification System that will be in place in 2019 to manage information on medicine shortages throughout the supply chain

Recommendations to mitigate medicine shortages

- **Specific regulatory measures to mitigate imminent medicine shortages:**
 - Flexibility to accept different pack sizes at national level based on Marketing Authorization
 - Flexibility to accept multilingual packages (e.g. eLeaflet as a solution)
 - Efficient Repeat Use Procedure
 - Incentives for medically essential low price products (e.g. lower variation fees/flat fee)

Patient-centric approach to medicines shortages

Medicines for Europe believes in the importance to provide patients timely access to medicines and is committed to provide a safe and continuous supply of medicines as a key public health objective. In this view, Medicines for Europe aims at ensuring a patient-centric proactive dialogue on the availability and access of medicines involving all the stakeholders: payers, regulators and supply chain actors.

Medicines for Europe believes that the medical use of generic medicines should be considered as an opportunity to increase patient access and prevent medicines shortages through increased choice and availability of treatments. Medicines shortages can be addressed when multisource alternatives are available.

Generic medicines have transformed healthcare in Europe by significantly increasing patient access to medicines in an era of rising demands for healthcare services and constrained finances. Over the last ten years, generic medicines have increased access to medicines by over 100% in seven key therapeutic areas without increasing the overall treatment cost.

Drivers of medicines shortages in an off-patent, multi-source sector

Members of Medicines for Europe are highly committed to quality. To achieve this quality, manufacturers comply with stringent regulatory and quality procedures. These procedures are costly and experience has proven that there is an inability of the market to reward the investment on these procedures. Additionally, the extreme pressure on prices due to short-term cost containment measures such as tendering, external reference pricing and payback mechanisms challenge the sustainability of our industry provoking the withdrawal of medicines from the market and increasing the risk of medicines shortages.

In order to tackle medicines shortages in a multi-source context, Medicines for Europe believes in an approach that addresses both the root causes of medicines shortages (preventing medicines shortages) and mitigates them once they occur (mitigating medicines shortages).

Recommendations to prevent shortages

Improve regulatory efficiency

The EU has high regulatory standards in place which need to be complied with before a medicine can be placed on the market. While we encourage these high standards, Medicines for Europe considers that enhancing regulatory efficiency and fit-for-purpose regulatory measures can foster greater access to and availability of medicines. To increase the efficiency and optimise the regulatory processes to reduce the administrative and cost burden of keeping the medicines on the market, we recommend to implement a flat fee structure for variations, optimise the use of Centralised and Decentralised procedures for generic medicines, increase flexibility to accept different pack sizes or multi-country packs to address market needs, increase use of telematics tool (e.g. FMD, ISO-IDMP, Art. 57, etc.) for communication of changes currently requiring variation submission in large portfolios and lower fees/costs for older molecules that still serve a healthcare need.

Ensure market predictability

Generic manufacturing is a competitive business which aims at having efficient operations to minimise costs and offer maximum discounts to payers. To date, the main focus of healthcare policies around generic medicines has been on cutting prices, instead of securing patient access to high-quality medicines. Average price reduction after patent expiry is 50%, increasing further over time up to 80-90%.

Cost-containment measures such as government mandated price reductions, internal and external reference pricing and procurement through tendering, undermine the long-term sustainability of manufacturers while increasing the risk of medicines shortages that ultimately affects patient health. This was also acknowledged by the World Health Organisation (WHO), which stated that *there are more appropriate pricing mechanisms for off-patent medicines than external reference pricing* (WHO HAI 2011 – Project on medicines availability – External reference Pricing). Similarly, most scientific articles reviewing shortages of generic medicines identify cost-containment measures and policies as the underlying root cause^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15}.

¹ Alevizakos M, Detsis M, Grigoras CA, et al. The Impact of Shortages on Medication Prices: Implications for Shortage Prevention. *Drugs*. 2016;76(16):1551-8.

² Barlas S. FDA strategies to prevent and respond to drug shortages: finding a better way to predict and prevent company closures. *P & T: a peer-reviewed journal for formulary management*. 2013;38(5):261-3.

³ Birgli. An Evaluation of Medicines Shortages in Europe with a more in-depth review of these in France, Greece, Poland, Spain, and the United Kingdom. Zug: Birgli, 2013. Available from: <http://static.correofarmaceutico.com/docs/2013/10/21/evaluation.pdf>.

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⁷ Kaposy C. Drugs, money, and power: the Canadian drug shortage. *Journal of bioethical inquiry*. 2014;11(1):85-9

⁸ Kweder SL, Dill S. Drug shortages: the cycle of quantity and quality. *Clinical pharmacology and therapeutics*. 2013;93(3):245-51.

⁹ Markowski ME. Drug Shortages: The Problem of Inadequate Profits. Cambridge, MA: Harvard Law School, 2012. Available from: <https://dash.harvard.edu/handle/1/11940215>.

¹⁰ McKeever AE, Bloch JR, Bratic A. Drug shortages and the burden of access to care: a critical issue affecting patients with cancer. *Clinical journal of oncology nursing*. 2013;17(5):490-5.

¹¹ Pauwels K, Huys I, Casteels M, et al. Drug shortages in European countries: a trade-off between market attractiveness and cost containment? *BMC health services research*. 2014;14:438.

¹² Pauwels K, Simoens S, Casteels M, et al. Insights into European drug shortages: a survey of hospital pharmacists. *PloS one*. 2015;10(3):e0119322.

¹³ Reed BN, Fox ER, Konig M, et al. The impact of drug shortages on patients with cardiovascular disease: causes, consequences, and a call to action. *American heart journal*. 2016;175:130-41.

¹⁴ Woodcock J, Wosinska M. Economic and technological drivers of generic sterile injectable drug shortages. *Clinical pharmacology and therapeutics*. 2013;93(2):170-6.

¹⁵ Yurukoglu AL, E. Ridley D.B. The Role of Government Reimbursement in Drug Shortages. US: Stanford University, 2016. Available from: <https://web.stanford.edu/~ayurukog/shortages.pdf>.

The most extreme examples of medicines shortages can be found in countries which have disproportionate pharmaceutical pricing policies on generic medicines. In Romania, due to inappropriate cost-containment measures (e.g. clawback tax, external reference pricing, etc.), approximately 2.000 generic medicines have been withdrawn from the market over the last two years alone (annex with links for ‘Clawback influence on shortages’ and ‘Statements of Patient Associations regarding shortages’). As a result, Romania has suffered from chronic shortages of essential but inexpensive medicines such as methotrexate.

Medicines for Europe recommends a predictable and sustainable pricing and reimbursement environment that will increase the number of players in the market to reduce the risk of medicines shortages. This can be achieved with measures that avoid retraction of manufacturers from the market. In particular, to adjust the number of winners of tenders to the market/country characteristics – guaranteeing that multiple players are supplying the market and in case one of the manufacturers cannot supply, other manufacturers in the market are able to supply. Furthermore, disproportionate sanctions should be prevented as they promote retraction of manufacturers from the market and increase the risk of supply. In case there are penalties applied to guarantee supply, these should be proportionate to the revenue of manufacturers and applied in accordance with the contract criteria. In Slovakia, under the umbrella of the Article 81 of Directive 2001/83/EC¹⁶, and to avoid medicines shortages, the government is issuing a legal obligation to manufacturers to supply within 24 hours. In case manufacturers fail to supply, they are subjected to penalties of up to 1 Million Euro. The way in which these penalties are applied (by SKU rather than INN) will lead to disproportionate fines amounting to multiples of generic medicines industry sales which will undermine the sustainability of the pharmaceutical industry and increase the risk of medicines shortages.

Finally, to ensure that the society will continue to benefit from these medicines, it will be important to develop a predictable and sustainable market model. At this moment, generic medicines account for over 56% of the medicines dispensed in Europe at only 22% of the costs, which is only 2-3% of total healthcare budgets.

Address negative healthcare impacts of parallel trade

Parallel exports from Eastern Europe to Western Europe are contributing to availability problems which undermine public health. Slovakia, Czech Republic and Romania are proposing measures to address medicines shortages caused by parallel exports: if a medicine is at risk of experiencing medicines shortages, distributors will have to notify the relevant authorities which will decide whether the medicine can be exported.

¹⁶ Article 81 of Directive 2001/83/EC: EU legislation that imposes legal obligation for the marketing authorisation holder to ensure, within the limits of their responsibilities, a continuous supply.

Recommendations to mitigate shortages

Specific regulatory measures to mitigate imminent shortage

Medicines for Europe encourages the enforcement of already existing regulatory measures to mitigate medicines shortages when they occur.

Such measures would serve two main purposes, namely to allow the concerned manufacturer to resume its activities in compliance with regulatory requirements within a reasonably short timeframe and to encourage other manufacturers producing a therapeutically equivalent medicine to rapidly supply the market.

Mitigating the potential impact of medicines shortages through regulatory discretion measures could consist of various elements such as e.g. in the context of a potential supply disruption, flexibility to accept different pack sizes on national level based on decentralised procedure Marketing Authorisation, harmonisation of pack sizes requirements across EU, incentives for medically essential low cost medicines (e.g. lower variation fees/flat fee). Furthermore, incentives to authorise alternative API supplier(s), simplified way of reporting variations, provide re-packaging flexibility to MAH to address shortages and efficient Repeat Use Procedure would be relevant measures to tackle medicines shortages. These measures are consistent with Medicines for Europe's plea for all possible efficiency gains in the EU regulatory system as outlined in the 42 recommendations of its Regulatory Efficiency report¹⁷.

Beyond regulatory mitigation measures, a more fundamental reflection is needed in order to design a new model aimed at balancing maintenance and regulatory fees for essential medicinal products with limited-to-no commercial attractiveness, and where two or less manufacturers supply the market (higher risk of supply disruption).

Manage available market stock information

In 2019, a European Medicines Verification System (EMVS) will be in place which could support authorities and manufacturers to better manage supply through the management of the information available in the EMVS. We believe that this system constitutes an opportunity to increase transparency in supply chain for supply chain actors, enabling better management of production and supply.

Currently manufacturers have a legal obligation to notify to 28 different competent authorities of supply disruption due to manufacturing and quality issues. Therefore, Medicines for Europe recommends the use of this system as a European harmonised reporting standard of medicines shortages throughout the supply chain. Despite the importance of having in place a proper and controlled communication system, we believe that the notification and aim of the supply chain actors to tackle medicines shortages should not be punished by exorbitant and disproportionate penalties.

¹⁷ http://www.medicinesforeurope.com/wp-content/uploads/2016/03/EGA_Regulatory_Efficiency_Report_2015_low.pdf

Conclusions

In conclusion, Medicines for Europe considers that continuous availability of medicines is a patient-centric shared concern and responsibility of payers, regulators and all supply chain actors. Medicines for Europe believes that preventing and mitigating shortages requires addressing economic causes of shortages, improving regulatory efficiency, more transparency in supply chain and proper and controlled communication.

Medicines for Europe

Medicines for Europe represents the generic, biosimilar and value added medicines industries across Europe. Its vision is to provide sustainable access to high quality medicines for Europe, based on 5 important pillars: patients, quality, value, sustainability and partnership. Its members employ 160,000 people at over 350 manufacturing and R&D sites in Europe, and invest up to 17% of their turnover in medical innovation.

Gemeinsame Position der Pharmaverbände zu Lieferengpässen

Auf einen Blick

Pharmazeutische Unternehmer haben höchstes Interesse an einer nachhaltigen Liefersicherheit. Sie folgen damit einerseits ihrer Verpflichtung, Patienten mit den von ihnen benötigten Arzneimitteln versorgen zu können. Andererseits schlägt jede Lieferunfähigkeit nicht nur mit Umsatz- und Absatzverlusten zu Buche, sondern es bestehen erhebliche Risiken von Strafzahlungen (Vertragsstrafen, Schadenersatz). Hinzu kommt die Gefahr eines Imageschadens.

Lieferengpässe – Ursachen

- Verzögerungen bei der Lieferung eines Wirkstoffs durch den Zulieferer
- Qualitätsprobleme beim Wirkstoffhersteller oder bei der Arzneimittelherstellung
- Störungen oder Ausfälle einer Produktionsanlage, u.a. durch Maschinenschäden, Unfälle oder Brände
- Einschränkungen beim Produktionsvolumen durch größere Überholungsmaßnahmen der Ausrüstung oder durch Kapazitätserweiterung
- Naturkatastrophen wie Tsunamis, Wirbelstürme oder Erdbeben
- Steigende globale Nachfrage
- Unerwarteter Anstieg der Nachfrage, z.B. durch Lieferausfall eines Wettbewerbers oder eine Krankheitswelle
- In manchen Fällen: Parallelexport von Arzneimitteln aus Deutschland in andere EU-Länder

Es gibt viele Ursachen für Engpässe und daher auch keine einfachen Lösungen. Wenn politische Entscheidungen getroffen werden, sollten die vorgesehenen Maßnahmen darauf überprüft werden, ob diese wirklich geeignet sind, zu einer Lösung beizutragen; sie sollten auf jeden Fall den Kostendruck und damit das Problem nicht noch verschlimmern.

Lieferengpässe – Lösungsmöglichkeiten

Über die bereits bestehenden Maßnahmen hinaus:

- Berücksichtigung mehrerer Anbieter bei Rabattverträgen als Regel
- Stärkung des Pharmastandorts Europa durch bessere Honorierung von Herstellungsstätten mit hoher Produktions- und Lieferqualität
- Grundsätzlicher Verzicht auf Ausschreibungen bei versorgungskritischen Medikamenten
- Endgültige Abschaffung der Importförderklausel
- Exportverbot bei Medikamenten mit Lieferengpässen

Die Arzneimittelversorgung ist letztendlich eine Gemeinschaftsaufgabe. Hierbei müssen – im Interesse der Patienten – die Politik durch die Rahmenbedingungen, die Krankenkassen und Krankenhäuser mit ihren Einkaufsgemeinschaften durch ihre Einkaufspolitik und ihre Erstattungsregelungen, die pharmazeutischen Unternehmen durch eine vorausschauende Herstellung sowie Großhandel und Apotheker durch ein adäquates Lager- und Bestellverhalten zusammenwirken.

Ausführliche Positionierung

Die Arzneimittelversorgung in Deutschland ist (noch) gut

Für Patienten ist die Unterscheidung von großer Bedeutung, ob es sich um einen Lieferengpass handelt, der zeitlich vorübergehend ist und bei dem der Patient auf andere Art und Weise adäquat versorgt werden kann, oder ob es tatsächlich einen Versorgungsengpass gibt, bei dem kein vergleichbares Arzneimittel ersatzweise zur Verfügung steht. Diese Differenzierung muss in der Diskussion berücksichtigt werden, auch wenn jeder Wechsel eines Arzneimittels einen Mehraufwand für den Arzt, den Apotheker und den Patienten bedeuten kann.

Einigkeit besteht jedoch unter Experten darin, dass die Arzneimittelversorgung in Deutschland grundsätzlich gut ist, da Versorgungsengpässe selten auftreten. Patienten haben hierzulande einen schnellen Zugang zu innovativen Medikamenten, und für die Basisversorgung stehen von vielen Herstellern eine Vielzahl von nicht mehr Patent-geschützten Medikamenten zur Verfügung. Dies ist wichtig, da die Erfahrung zeigt, dass Anbieter- und Produktvielfalt ein probates Mittel gegen Versorgungsengpässe ist.

Daher sollte unbedingt darauf geachtet werden, dass diese Vielfalt erhalten bleibt.

Ursachen für Lieferengpässe

- Arzneimittel sind komplexe Produkte

Arzneimittel sind Waren besonderer Art, deren Entwicklung, Zulassung, Herstellung, Lagerung, Vertrieb und Überwachung einer hohen Regulierungsdichte und hohen Qualitätsstandards unterliegen. Dies gilt insbesondere für Arzneimittel, die, wie Impfstoffe, biotechnologisch oder wie Spritzen unter Sterilbedingungen hergestellt werden. Das erfordert komplexe Produktionsprozesse, für die spezielles Know-how und entsprechende Ressourcen benötigt werden. Nicht jeder Arzneimittelhersteller ist auf die Herstellung komplexer Arzneimittel wie Biopharmazeutika (gentechnisch hergestellte Arzneimittel) oder Zytostatika (Krebsmittel) spezialisiert. Und eine Produktion ist generell umso störanfälliger, je komplexer sie ist. Ein Beispiel hierfür sind Impfstoffe. Hinzu kommt, dass die Herstellung von Medikamenten ein zeitintensiver Prozess ist, der mehrere Monate, in Einzelfällen auch weit über ein Jahr dauert. Deshalb ist es nicht möglich, quasi auf Zuruf die Liefermenge zu erhöhen. Aufgrund dieser Komplexität der Herstellung sind auch die Ursachen für Lieferengpässe sehr vielfältig:

- Verzögerungen bei der Lieferung eines Wirkstoffs durch den Zulieferer oder Qualitätsprobleme beim Wirkstoffhersteller
- Qualitätsprobleme bei der Arzneimittelherstellung
- Störungen oder Ausfälle einer Produktionsanlage, u.a. durch Maschinenschäden, Unfälle oder Brände

- Einschränkungen beim Produktionsvolumen durch größere Überholungsmaßnahmen der Ausrüstung oder durch Erweiterung von deren Kapazität
- Naturkatastrophen im Produktionsland wie Tsunamis, Wirbelstürme oder Erdbeben
- Steigende globale Nachfrage
- Unerwarteter Anstieg der Nachfrage, z.B. durch den Lieferausfall eines Wettbewerbers
- In manchen Fällen: Parallelexport von Arzneimitteln von Deutschland in andere EU-Länder

Viele dieser Ursachen sind weder absehbar noch plan- oder kontrollierbar.

- Zunahme regulatorischer Anforderungen

In den letzten Jahren sind die regulatorischen Auflagen, die bei der Entwicklung, Zulassung, Herstellung, Lagerung, beim Import oder Vertrieb von Arzneimitteln strikt zu beachten sind, erheblich angestiegen. Immer neue regulatorische Anforderungen erhöhen jedoch auch die Kosten und Aufwendungen der pharmazeutischen Unternehmer für die Zulassung von Arzneimitteln, deren Aufrechterhaltung, die Herstellung und Vermarktung und die vielfältigen Maßnahmen zur Gewährleistung der Arzneimittelsicherheit.

Das führt z. B. im Bereich der Generika mit dazu, dass Unternehmen sich gezwungen sehen, fortlaufend zu überprüfen, ob die von ihnen für die Versorgung bereitgestellten Arzneimittel noch wirtschaftlich angeboten werden können. Denn das Wirtschaftlichkeitsgebot gilt nicht nur für die gesetzlichen Krankenkassen, sondern eben auch für die Unternehmen.

- Preis- und Rabattdruck

Preis- und Erstattungsregelungen für Arzneimittel tragen sowohl im ambulanten wie im Klinikbereich dazu bei, dass Arzneimittelhersteller bestimmte Arzneimittel oder Darreichungsformen nicht mehr anbieten können. Beispielsweise durch exklusive Rabattverträge zwischen Krankenkasse und Unternehmen werden andere Unternehmen für die betreffende Kasse faktisch einem Lieferstopp unterworfen. Diese versuchen dann, ihre Produktionsstätten mit der Herstellung anderer Arzneimittel auszulasten. Fällt nun eines der Rabattvertragsunternehmen aus, können die anderen den plötzlich eintretenden Mehrbedarf im Regelfall nicht decken. Gerade wenn Krankenkassen nur mit einem einzigen Hersteller Rabattverträge schließen, ist die Gefahr von Lieferengpässen hoch. Dies führt bei manchen Arzneimitteln zur Marktverengung, d.h. diese werden nur noch von wenigen Unternehmen angeboten. Je weniger Anbieter es jedoch für ein Arzneimittel oder auch einen Wirkstoff gibt, desto störanfälliger ist die Liefersicherheit. Seit vielen Jahren ist der Preis- und Rabattdruck auf Arzneimittel in Deutschland immer weiter gesteigert worden, wobei der Kostendruck im Bereich der Generika europaweit mit am höchsten ist.

- Steigende globale Nachfrage

Weltweit erhalten immer mehr Menschen Zugang zu Arzneimitteln. Dies ist in vollem Einklang mit Ziel 3 der Nachhaltigen Entwicklungsziele der Weltgesundheitsorganisation, Gesundes Leben für alle – ein gesundes Leben für alle Menschen jeden Alters zu gewährleisten und ihr Wohlergehen zu fördern.

Aus dieser an sich positiven Entwicklung leitet sich jedoch auch eine entsprechend stark steigende globale Nachfrage nach Arzneimitteln und ihren Wirkstoffen ab. Mit diesem sprunghaften Nachfrage-Anstieg können aber der Bau neuer Produktionsstätten für Wirkstoffe und Arzneimittel und die erforderliche behördliche Freigabe dieser Herstellstätten zeitlich nicht immer Schritt halten.

- Umbau, Ausbau, Erweiterung von Produktionskapazitäten

Arzneimittel- und Wirkstoffhersteller arbeiten weltweit an Erweiterungen der Produktionskapazitäten. Allerdings können vom Beginn der Arbeiten bis zur behördlichen Abnahme der Produktionsstätte bis zu fünf Jahre Zeit vergehen. Der Grund hierfür ist, dass Produktionsstätten für Arzneimittel und Wirkstoffe hohen Qualitätsstandards entsprechen müssen. Zudem können neue Produktionsanlagen erst nach erfolgreichem Probetrieb und der Freigabe durch die Überwachungsbehörde in Betrieb genommen werden. Bei der inzwischen üblichen globalen Arzneimittelproduktion erfolgt diese Freigabe nicht nur von einer Behörde, sondern – je nachdem wie viele Länder daraus beliefert werden – von mehreren. Auch dies trägt dazu bei, dass weitere Kapazitäten ihre Zeit brauchen.

Lösungsansätze für die Minimierung von Liefer-/ Versorgungsengpässen

Die Arzneimittelhersteller nehmen Arzneimittelengpässe sehr ernst. Daher wirken sie bei der Suche nach Lösungsansätzen aktiv mit, z.B. im Pharmadialog der Bundesregierung und in dem daraufhin eingerichteten Jour Fixe Lieferengpässe. Dort werden mehrmals jährlich mit allen Beteiligten Lieferprobleme diskutiert, bewertet und möglichst einer Lösung zugeführt. Bisher wurden insbesondere folgende Aktivitäten unternommen:

- Einrichtung eines Onlineregisters, das über Engpässe vorzugsweise bei solchen Arzneimitteln informiert, die bei schweren Krankheiten eingesetzt werden, und für die es keine Alternativpräparate gibt. Dieses Register ist seit dem 01. April 2013 auf der Website des BfArM für jedermann einsehbar. Das Register verbessert damit die Transparenz über Engpässe und soll Ärzte, Apotheker und Kliniken in die Lage versetzen, sich auf solche Engpässe einzustellen.
Basis dieser Meldungen ist folgende Definition eines Lieferengpasses in Deutschland: Ein Lieferengpass ist eine über voraussichtlich 2 Wochen hinausgehende Unterbrechung einer Auslieferung im üblichen Umfang oder eine deutlich vermehrte Nachfrage, der nicht angemessen nachgekommen

werden kann. Weiterhin wurden Listen von Wirkstoffen erarbeitet, für die Hersteller im Rahmen ihrer Selbstverpflichtung Lieferengpässe melden. Für Krankenhausware hat der Gesetzgeber im Mai 2017 eine gesetzliche Meldepflicht für Lieferengpässe eingeführt.

- Proaktives Management von Lieferengpässen in enger Abstimmung zwischen Hersteller sowie Bundes- und Landesbehörden; dadurch ist es z.B. möglich, durch rasche Genehmigung von Importen aus Drittländern die Dauer eines Liefer- oder Versorgungsengpasses zu verkürzen.
- Erarbeitung und Verabschiedung von „Empfehlungen des Jour Fixe zu Liefer- und Versorgungsengpässen zur Vertragsgestaltung zwischen Betreibern von Krankenhausapotheken / krankenhausversorgenden Apotheken und pharmazeutischen Unternehmen mit dem Ziel einer Verbesserung der Lieferfähigkeit versorgungsrelevanter Arzneimittel in Kliniken“ vom 11. Juli 2019¹. Diese sehen z.B. vor, dass vereinbarte Mengen auch wirklich abgenommen werden, und ein erweiterter Lagerbestand oder die Zusagen für eine erhöhte Liefersicherheit von dem Vertragspartner auch vergütet wird.

Es wird ein kontinuierliches Monitoring der Umsetzung dieser Empfehlungen erfolgen, um die Effekte nachzuvollziehen, die sich aus der Anwendung der Empfehlung ergeben, und um Hinweise zu Optimierungspotentialen zu identifizieren. Mit konkreten Ergebnissen kann aber erst in mehreren Jahren gerechnet werden.

Weitere Maßnahmen gegen Arzneimittellieferengpässe:

Neben den genannten Bereichen muss der Pharmastandort Europa wieder attraktiver werden, und die Regelungen im Bereich der Erstattung gehören auf den Prüfstand. Das gilt für den ambulanten Bereich mit den dort üblichen Rabattverträgen, die zu einer Marktverengung beitragen.

Das gilt aber auch für die in Deutschland geltende Importförderklausel, die Lieferengpässe in anderen EU-Ländern befördert. Positiv ist, dass für Krebsmittel zum Spritzen und für Biologika die Importförderklausel nicht mehr Anwendung finden soll. Im nächsten Schritt sollte die Importförderklausel aber grundsätzlich abgeschafft werden. Und die ersten Krankenkassen haben begonnen, bei ihren Ausschreibungen für Rabattarzneimittel mehrere Anbieter zu berücksichtigen. Damit kommen sie der im Sommer 2019 eingeführten gesetzlichen Aufforderung nach, die Vielfalt der Anbieter und die Sicherstellung einer bedarfsgerechten Versorgung der Versicherten zu berücksichtigen.

Sollte diese Aufforderung nicht umfassend umgesetzt werden, sollte dieser Passus im Sinne einer gesetzlichen Regelung für die Mehrfachvergabe bei Rabattverträgen

¹ https://www.bfarm.de/DE/Arzneimittel/Arzneimittelzulassung/Arzneimittelinformationen/Lieferengpaesse/jourfixe/_node.html

präzisiert werden. Zudem sollte bei versorgungskritischen Arzneimitteln grundsätzlich auf Ausschreibungen verzichtet werden. Anbietervielfalt mit ausreichenden Produktions- und Lagerkapazitäten bieten nämlich beim Ausfall eines Anbieters die Möglichkeit, auf andere Bieter zurückgreifen zu können, und damit die Voraussetzung für eine Stabilisierung der Lieferketten:

Die Arzneimittelversorgung ist letztendlich eine Gemeinschaftsaufgabe. Hierbei müssen – im Interesse der Patienten – die Politik durch die Rahmenbedingungen, die Krankenkassen und Krankenhäuser mit ihren Einkaufsgemeinschaften durch ihre Einkaufspolitik und ihre Erstattungsregelungen, die pharmazeutischen Unternehmen durch eine vorausschauende Herstellung sowie Großhandel und Apotheker durch ein adäquates Lager- und Bestellverhalten zusammenwirken.

Stand: 13.12. 2019

PGEU SURVEY ON MEDICINE SHORTAGES 2019

Pharmaceutical Group of the European Union [PGEU]



PGEU Medicine Shortages Survey 2019 Results

Each year PGEU conducts a survey among their membership to map the impact of medicine shortages across Europe from the community pharmacists' perspective.

The 2019 Survey was open to all [PGEU member organisations](#) and has been conducted between 4 November – 16 December 2019.

24 PGEU members (1 response per country) provided their responses to the survey coming from the following countries:

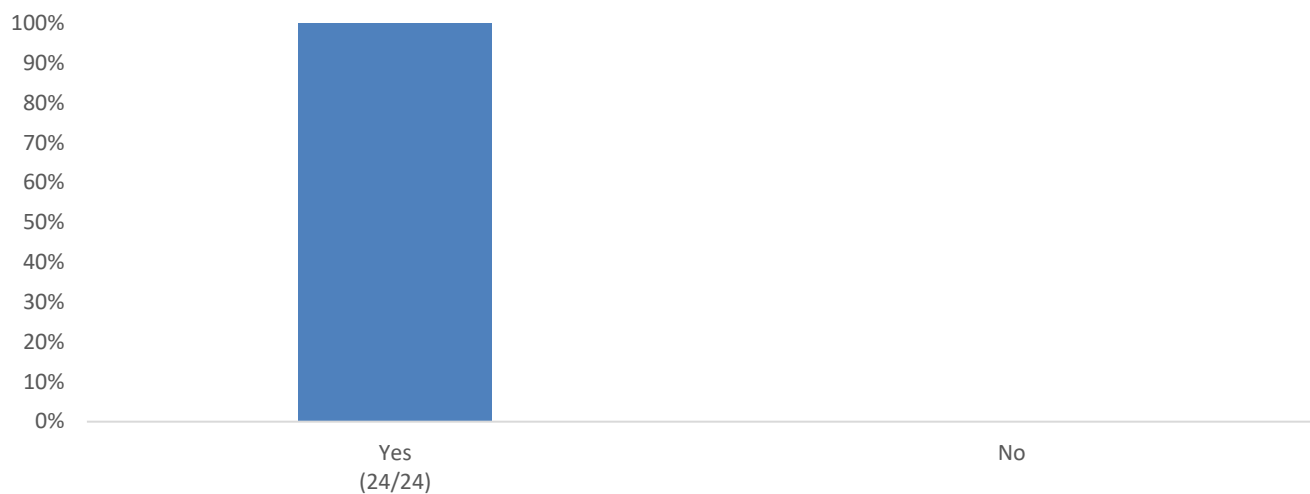
Austria	Cyprus	Germany	Latvia	Poland	Slovenia
Belgium	Czech Republic	Greece	Malta	Portugal	Spain
Bulgaria	Denmark	Ireland	Netherlands	Romania	Sweden
Croatia	France	Italy	Norway	Slovak Republic	United Kingdom

For the purpose of this survey, the term “medicine shortage” was defined as *every (temporally) inability for a community or hospital pharmacy to supply patients with the medicinal product requested as a result of factors beyond their control, requiring the dispensing of an alternative agent or even discontinuation of an ongoing medical therapy*. In terms of reporting/notification of medicine shortages, respondents were asked to apply their national definition if available.

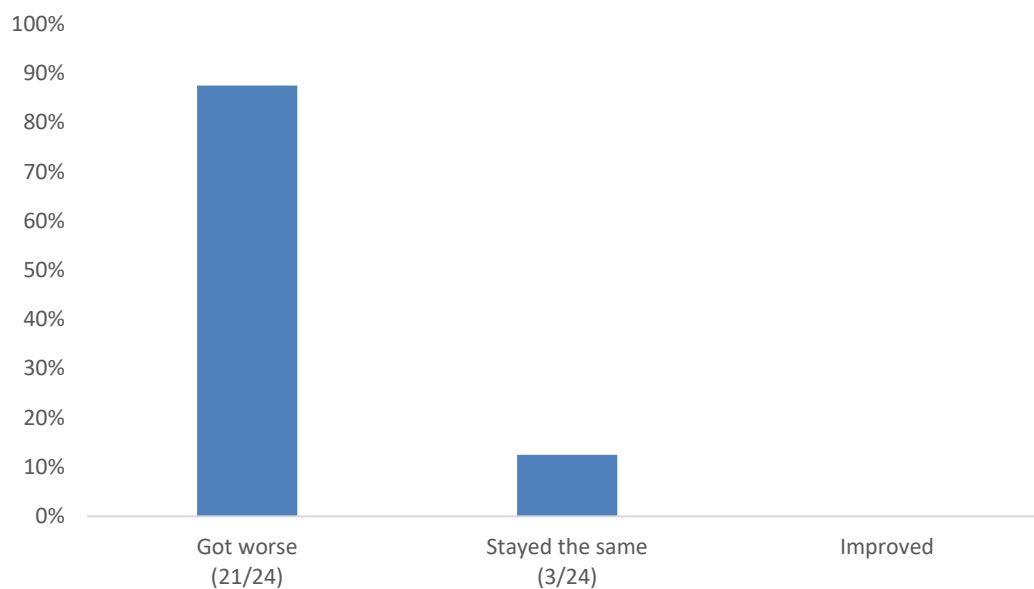
Among the key findings of the survey are:

- The high incidence and ongoing rise of the number of medicine shortages in most European countries;
- The daily and burdensome impact of medicine shortages on patients and pharmacy practice across Europe;
- The existing gap in needed information, tools and legal solutions available to community pharmacists in many European countries for providing solutions to patients in case of a shortage.

1. In the last 12 months, have you experienced medicines shortages in your country?
(% of responding countries)

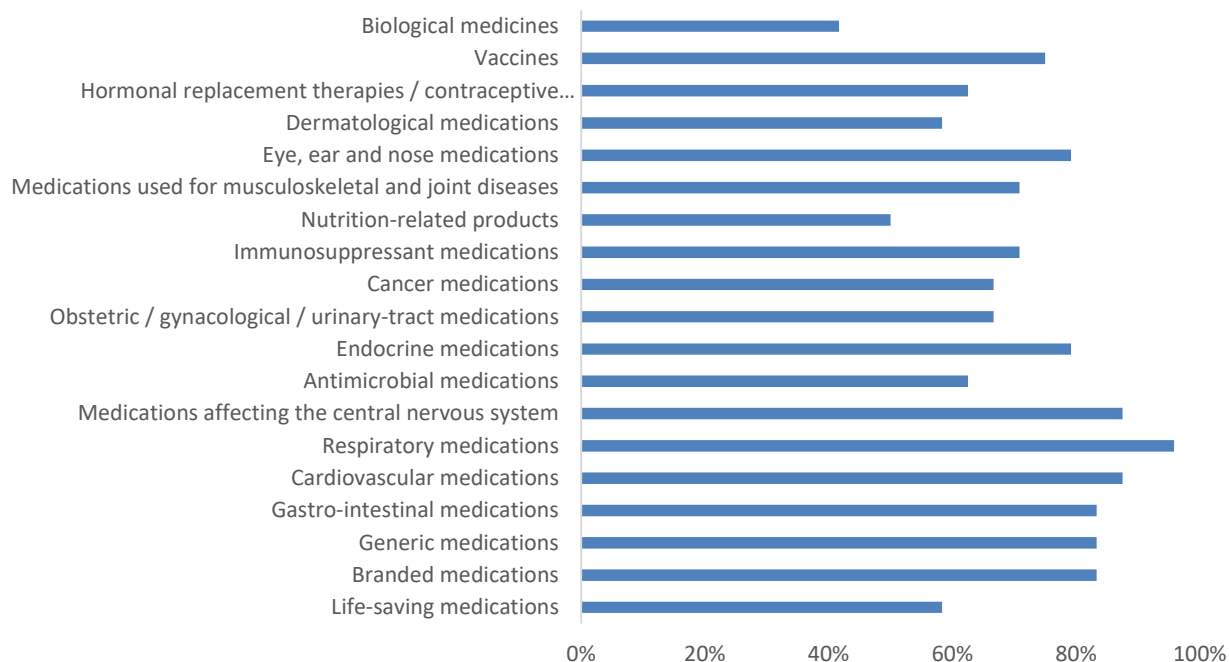


2. If yes, compared to the previous 12 months, the situation has:
(% of responding countries)



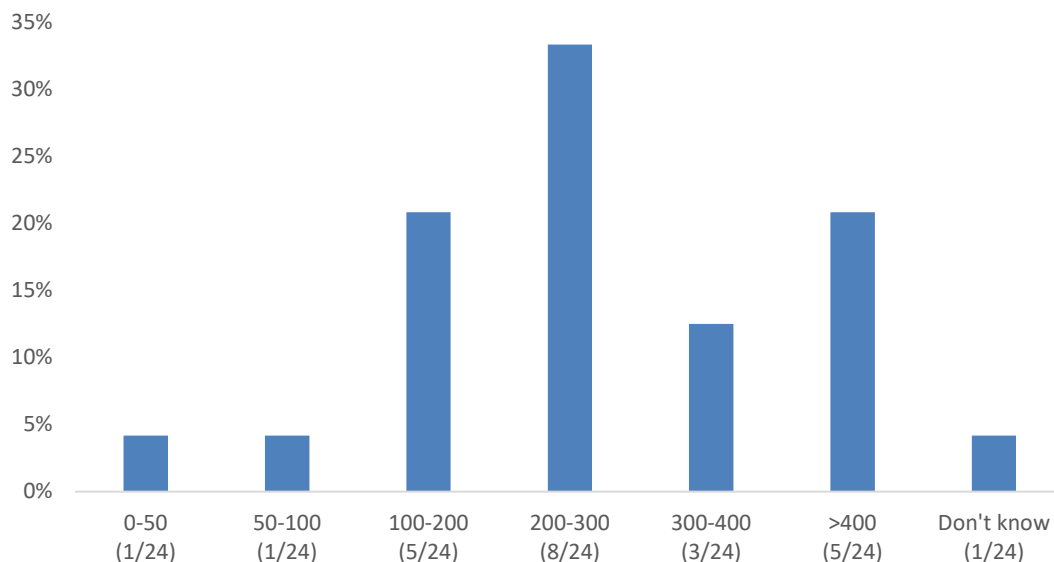
3. If yes, which medicines have been in short supply?

Tick all that apply (% of responding countries)



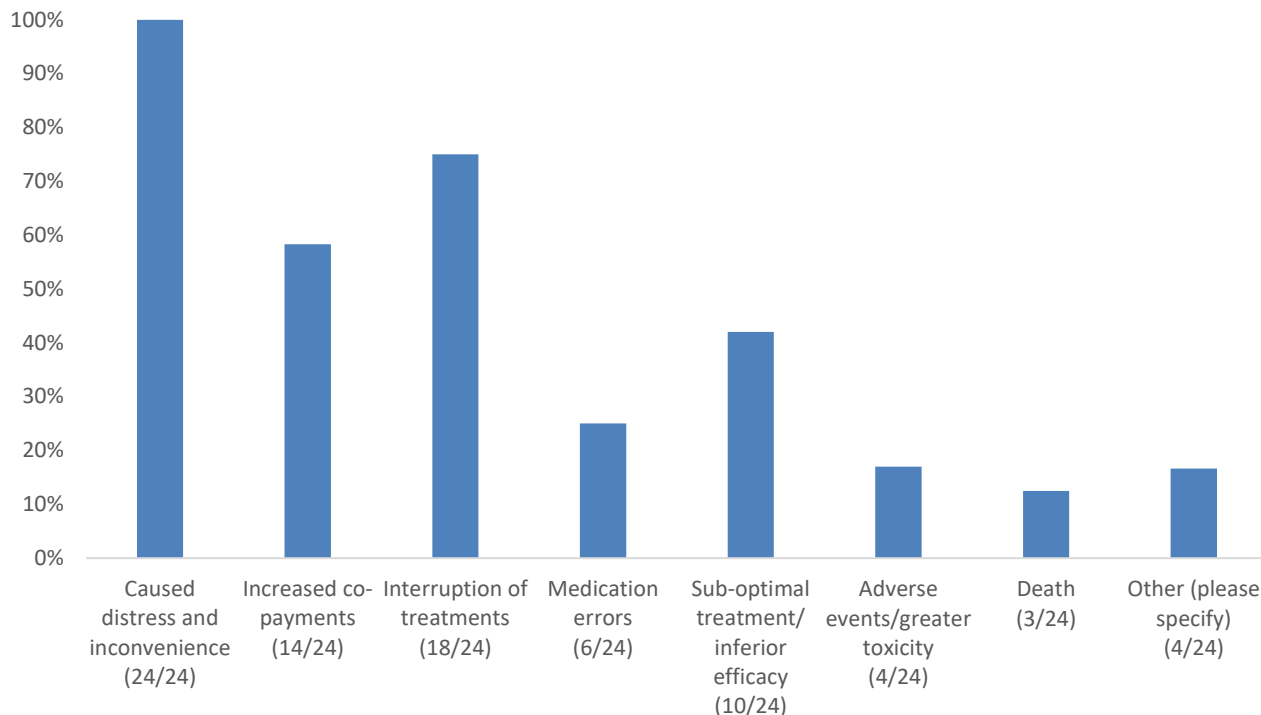
4. How many medicines are short in supply at the time of completing this survey?¹

(% of responding countries)



¹ The quantification takes into account the national definition of a medicine shortages in each responding country, which can show differences between them. The comparison of these numbers should therefore be interpreted as an indication rather than exact comparison.

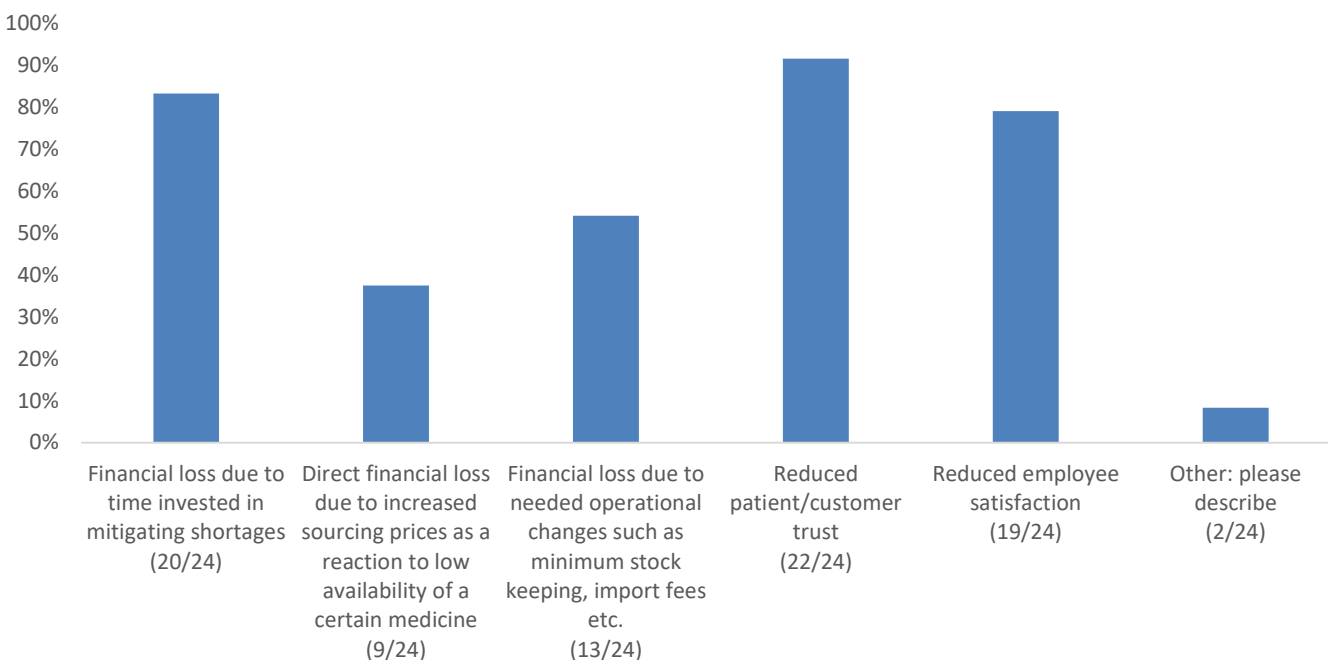
5. In your opinion, how have medicines shortages adversely affected patients in your country? Tick all that apply (% of responding countries)



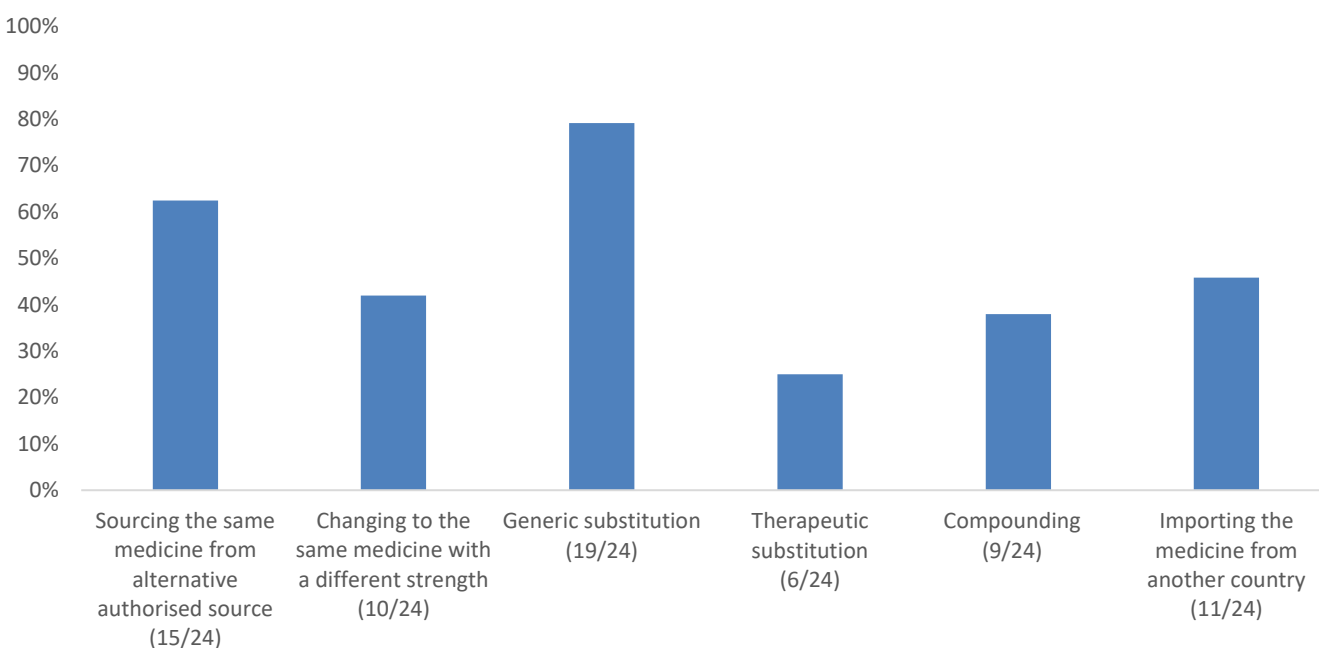
Comments received:

- **Belgium:** It is hard to prove or measure what the consequences of actual shortages have been in recent years on patients. However, it is obvious that the burden on pharmacists and patients became more and more problematic. It is probable that continued and unpredictable shortage of essential medicines such as diuretics and anticoagulants have caused destabilization in compromised patients, hospital admissions and likely also early deaths in a limited number of complex and severely compromised patients.
- **Bulgaria:** In Bulgaria, pharmacists are not permitted to provide substitutes for medicines and the patient should make a visit to a GP for a new prescription.
- **France:** Increased payments as a result of new basic medical consultation to change therapy due to medicines unavailability.
- **Spain:** Some medicines have to be imported from an EU country when it is not available. Once the medicine is received, patients should go to approved establishments by the Spanish Autonomous communities to pick up their medication. This situation have a sheer impact on patients in terms of access to medicines and time invested by the patient.

6. In your opinion, how have medicines shortages affected community pharmacies in your country? Tick all that apply (% of responding countries)



7. Which solutions can legally be offered by pharmacists in case of a shortage Tick all that apply (% of responding countries)



7. Comments:

- Austria: Generic Substitution is not allowed in Austria
- Belgium: Sourcing the medicines from other pharmacies systematically is not permitted. It is accepted in urgencies of exceptional circumstances such as shortages.
- Bulgaria: None from listed above options. In Bulgaria pharmacists are not permitted to provide substitutes for medicines in short supply.
- Germany: Most of the above mentioned solutions may only be offered in correspondence to the prescriber and potential amendments to the prescription.
- Greece: Importing through the Institute of Pharmaceutical Research and Technology.
- Slovenia: Patients seek medicine in another country and get reimbursed by the insurance. Therapeutic substitution is possible, but only by the prescriber.
- Spain: In Spain only approved establishments by the Spanish Autonomous communities are allowed to dispense medications imported from European countries when the substitution or switching by the pharmacist / prescriber is not possible. At this point it is important to highlight that there are some kind of medications whose substitution is not permitted, such as those medicines with a narrow therapeutic index or inhaled therapy in respiratory diseases (see Order SCO / 2874/2007, of September 28th)
- Sweden: Importing medicines are made after a special approval for a non-licensed medicine by the Swedish Medical Product Agency. Preparing compounded formulation is only permitted if there are no other alternatives. The formulation is normally made by special pharmacies as APL (<https://www.apl.se/in-english.html>) specialised in ex tempore preparations.
- United Kingdom: We now have the serious shortage protocol set in legislation, which will be utilised through the Department of Health in instances of a serious shortage of a specific named product. These protocols are fixed with a start and end date. So far, the UK has had two protocols in place.



PGEU GPUE

Pharmaceutical Group of European Union
Groupement Pharmaceutique de l'Union Européenne

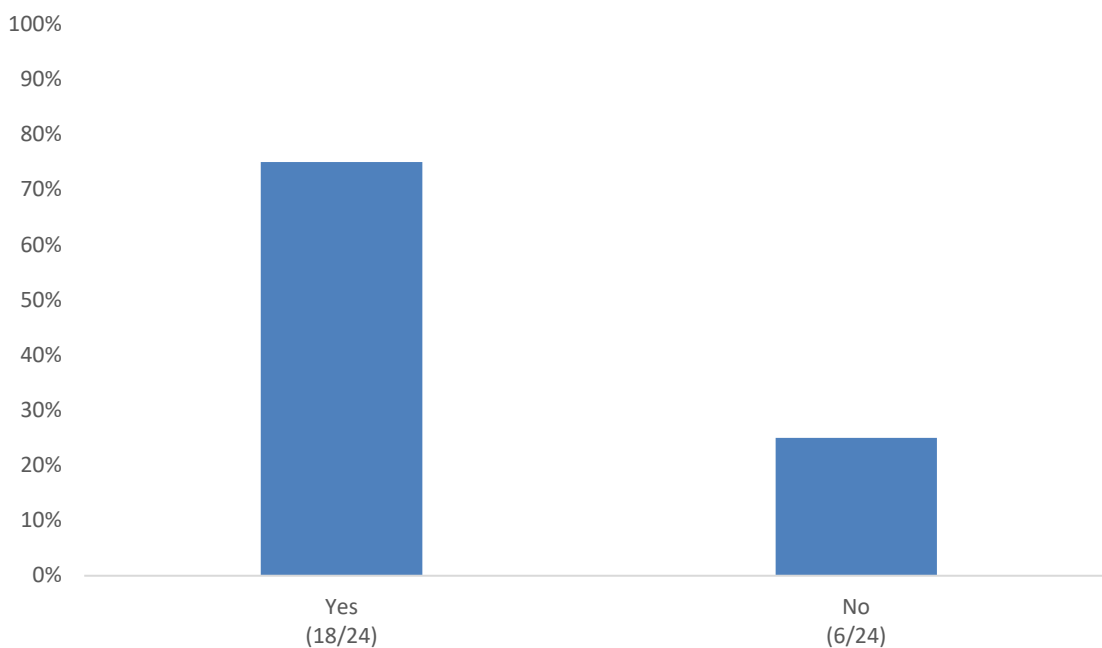
8. On average, per week, how much time does pharmacy staff spend dealing with medicine shortages?



6,6 hours/week on average

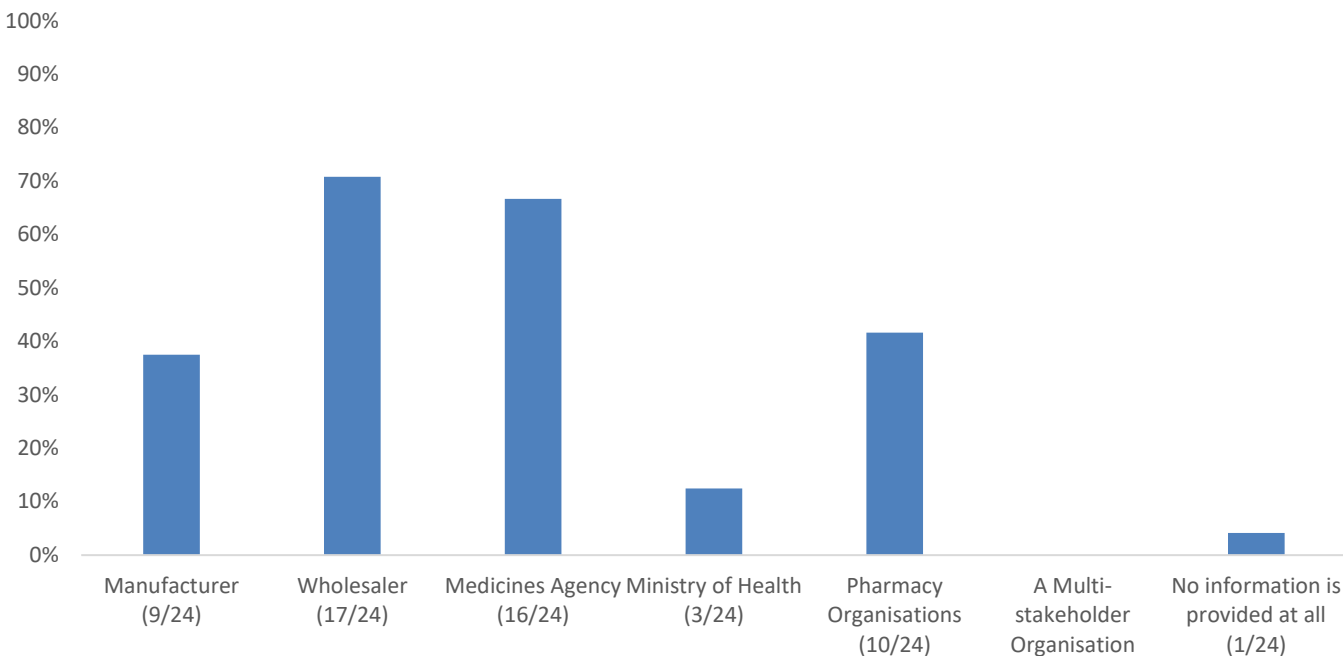
(Answers ranged from 2 hours/week to 15 hours/week)

9. Does your country have a reporting system for shortages in place which can be used by community pharmacists?
(% of countries)



10. Who provides data / information on medicines shortages to pharmacists in your country?

Tick all that apply (% of countries)



Comments:

- Poland: There is no legal obligation to provide public information about shortages. In crisis situation information is provided by different parties.
- Portugal:
 - a) Manufacturers are obliged to notify INFARMED (regulator) on the cause and estimated length of production problems
 - b) Pharmacies report to ANF (daily), on a voluntary basis, information regarding the medicine (name, strength, pharmaceutical form), package and price, name of the market authorization holder, name of the supplier (wholesaler) and number of units in shortage. The registry of shortages is undertaken during the verification of the orders received from the wholesalers in the Pharmacy. The pharmacy software generates a file which is sent by e-mails to the IT department of ANF. The report produced is shared with Authorities on a monthly basis
 - c) Pharmacies must notify all medicines on shortage to INFARMED; the Portuguese Medicines Agency, automatically through a webservice. Wholesalers should notify shortages to an email address from INFARMED, while the webservice is being developed.
- Romania: Although this information is provided to the authority, the information doesn't reach the pharmacy on a regular basis or systematically. In most cases it is transmitted locally by one pharmacy to another, or by wholesalers when you place an order.

MAIN FINDINGS

- **All responding countries experienced medicine shortages** in community pharmacies in the past 12 months, and in the vast majority (87%) of countries respondents indicated that the situation got worse compared to 2018.
- **All classes of medicines are affected by medicine shortages** in community pharmacies across the different responding European countries. **Respiratory medications** have been short in supply in the highest percentage of countries (87%) whilst **biological medicines** have been short in supply in the lowest percentage of countries (42%).
- In the majority of responding countries (67%), **over 200 medicines** were listed as in short supply at the time of completing this survey, with 5 countries indicating that there were even **more than 400 medicines** short in supply.
- **All responding countries** indicated that they believe medicine shortages cause **distress and inconvenience** to patients. **Interruption of treatments** (75% of countries), **increased co-payments** as a result of more expensive/non-reimbursed alternatives (58%) and **suboptimal treatment/inferior efficacy** (42%) are also perceived as negative consequences of medicine shortages on patients.
- Medicine shortages are believed to affect community pharmacy businesses in most countries by **reduced patient trust** (92% of countries), **financial loss** due to time invested in mitigating shortages (82%) and **reduced employee satisfaction** (79%).
- Across European countries, **strong differences** exist in terms of **legal solutions** community pharmacists can offer in case of a shortages. **Generic substitution** (79 % of countries), **sourcing the same medicine from alternative authorised sources** (such as other pharmacies) (63%), and **importing the medicine** from a country where it is available (46%) are the solutions which can be provided in most of the European countries. However, some of these solutions are subject to restrictions (e.g. new prescription is needed) and can be cumbersome and time-consuming for the patient and the pharmacist.
- The time pharmacy staff has to spend on dealing with medicine shortages has increased from 5,6 hours per week (2018) to **6,6 hours per week** on average.
- **25%** of responding countries indicated that there is still **no reporting system for shortages** in place which can be used by community pharmacists in their country, despite that pharmacists often experience or foresee supply difficulties before the industry or wholesalers are aware that there is, or will be, a problem.
- Community pharmacists receive their **needed information** on shortages in most countries from **wholesalers** (71%), **medicines agencies** (67%) and **pharmacy organisations** (42%).

[spiegel.de](https://www.spiegel.de)

Coronavirus könnte deutsche Arzneimittel-Versorgung gefährden - DER SPIEGEL - Wirtschaft

Martin U. Müller, DER SPIEGEL

4 Minuten

Wirkstoffe aus China Coronavirus könnte Arznei-Versorgung in Deutschland gefährden

Die Region um Wuhan ist weitgehend isoliert, um die Welt vor der Ausbreitung des Coronavirus zu schützen. Gerade das aber könnte jetzt die Gesundheit von Patienten auch in Europa in Gefahr bringen.

04.02.2020, 20.30 Uhr



Tabletten (Symbolfoto)

Foto: Gudrun Senger/ Gudrun Senger/photothek.net

Das Coronavirus könnte zu Engpässen im deutschen Arzneimittelmarkt führen. Grund ist die massive Abhängigkeit Deutschlands von Wirkstoffproduzenten in Asien – ein Großteil davon sitzt in [China](#), manche davon auch in der besonders betroffenen Provinz Hubei.

Zwar liegen der zuständigen Aufsichtsbehörde, dem Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), mit Stand Dienstagabend keine Hinweise vor, dass es aufgrund des [Coronavirus](#) zu kurzfristigen Liefer- oder Versorgungsengpässen kommen werde.

Doch im Hintergrund befürchten Experten, dass das bald eintreten könnte. Eine Recherche des BfArM habe ergeben, dass für 19 Arzneimittel ein Wirkstoffhersteller in der Stadt Wuhan, dem Epizentrum des Corona-Virus, gemeldet sei, heißt es in einer internen Nachricht des Bundesverbands der [Pharmazeutischen Industrie](#). 17 der Wirkstoffe seien versorgungsrelevant. Aufgrund des Ausbruchs des Coronavirus könne nicht ausgeschlossen werden, dass es zum Beispiel durch Zwangsferien, Quarantänen und Unterbrechungen von Lieferwegen zu Lieferengpässen von Arzneimitteln kommen könne.

Hinzu kommt: Etliche Rohstoffe für Medikamente werden in der chinesischen Provinz Zhejiang, relativ weit von Wuhan entfernt, hergestellt. Je schneller und weiter sich das Virus ausbreitet, desto größer ist die Gefahr, dass sich die Lieferengpässe, die bereits vor dem Ausbruch des aktuellen Coronavirus die Gesundheit vieler deutscher Patienten gefährdeten, noch ausweiten.

[Deutschland hängt am Tropf von Schwellenländern wie China,](#)

wenn es um die Versorgung mit lebenswichtigen Arzneimitteln

geht. Einst nannte sich die Bundesrepublik "Apotheke der Welt" – heute steht ein Großteil der Fabriken, in denen die Grundsubstanzen für Medikamente hergestellt werden, in China oder Indien. Die meisten Wirkstoffe – so genannte kleine Moleküle – sind nicht besonders schwer zu produzieren. Sie machen einen Großteil aller Arzneimittel aus, darunter fallen Blutdrucksenker, Schmerzmittel, Antibiotika oder Herzmedikamente genauso wie Antidepressiva, Chemotherapien und Betäubungsmittel. Sie werden fast ausschließlich außerhalb der Europäischen Union produziert.

Das BfArM stehe in engem Austausch mit der Europäischen Arzneimittelagentur und habe auch den Jour Fixe zu Liefer- und Versorgungsengpässen aktiv eingebunden, um belastbare Informationen zu erhalten, teilt ein Sprecher mit. "Sollten sich Hinweise auf eine Nichtverfügbarkeit von Arzneimitteln durch den Ausbruch des Coronavirus ergeben, wird das BfArM diese umgehend und in geeigneter Form kommunizieren", so der Sprecher.

S

Mangelware Medizin?

Corona, China und der Arzneimittelmarkt - Film von Michael Mueller



Eine drohende Corona-Pandemie könnte zu großen Engpässen von lebensnotwendigen Medikamenten führen. Was lässt sich in Deutschland gegen Pillennotstand tun?

28 min | 26.03.2020 | UT

Video verfügbar bis 24.03.2021

Mehr von ZDFzoom

Hintergründe zum Coronavirus

Politik und Gesellschaft

Coronavirus bleibt gefährlich

[Thema](#)

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Verbraucher | Volle Kanne

Corona-Gipfel: Was sind jetzt die Regeln?

Politik | Frontal 21

Wettkampf um Corona-Impfstoff

Verbraucher | Volle Kanne

Corona-Update September

Seit Jahren steigt die Zahl der nicht lieferbaren Medikamente, werden wir abhängiger von Produzenten in China oder Indien. "ZDFzoom"-Reporter Michael Mueller über Lieferengpässe und den Preiskampf auf dem deutschen Arzneimittelmarkt.

Deutschland war als Produktionsstandort von Arzneimitteln einmal die sogenannte Apotheke der Welt. Heute herrscht in deutschen Apotheken Mangel. Mehr als 250 Lieferengpässe für Medikamente listet das Bundesinstitut für Arzneimittel und Medizinprodukte im Durchschnitt auf. Und das erfasst nur die Lieferschwierigkeiten, die von den Pharmaunternehmen gemeldet werden. Im Zentrum der Auseinandersetzung stehen der Preiskampf auf dem deutschen Arzneimittelmarkt zwischen Krankenkassen und Pharmaindustrie. Und in Folge die Abhängigkeit von Billiglohnländern wie China und Indien. "Die Chinesen brauchen gar keine Atombombe. Sie liefern einfach keine Antibiotika mehr", so Pharmazeutin Prof. Ulrike Holzgrabe.

In aktuellen Krisen wie dem Ausbruch des neuartigen Coronavirus verschärft sich die Lage auf dem deutschen und europäischen Arzneimittelmarkt, vor allem für die Pharmakonzerne, die von der Wirkstoffproduktion in Asien abhängig sind. Es gibt zum Beispiel heute in Europa fast keine Antibiotika-Produktion mehr. Wenn "wie jetzt aufgrund des Coronavirus die Lieferwege gestört sind, dann hat das unmittelbare Konsequenzen", sagt Christoph Stoller, Generalmanager von Teva/ratiopharm in Deutschland und Österreich. Und dann werden aus Lieferengpässen irgendwann Versorgungsengpässe.

Die Politik hat das Problem zwar erkannt, so will Gesundheitsminister Jens Spahn eine Meldepflicht für drohende Lieferengpässe einführen und die Unternehmen im Notfall dazu zwingen, größere Vorräte anzulegen. Aber die Lösung scheint komplizierter: Anlässlich der aktuellen globalen Krise beraten Gesundheitsminister und Experten in Brüssel jetzt, was zu tun ist. Mittel- und langfristig kann man der Abhängigkeit von Billiglohnländern nur begegnen, wenn wieder mehr Wirkstoff-Produktionen nach Europa geholt werden. Doch das "wird mindestens zehn Jahre dauern, zehn Jahre von heute an, wenn wir es jetzt beschließen", sagt Pharma-Expertin Prof. Ulrike Holzgrabe. Es braucht einen Paradigmenwechsel im Gesundheitssystem, weg vom Preisdruck auf die Medizin. Das aber wird langwierig und teuer für alle Beteiligten.

- Kamera - Oliver Biebl, Paul Kraneis

Auch interessant

Comedy | heute-show

heute-show vom 9. Oktober 2020

Nachrichten | Politik

Wie die Welt gegen das Coronavirus kämpft

Serien | Ingo Thiel

Die Spur der Mörder

Filme | Tonio & Julia

Dem Himmel so nah

Serien | Katie Ford

Eine Liebe in Deutschland

nach oben



May 17, 2019

RE: Request to start an investigation into the factors leading to medicines shortages

Dear Commissioner Andriukaitis, dear Ms Bucher,

Recent studies, such as the 2018 Medicines Shortages Survey of the European Association of Hospital Pharmacists (EAHP)¹ and an investigation by France Assos Santé into the recurring difficulties of access to certain vaccines and medicines by French citizens², have shown that the problems caused by medicines shortages all across the European Union continue to accumulate. The undersigned associations are extremely concerned by this development, in particular since the quality and safety of care is significantly affected. Patients are at risk of suffering deterioration in their health status if they cannot receive their prescribed medicines in a timely manner. Simultaneously, the amount of time that different healthcare professionals are able to spend with patients is reduced by the increased necessity of investing more and more working hours into the management of shortages.

As representatives of organisations of patients, consumers, healthcare professionals and public health advocates, we consider that the mandate of the European Commission to assist in alleviating medicines shortage problems includes, but also goes beyond, facilitating best practice-sharing. Given that medicines shortages are impacting patient care in all Member States, a strong EU commitment under the leadership of the European Commission is needed to contain the problems and ensure remedy, as acknowledged by the European Commission itself in its contribution to the informal

¹ http://www.eahp.eu/sites/default/files/report_medicines_shortages2018.pdf

² https://www.france-assos-sante.org/communiqué_presse/enquete-csa-pour-fas-les-francais-veulent-une-europe-plus-forte-et-plus-protectrice-en-matiere-de-sante/

EU27 leaders' meeting in Sibiu (Romania) on 9 May 2019³. Such engagement should be carried out in coherent addition to the efforts by the joint task force of the Heads of Medicines Agencies and the European Medicines Agency on the availability of authorised medicines for human and veterinary use.

The undersigned associations request the European Commission to **start an investigation into the factors leading to medicines shortages** to provide clear and transparent information on the root causes of these problems, including on responsible entities and affected population groups, to healthcare professionals, patients and the general public. Further evidence on EU's medicines shortage crisis should also inform the planning of the activities of the Directorate General for Health and Food Safety during the next legislative period.

We, the undersigned associations, solicit a meeting at your earliest convenience to further discuss this investigation request.

Yours sincerely,

Signatory organisations (in alphabetical order)

- AFA – Crohn RCH France
- AFH – Association française des hémophiles
- AGE Platform Europe
- AIDES
- Altroconsumo
- Amalyste
- APAA - Autoimmune Diseases Patient Association Romania
- ARAS – Asociatia Romana Anti-Sida
- ASPLA - Asociatia Prietenii lui Adrian
- BAPD – Bulgarian Association for Patients' Defense
- CHV – Collectif Hépatites Virales
- DECO PROTESTE
- EAHP – European Association of Hospital Pharmacists
- EAP – European Academy of Paediatrics
- EATG – European AIDS Treatment Group
- ECL Access to Medicines Task Force
- EFCCA – European Federation of Crohn's & Ulcerative Colitis Association
- EHC – European Haemophilia Consortium
- EIWH – European Institute of Women's Health
- EKPIZO - Consumers' Association "The Quality of Life"
- EPHA – European Public Health Alliance
- Épilepsie France
- France Assos Santé
- France Lymphome Espoir
- Give Life Foundation
- HAI – Health Action International
- OCU - Organización de Consumidores y Usuarios
- ORS – Romanian Health Observatory
- Prescrire
- Test Achats
- TRT-5

Contact information :

Charlotte Roffiaen (France Assos Santé): europa@france-assos-sante.org

Stephanie Kohl (European Association of Hospital Pharmacists): stephanie.kohl@eahp.eu

³ Europe in May 2019: Preparing for a more united, stronger and more democratic Union in an increasingly uncertain world (p.33).



September 2, 2019

RE: Proposal of public hearing and own initiative report on medicines shortages in the EU

Dear MEP Pascal Canfin,

Recent studies, such as the 2018 Medicines Shortages Survey of the European Association of Hospital Pharmacists (EAHP)¹ and an investigation by France Assos Santé into the recurring difficulties of access to vaccines and medicines by French citizens² have shown that medicines shortages have increased dramatically all across the European Union. In France, the number of reported shortages increased 20-fold between 2008 and 2018³ and it is predicted to reach 1200 medicines and vaccines in 2019⁴. In Belgium, 497 drugs - 5 % of the medicines marketed in the country - are not available⁵. More and more patients are suffering deterioration in their health status as they cannot receive their prescribed medicines in a timely manner, creating a serious public health threat in Europe.

Concerns were raised by over 30 organisations representing patients, consumers, healthcare professionals and public health advocates in a letter addressed to the European Commission in May, in which the organisations asked for an investigation into the factors leading to shortages. Recently, other organisations also highlighted the problems caused by medicines shortages and called the EU for action, including the European Society for Medical Oncology (ESMO)⁶ and the Pharmaceutical Group of the European Union (PGEU)⁷.

¹ http://www.eahp.eu/sites/default/files/report_medicines_shortages2018.pdf

² https://www.france-assos-sante.org/communiqu%C3%A9_presse/enquete-csa-pour-fas-les-fran%C3%A7ais-veulent-une-europe-plus-forte-et-plus-protectrice-en-mati%C3%A8re-de-sant%C3%A9/

³ <https://solidarites-sante.gouv.fr/actualites/presse/communiqu%C3%A9s-de-presse/article/lutter-contre-les-penuries-et-am%C3%A9liorer-la-disponibilit%C3%A9-des-m%C3%A9dicaments-en>

⁴ https://www.france-assos-sante.org/communiqu%C3%A9_presse/penuries-de-m%C3%A9dicaments-la-situation-saggrave/

⁵ <https://plus.lesoir.be/236531/article/2019-07-15/la-penurie-de-m%C3%A9dicaments-atteint-des-sommet>

⁶ <https://www.esmo.org/content/download/197306/3552860/file/ESMO-Shortages-of-Inexpensive-Essential-Medicines-Call-to-Action.pdf>

⁷ <https://www.pgeu.eu/wp-content/uploads/2019/03/190514E-PGEU-Position-Paper-on-Medicine-Shortages.pdf>

Given that medicines shortages are impacting patient care in all Member States, a strong EU commitment is very much needed, as outlined by European Commission itself in its contribution to the informal EU27 leaders' meeting in Sibiu (Romania) on 9th May 2019⁸. The European Parliament could play a crucial role in underlining the urgency of the problem and making it a political priority of the European Union's 2019-2024 legislature. Consequently, we propose to the ENVI Committee **to organise a public hearing and to submit an own initiative report on shortages in the EU.**

We, the undersigned associations, solicit a meeting at your earliest convenience to further discuss this request.

Yours sincerely,

Signatory organisations (in alphabetical order)

- AFH – Association française des hémophiles
- AFSA – Association Française du syndrome d'Angelman
- AFTOC – Association Française de Personnes Souffrant de Troubles Obsessionnels et Compulsifs
- AGE Platform Europe
- AIDES
- AIM – International Association of Mutual Benefit Societies
- Altroconsumo
- APAA – Autoimmune Diseases Patient Association Romania
- ARAS – Asociatia Romana Anti-Sida
- ASPLA – Asociatia Prietenii lui Adrian
- BEUC – The European Consumer Organisation
- CLVC – Association nationale de défense des consommateurs et usagers
- DECO PROTESTE
- EAHP – European Association of Hospital Pharmacists
- EAP – European Academy of Paediatrics
- EATG – European AIDS Treatment Group
- ECCO – European CanCer Organisation
- ECL Access to Medicines Task Force
- EFAPPE – Fédération des Associations de personnes handicapées par des épilepsies sévères
- EFCCA – European Federation of Crohn's & Ulcerative Colitis Association
- EHC – European Haemophilia Consortium
- EPHA – European Public Health Alliance
- Épilepsie-France
- France Assos Santé
- France Lymphome Espoir
- France Parkinson
- Give Life Foundation
- HAI – Health Action International
- La Ligue contre le cancer
- La LUSS
- Le Lien
- OCU - Organización de Consumidores y Usuarios
- ORS – Romanian Health Observatory
- Prescrire
- Renaloo
- SOS-Hépatites
- Test Achats | Test Ankoop
- TRT-5 | CHV – Collectif Hépatites Virales
- UFC-Que Choisir
- UNAPECLE – Union des Associations de Parents d'Enfants atteints de Cancer ou Leucémie
- Vlaams Patiëntenplatform

Contact information :

Charlotte Roffiaen (France Assos Santé): europa@france-assos-sante.org

Stephanie Kohl (European Association of Hospital Pharmacists): stephanie.kohl@eahp.eu

⁸ Europe in May 2019: Preparing for a more united, stronger and more democratic Union in an increasingly uncertain world (p.33).



Essential medicines and health products

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Access to essential medicines as part of the right to health

Access to essential medicines as part of the right to the highest attainable standard of health ("the right to health") is well-founded in international law. The right to health first emerged as a social right in the World Health Organization (WHO) Constitution (1946)* and in the Universal Declaration of Human Rights (1948)*. The binding International Covenant on Economic, Social, and Cultural Rights (ICESCR) of 1966* details the progressive realization of the right to health through four concrete steps, including access to health facilities, goods and services.

The authoritative General Comment 14 (2000)* further applies the principles of accessibility, availability, appropriateness and assured quality to goods and services, which include essential medicines "as defined by the WHO Action Programme on Essential Drugs".

Access to medical products and technologies as part of the right to health recognized in countries constitutions or national legislation is the first country progress indicator for Strategic Objective 11 (Improved access, quality and use of medical products and technologies) of the WHO Medium Term Strategic Plan for 2008-2013*.

[\(WHO\) Constitution \(1946\) \(pdf, 0.60kb\)](#)

[Universal Declaration of Human Rights \(1948\)](#)

[International Covenant on Economic, Social, and Cultural Rights \(ICESCR\) of 1966](#)

[General Comment 14 \(2000\)](#)

[WHO Medium Term Strategic Plan for 2008-2013](#)

WHO has done several studies on national constitutional commitments and legal enforcement of access to essential medicines as part of the right to health

- WHO articles and documents
- Original data collected by WHO
- WHO Human rights web site
- Reports by the UN Special Rapporteur
- References and other links

Meetings & events



- 69th INN Consultation on International Nonproprietary Names (INN) for Pharmaceutical Substances 22-25 October 2019
- 19th International Conference of Drug Regulatory Authorities (ICDRA) New Delhi - India

Training resources



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2020

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IMPRESSUM

PATIENTENVERSORGUNG IM ÜBERBLICK

Die Apotheken haben den gesetzlichen Auftrag, die Arzneimittelversorgung der Bevölkerung sicherzustellen. Dies betrifft jede einzelne Apotheke, aber auch die flächendeckende Verteilung aller Apotheken in ganz Deutschland. Neben der Versorgung mit Fertigarzneimitteln erfüllen Apotheken auch Gemeinwohlpflichten, wie z. B. den Nacht- und Notdienst oder die Anfertigung von Rezepturen.

19.075

öffentliche Apotheken versorgen die Menschen in Deutschland mit Arzneimitteln.

1 Mrd.

Patientenkontakte pro Jahr haben öffentliche Apotheken.

3,3 Mio.

Patienten werden täglich versorgt in öffentlichen Apotheken.

300.000

Botendienste werden täglich durchgeführt.

6 Mio.

industriell hergestellte Arzneimittel werden jährlich von Apothekern geprüft.

88 %

der Patienten, die regelmäßig drei oder mehr Arzneimittel einnehmen, haben eine Stammapotheke.

83 %

der Bundesbürger haben Vertrauen zu ihrem Apotheker.

93 %

der Bundesbürger sind mit den Apotheken vor Ort entweder zufrieden oder sogar sehr zufrieden.

NACHT- UND NOTDIENST

Der Nacht- und Notdienst ist eine der wichtigsten Gemeinwohlpflichten der Apotheken. Jede Apotheke wird dazu von ihrer Landesapothekerkammer nach Bedarf in regelmäßigen Abständen eingeteilt. Apotheken erhalten für den Mehraufwand einen Zuschuss aus dem Notdienstfonds des Deutschen Apothekerverbandes, der sich aus einem Zuschlag auf die Abgabe eines jeden verschreibungspflichtigen Arzneimittels finanziert.* Der „Apothekenfinder 22 8 33“ ist ein Service für Patienten, um die nächstgelegene (Notdienst-) Apotheke schnell und unkompliziert zu finden.

Nacht- und Notdienste im Jahr 2019	460.000
davon Volldienste (20.00 Uhr bis 6.00 Uhr)	400.000
Teildienste	60.000
geöffnete Apotheken pro Nacht- und Notdienst	1.300
versorgte Patienten pro Nacht- und Notdienst	20.000

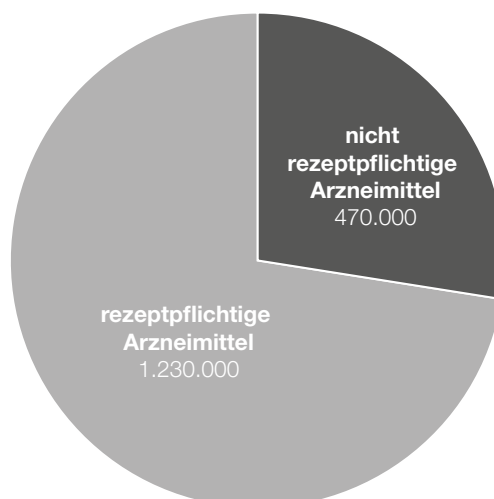
Apotheken müssen unterschiedlich häufig Notdienst leisten. Dies zeigt ein Beispiel aus dem Freistaat Bayern, einem Flächenland: Eine Apotheke im städtischen München hat 14 Mal Notdienst pro Jahr, im ländlicheren Rothenburg dagegen 70 Mal.

Rezepte ohne Notdienstgebühr für GKV-Versicherte 2019

In den Nacht- und Notdienst der Apotheken kommen viele Patienten wegen dringender Selbstmedikation (z. B. „Pille danach“) oder sie lösen Rezepte ein. Das können z. B. Privatrezepte oder rosa Rezepte zulasten der Gesetzlichen Krankenversicherung (GKV) sein. Hat ein notdiensthabender Arzt das Feld „noctu“ (lat. nachts) auf dem rosa Rezept angekreuzt, muss der Patient die ansonsten anfallende Notdienstgebühr von 2,50 Euro nicht selbst zahlen, sondern seine Krankenkasse übernimmt sie für ihn. Bei fast zwei Millionen Packungen wurden gesetzlich Versicherte im Jahr 2019 von dieser Gebühr befreit.

Insgesamt

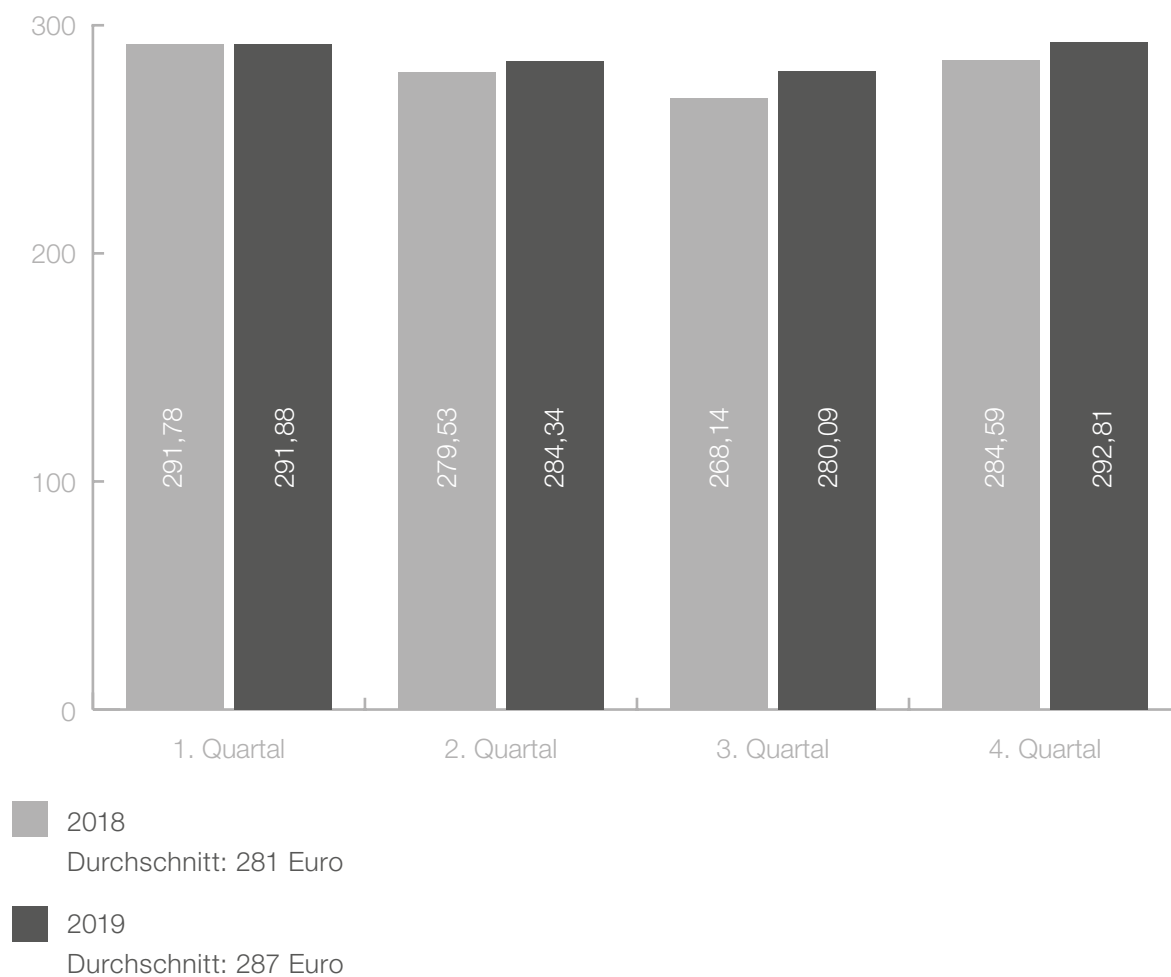
1.700.000 Packungen



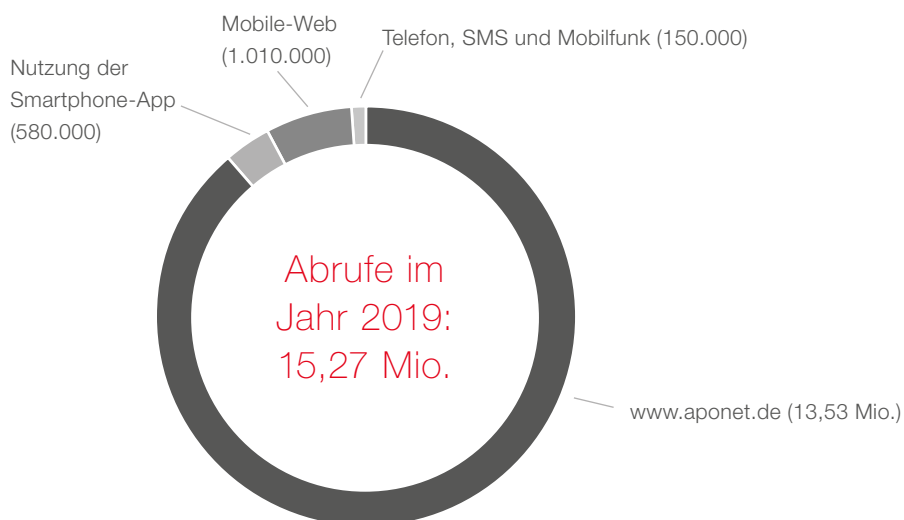
* Seit 1. Januar 2020 beträgt der Notdienstzuschlag zur Finanzierung der Notdienstpauschale statt bislang 16 nun 21 Cent pro rezeptpflichtigem Arzneimittel.

Quelle: Nacht- und Notdienstfonds, aponet.de, Deutsches Arzneiprüfungsinstitut e.V. (DAPI)

Notdienstpauschale pro geleistetem Volldienst in EUR



Apothekenfinder 22 8 33

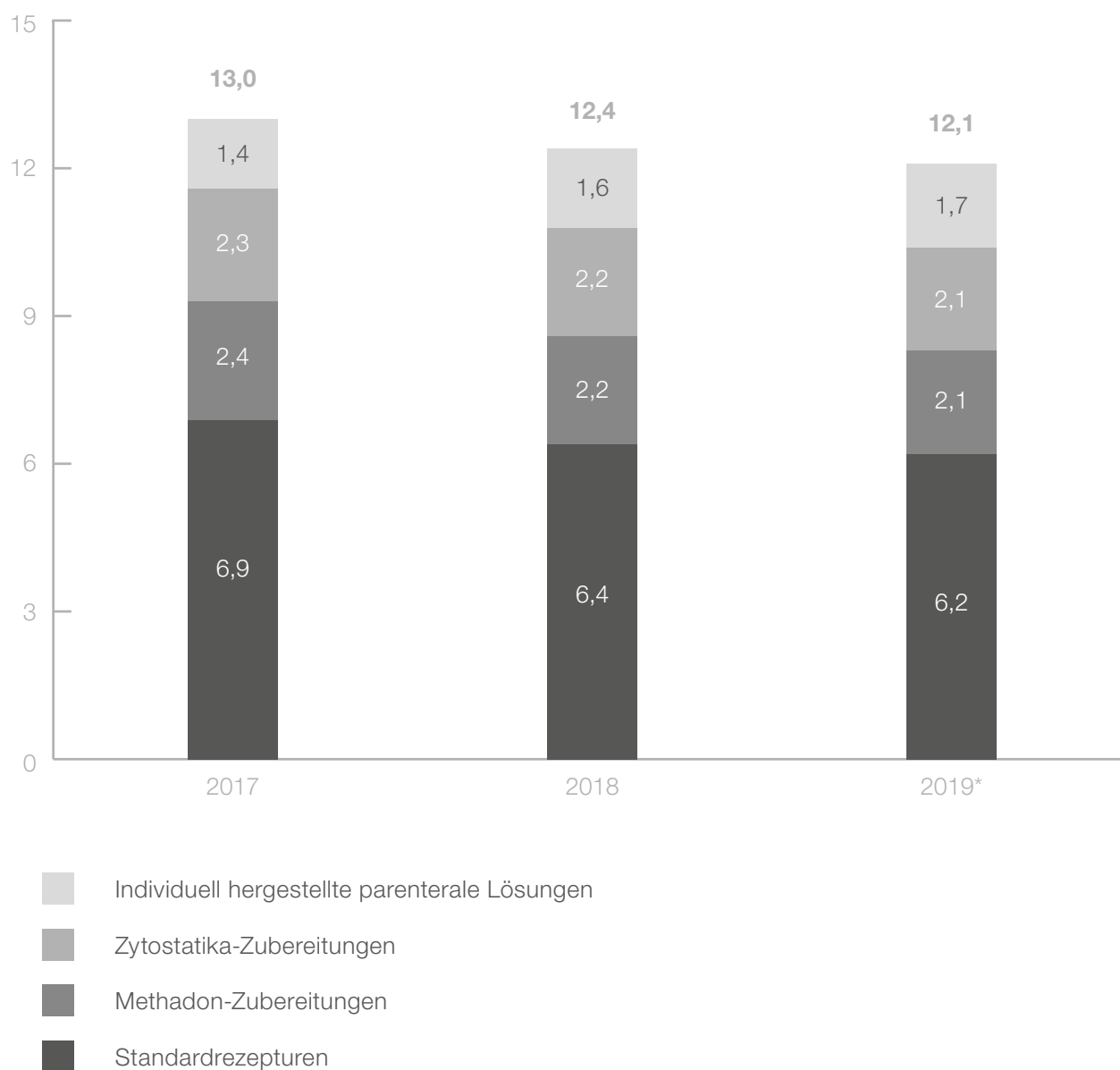


Quelle: aponet.de, Nacht- und Notdienstfonds

REZEPTUREN

In vielen Fällen gibt es für den spezifischen Arzneimittelbedarf eines Patienten kein Fertigarzneimittel. Apotheken schließen diese Lücke, indem sie auf ärztliche Verschreibung hin individuelle Rezepturen anfertigen. 2019 wurden für die Versicherten der Gesetzlichen Krankenversicherung (GKV) schätzungsweise rund 12 Millionen Rezepturen hergestellt.

in Mio.



* Prognose

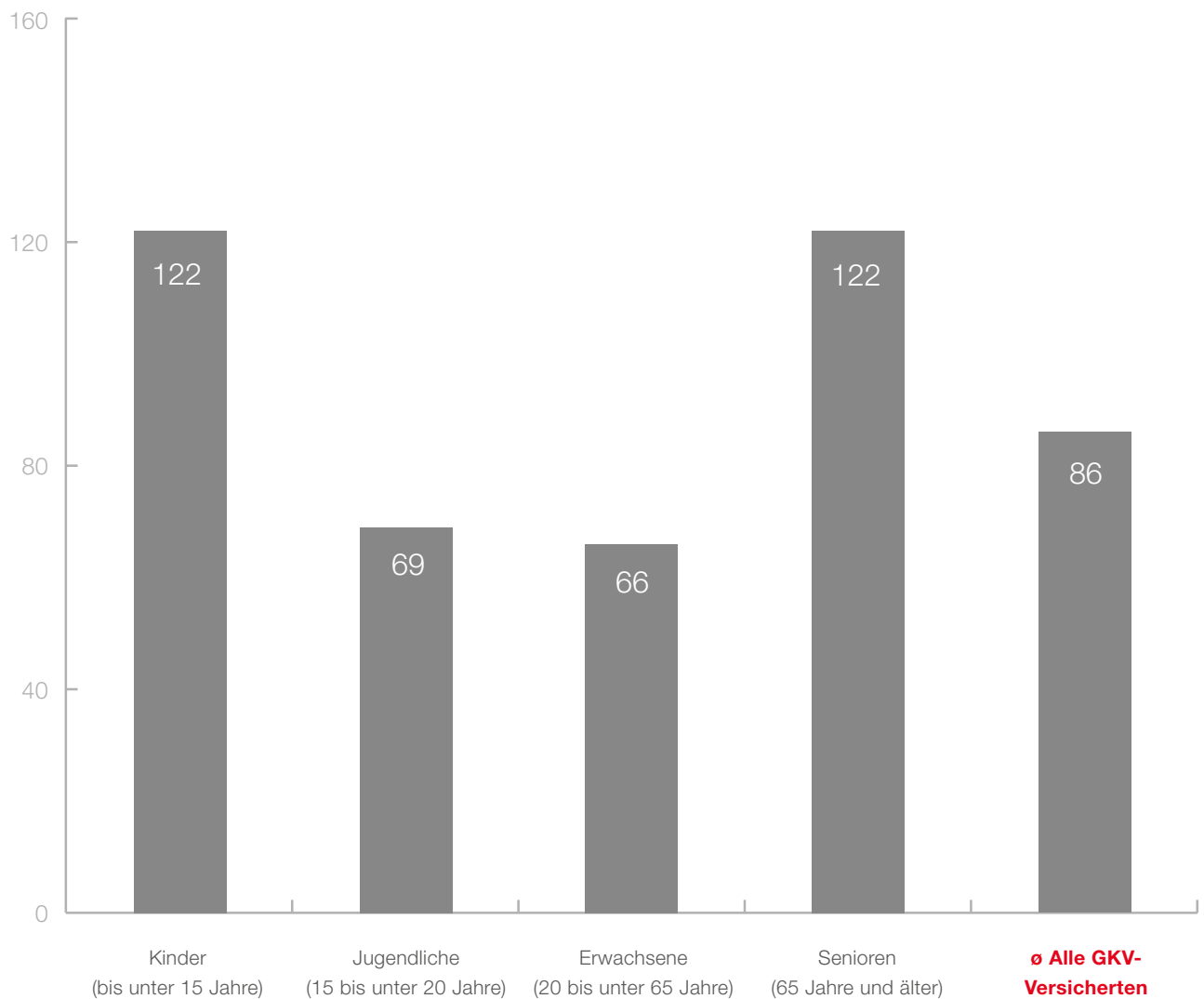
Quelle: Wissenschaftliches Institut der AOK (WiO), ABDA-Statistik

STANDARDREZEPTUREN

Über sechs Millionen Standardrezepturen für gesetzlich versicherte Patienten fertigen die Apotheken pro Jahr auf ärztliche Verordnung an. Ob Hautcreme oder Fieberzäpfchen – jede Apotheke kann sie patientenindividuell herstellen. Besonders viele Kinder profitieren davon, z. B. wenn ein Medikament in einer bestimmten Dosis nicht als Fertigarzneimittel verfügbar ist. Auch viele Senioren brauchen „Sonderanfertigungen“.

Standardrezepturen nach Altersgruppen

Anzahl je 1.000 GKV-Versicherte



Auswertung für das Jahr 2018

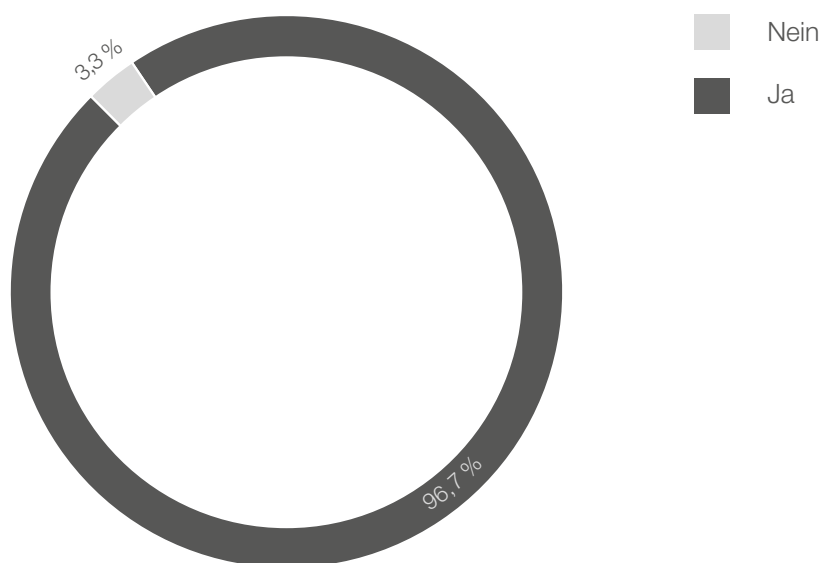
Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

BOTENDIENSTE

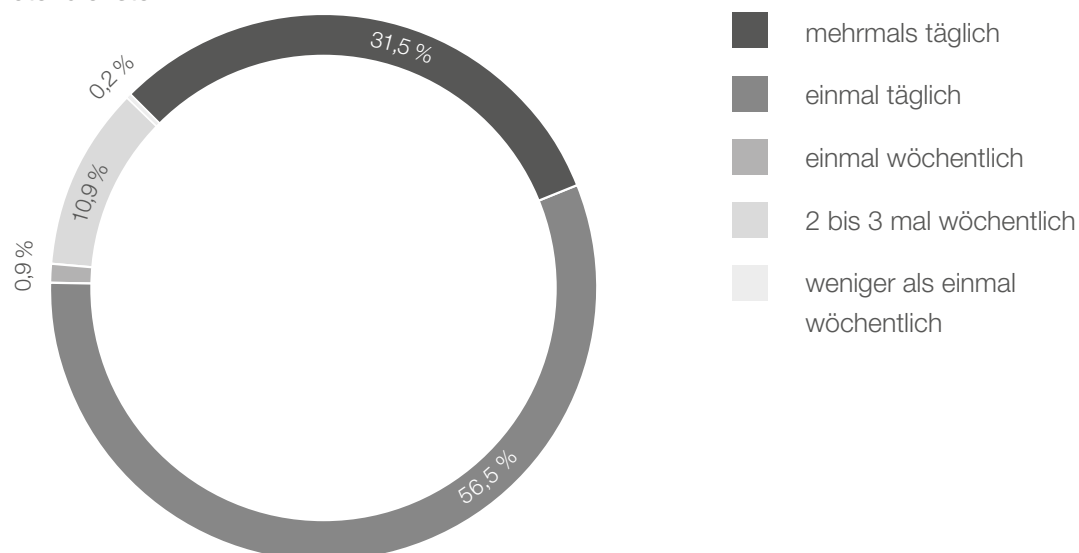
Fast alle Apotheken bieten insbesondere immobilen Patienten Botendienste an, um ihnen Wege zu ersparen. Diese Leistung wird ca. 300.000 mal täglich vom Apothekenpersonal erbracht. Die Beratung zum Arzneimittel erfolgt entweder vorab in der Apotheke, telefonisch oder begleitend durch pharmazeutisches Personal bei der Übergabe.

Angebot und Häufigkeit von Botendiensten

Anteil der Apotheken, die Botendienste anbieten



Häufigkeit der Botendienste



Anmerkung: repräsentative Befragung von öffentlichen Apotheken aus ABDA-Datenpanel 2018

Quelle: ABDA-Datenpanel

DIGITALE APOTHEKE

Langsam nimmt die Digitalisierung im Gesundheitswesen Fahrt auf. Apotheken haben aber früher als andere Akteure begonnen, Informationstechnologie (IT) für ihre tägliche Arbeit einzusetzen: von der Bestellung der Arzneimittel beim Großhandel und der Verwaltung der Lagerbestände über die Umsetzung von Rabattverträgen und die datenbankgestützte Prüfung von Neben- oder Wechselwirkungen von Medikamenten bis hin zur Abrechnung mit den Krankenkassen über die Rechenzentren. Inzwischen nimmt nun auch die Digitalisierung von Prozessen und Leistungen im Vorfeld der Apotheke an Fahrt auf – mit dem E-Rezept, dem E-Medikationsplan oder der E-Patientenakte. Ziel ist eine bessere Versorgung der Patienten.

15.270.000

mal pro Jahr suchen Patienten zumeist online im „Apothekenfinder 22 8 33“ die nächstgelegene Notdienstapotheke, deren Öffnungszeiten und Adressdetails dort aktuell hinterlegt sind.

14.000.000

Datensätze sind in der Apotheken-EDV hinterlegt, um Rabattverträge den Krankenkassen, Herstellern und Arzneimitteln zuzuordnen (Januar 2020).

6.200.000

mal pro Tag werden in den Apotheken Arzneimittel gescannt, um Arzneimittelfälschungen mithilfe eines Data-Matrix-Codes im securPharm-System auszuschließen.

1.000.000

Vertrags- und Präqualifizierungsprüfungen pro Woche nehmen die Apotheken auf dem Online-Vertragsportal (OVP) vor, um ihre Patienten mit Hilfsmitteln zu versorgen.

103.000

in Deutschland zugelassene Arzneimittel sind mittels Pharmazentralnummer (PZN) in der Apotheken-EDV abrufbar (Januar 2020).

18.800

verschiedene Arzneimittel (Pharmazentralnummern) sind von den Krankenkassen als Rabattarzneimittel gelistet (Januar 2020).

9.000

Abbildungen von Fertigarzneimitteln sind in der ABDA-Datenbank hinterlegt, damit die Arzneimittelsicherheit in den Apotheken verbessert wird.

74,1

Prozent der Apotheken halten ein elektronisches Medikamenten-Vorbestellsystem für sinnvoll.

3

Pilotprojekte zum elektronischen Rezept in Baden-Württemberg, Hessen und Berlin haben die Apotheker schon gestartet – in Berlin dient eine eigens entwickelte Web-App zum Einlösen des E-Rezepts.

EINSTELLUNG ZUM E-REZEPT

Für Apotheken ist die bevorstehende Einführung des E-Rezepts eine entscheidende Veränderung. Umfragen ergeben, dass die Haltung zum E-Rezept ambivalent ist. Vier von fünf Inhabern (81,8 Prozent) befürchten mehr Versandhandel durch das E-Rezept. Das elektronische Rezept soll das rosa Papierrezept ab 2022 ersetzen. Die technischen Standards dafür legt die gematik GmbH im Auftrag des Bundesministeriums für Gesundheit (BMG) fest.

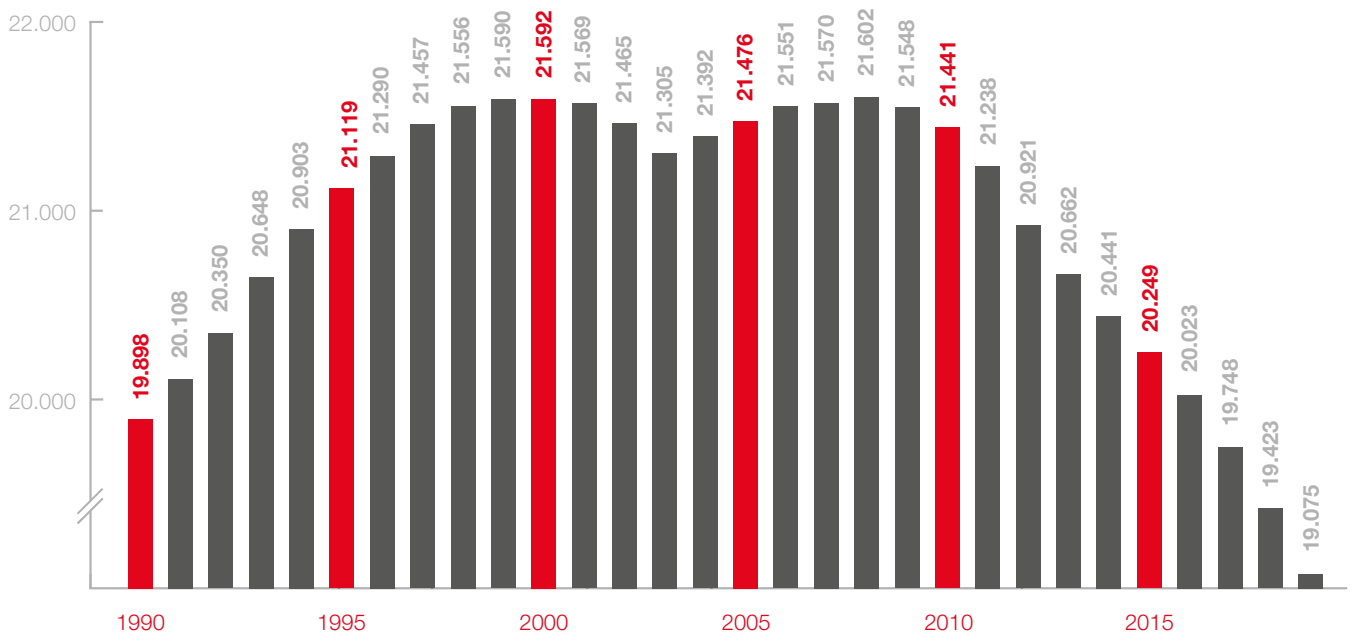
Welche Erwartungen verbinden Apothekeninhaber mit der Einführung des elektronischen Rezepts?

Mehr Versandhandel bei Arzneimitteln	81,8 %
Weniger Stammkundenbindung	49,4 %
Härterer Wettbewerb unter Offizinapotheken	46,8 %
Schnellerer und komfortablerer Arzneimittelbezug für Patienten	26,8 %
Weniger Rezeptfälschungen	23,2 %
Weniger Arztrücksprachen	18,4 %
Weniger Retaxationen von den Krankenkassen	15,0 %
Keine der genannten Erwartungen	5,0 %

ENTWICKLUNG DER APOTHEKENZAHL

Die Zahl der öffentlichen Apotheken in Deutschland sinkt seit 2009 und hat 2019 mit 19.075 den niedrigsten Stand seit Mitte der 1980er-Jahre erreicht. Zu den Ursachen gehören neben dem Wettbewerb der Apotheken untereinander auch die gesundheitspolitischen Rahmenbedingungen. Die flächendeckende Versorgung der Bevölkerung mit Arzneimitteln ist derzeit noch nicht gefährdet.

	1990	1995	2000	2005	2010	2015		2017	2018	2019
Apothekenzahl (inkl. Filialapotheken)	19.898	21.119	21.592	21.476	21.441	20.249		19.748	19.423	19.075
davon										
Haupt-/Einzel- apotheken*	19.898	21.119	21.592	20.248	17.963	15.968		15.236	14.882	14.473
Filialapotheken	—	—	—	1.228	3.478	4.281		4.512	4.541	4.602
Neueröffnungen	—	372	187	326	263	154		120	97	107
Schließungen	—	156	185	242	370	346		395	422	455
Apothekenentwicklung	—	+216	+2	+84	−107	−192		−275	−325	−348



Angaben jeweils Jahresende

* Apotheken mit Betriebserlaubnis nach § 2 Apothekengesetz

Quelle: ABDA-Statistik

APOTHEKENZAHL NACH BUNDESLÄNDERN

Die Zahl der Apotheken in den einzelnen Bundesländern hängt u. a. von der Einwohnerzahl, der Bevölkerungsstruktur und der Landesfläche ab. Das bevölkerungsreichste Bundesland Nordrhein-Westfalen, das in die beiden Kammerbezirke Nordrhein und Westfalen-Lippe aufgeteilt ist, weist mit mehr als 4.000 zugleich die höchste Zahl an Apotheken auf.

Bundesland	Öffentliche Apotheken		davon Haupt-/ Einzelapotheken *	davon Filialapotheken
	Anzahl	Apothekendichte **		
Baden-Württemberg	2.414	22	1.798	616
Bayern	3.073	23	2.345	728
Berlin	776	21	611	165
Brandenburg	569	23	416	153
Bremen	143	21	96	47
Hamburg	395	21	290	105
Hessen	1.454	23	1.101	353
Mecklenburg-Vorpommern	395	25	305	90
Niedersachsen	1.872	23	1.420	452
Nordrhein-Westfalen	4.019	22	3.054	965
Nordrhein	2.151	22	1.657	494
Westfalen-Lippe	1.868	23	1.397	471
Rheinland-Pfalz	964	24	746	218
Saarland	286	29	233	53
Sachsen	963	24	738	225
Sachsen-Anhalt	581	26	438	143
Schleswig-Holstein	636	22	483	153
Thüringen	535	25	399	136
Insgesamt	19.075	23	14.473	4.602

Angaben jeweils Jahresende 2019

* Apotheken mit Betriebserlaubnis nach §2 Apothekengesetz

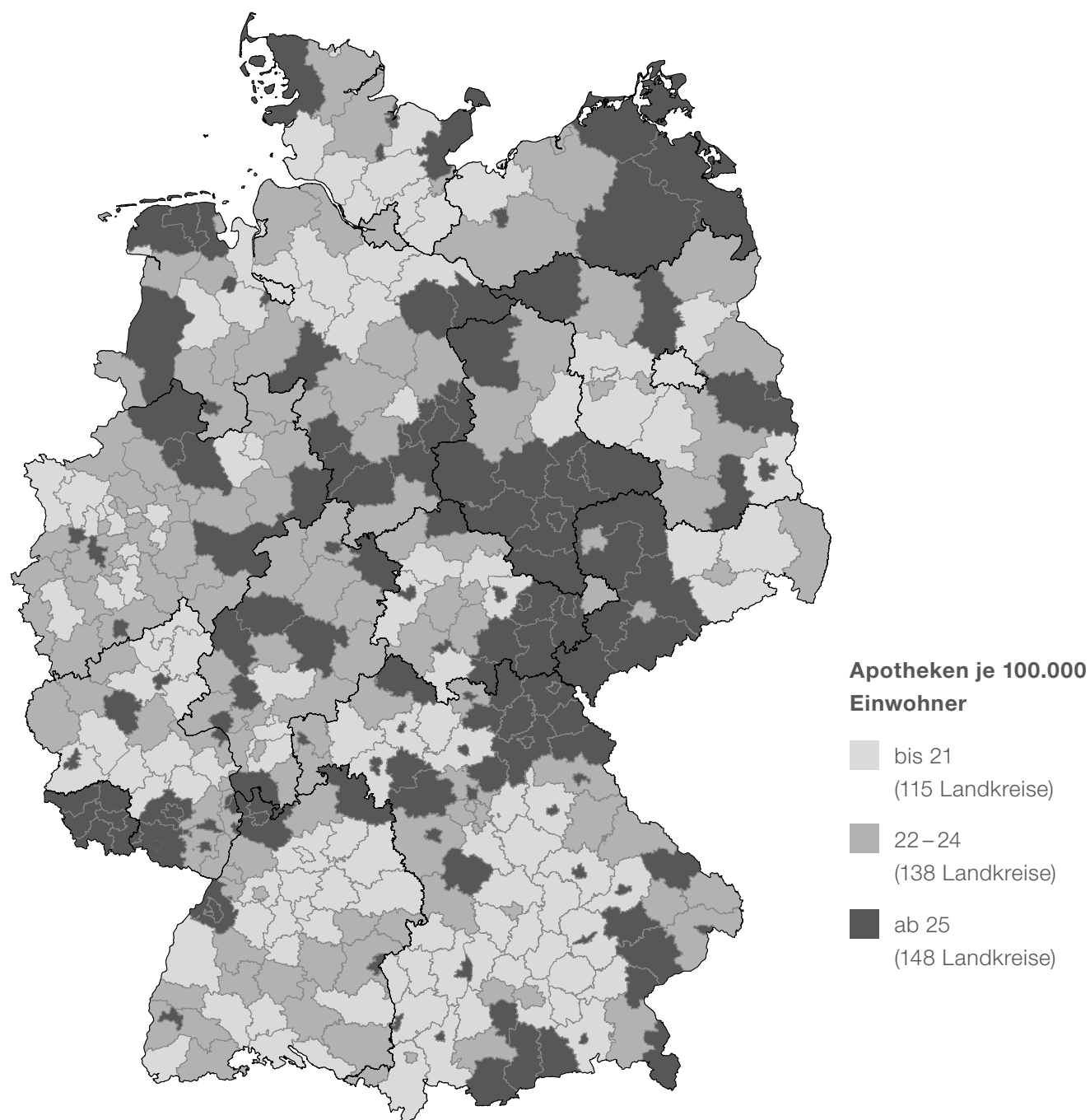
** Apotheken je 100.000 Einwohner

Quelle: ABDA-Statistik

FLÄCHENDECKUNG

Im Durchschnitt versorgen 23 Apotheken etwa 100.000 Einwohner in Deutschland. Doch es gibt durchaus regionale Unterschiede zwischen Ostsee und Alpen: Je nach Einwohnerzahl, Ausdehnung und Struktur von Städten und Landkreisen kann die Apothekendichte variieren. Die flächendeckende Versorgung der Bevölkerung mit Arzneimitteln ist derzeit aber überall gewährleistet.

Apothekendichte nach Landkreisen 2019



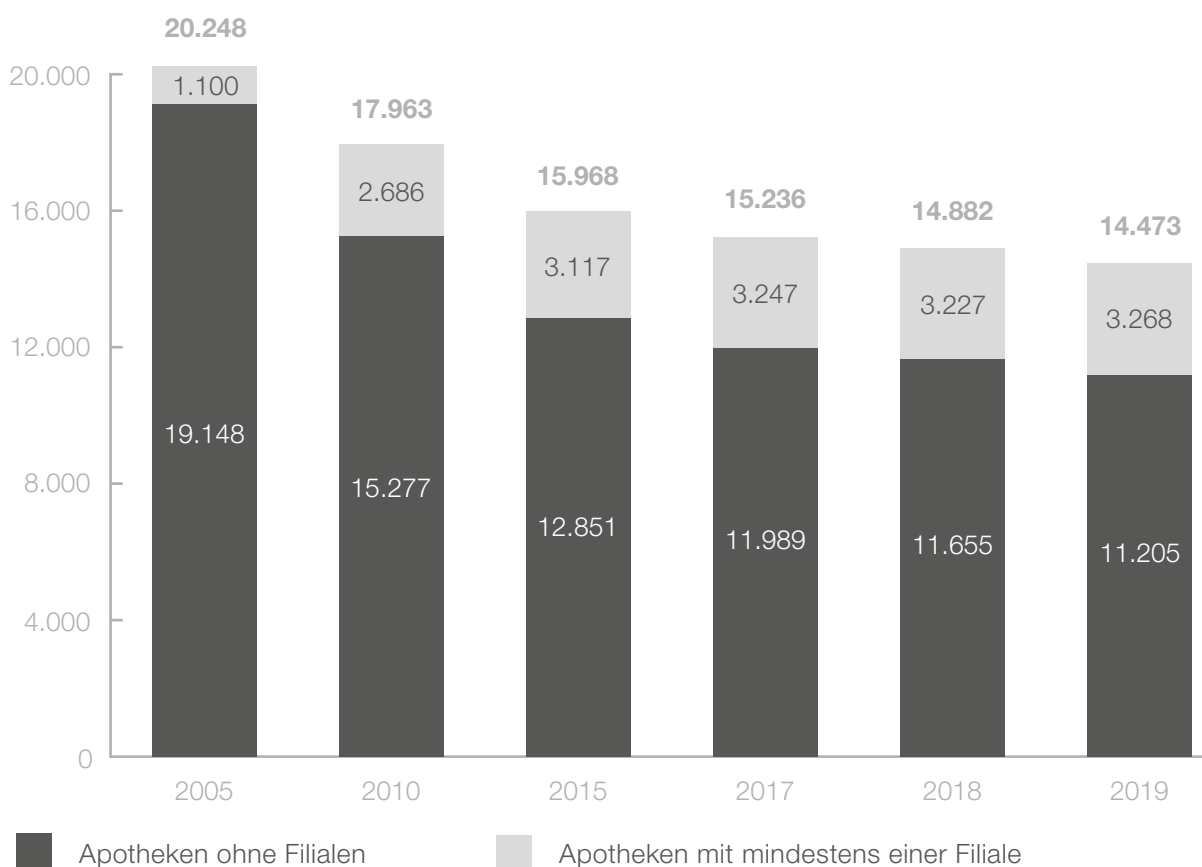
Anmerkung: geänderte Klasseneinteilung

Quelle: ABDA-Statistik

FILIALSTRUKTUR

Von den insgesamt 19.075 Apotheken waren Ende 2019 genau 14.473 Einzelapotheken bzw. Hauptapotheken mit Filiale(n). Die Filialisierung nimmt zu. Seit dem Inkrafttreten des GKV-Modernisierungsgesetzes 2004 darf eine Apotheke bis zu drei Filialen haben. Jede Filiale muss einen verantwortlichen Apotheker als Filialleiter haben. Haupt- und Filialapotheken müssen in räumlicher Nähe zueinander liegen.

	2005	2010	2015	2017	2018	2019
Apotheken ohne Filialen (Einzelapotheken)	19.148	15.277	12.851	11.989	11.655	11.205
Hauptapotheke mit einer Filiale	989	2.057	2.229	2.282	2.231	2.257
Hauptapotheke mit zwei Filialen	94	466	612	665	678	688
Hauptapotheke mit drei Filialen	17	163	276	300	318	323
Haupt-/Einzelapotheken	20.248	17.963	15.968	15.236	14.882	14.473



Angaben jeweils Jahresende

Quelle: ABDA-Statistik

SPEZIFISCHE APOTHEKENFORMEN

Krankenhausapotheken gehören nicht zu den öffentlichen Apotheken. Alle öffentlichen Apotheken sind inhabergeführt. In Bezug auf die Eigentumsform werden manche Apotheken von mehreren Apothekern als Offene Handelsgesellschaft (OHG) geführt. Pachtapotheken entstehen übergangsweise, wenn z. B. der Inhaber die Apotheke aus Altersgründen nicht mehr betreiben kann. Zur Sicherung der Versorgung auf lokaler Ebene können auch Rezeptsammelstellen genehmigt werden, über die Rezepte z. T. digital übermittelt und von einer autorisierten Apotheke beliefert werden.

	2017	2018	2019
Krankenhausapotheken (§ 14 ApoG*)	379	375	372
Krankenhausversorgende Apotheken (§ 1a Abs. 1 ApBetrO**)	171	169	164
OHG-Apotheken (§ 8 ApoG)	709	722	749
Pachtapotheken (§ 9 ApoG)	774	732	657
Zweigapotheken (§ 16 ApoG)	12	11	10
Notapotheken (§ 17 ApoG)	0	0	0

Rezeptsammelstellen (§ 24 ApBetrO) 2019

Baden-Württemberg	119	Nordrhein-Westfalen	35
Bayern	135	Nordrhein	3
Berlin	–	Westfalen-Lippe	32
Brandenburg	74	Rheinland-Pfalz	79
Bremen	–	Saarland	8
Hamburg	–	Sachsen	121
Hessen	176	Sachsen-Anhalt	127
Mecklenburg-Vorpommern	103	Schleswig-Holstein	44
Niedersachsen	105	Thüringen	83

Insgesamt

1.209

* Apothekengesetz

** Apothekenbetriebsordnung

Quellen: ABDA-Statistik, IQVIA Commercial GmbH & Co. OHG

VERSANDHANDEL

Seit 2004 ist in Deutschland der Versandhandel mit rezeptpflichtigen und -freien Medikamenten erlaubt. Im Bereich der Selbstmedikation hat der Versandhandel bereits einen zweistelligen prozentualen Marktanteil erreicht. Bei verschreibungspflichtigen Arzneimitteln liegt er deutlich niedriger.

Rezeptfreie Arzneimittel und Nichtarzneimittel	Absatz 2019			Umsatz* 2019		
	in Mio. Packungen	Veränderung zum Vorjahr	Marktanteil	in Mio. Euro	Veränderung zum Vorjahr	Marktanteil
Öffentliche Apotheken	796	–0,2 %	84,6 %	7.837	2,2 %	83,6 %
Versandhandel (Inland und Ausland)	145	7,3 %	15,4 %	1.537	6,7 %	16,4 %

Veränderte Datenquelle im Vergleich zur Vorjahrespublikation.

GKV-Arzneimittelausgaben**

	2016		2017		2018		2019	
	in Mio. Euro	Marktanteil	in Mio. Euro	Marktanteil	in Mio. Euro	Marktanteil	in Mio. Euro	Marktanteil
Öffentliche Apotheken	32.355	98,9 %	33.607	98,8 %	34.384	98,7 %	35.431	98,8 %
Ausländischer Versandhandel	367	1,1 %	407	1,2 %	437	1,3 %	427	1,2 %

Apotheken mit Versandhandelserlaubnis (§ 11a ApoG)



* bewertet zum effektiven Verkaufspreis

** Der Großteil der GKV-Ausgaben entfällt auf verschreibungspflichtige Arzneimittel.

*** professioneller Webshop und Listing bei Preis-Suchmaschinen

ZAHL UND ALTER DER PHARMAZEUTEN

In Deutschland gab es Ende 2019 über 67.000 berufstätige Apotheker – Tendenz steigend. Der weitaus größte Teil arbeitet in öffentlichen Apotheken. Aber auch in der pharmazeutischen Industrie, in Krankenhausapotheken, Universitäten und Behörden finden Apotheker Beschäftigung. Mehr als zwei Drittel der Approbierten sind Frauen.

Berufstätige Apotheker in:	2017	2018	2019	Frauenanteil 2019
öffentlichen Apotheken	51.098	52.048	52.876	73,1 %
davon Apothekenleiter*	15.836	15.476	15.067	49,1 %
Krankenhausapotheken	2.382	2.445	2.539	71,3 %
Industrie, Verwaltung, Fachorganisationen, Wissenschaft	10.899	11.287	11.767	61,3 %
Pharmazeutische Industrie	6.530	6.851	7.221	62,1 %
Bundeswehr	241	228	231	36,8 %
Behörden und Körperschaften	954	1.009	1.062	64,7 %
Universitäten	1.219	1.216	1.240	50,5 %
Lehranstalten und Berufsschulen	482	494	546	78,0 %
Sonstige Bereiche	1.473	1.489	1.467	61,1 %
Insgesamt	64.379	65.780	67.182	71,0 %

Durchschnittsalter der Apotheker **

Alter in Jahren bei berufstätigen Apothekern in:	gesamt	weiblich	männlich
öffentlichen Apotheken	47,2	45,7	51,2
davon Apothekenleiter	51,5	50,0	53,0
davon approbierte Mitarbeiter	44,7	44,2	47,4
Krankenhausapotheken	43,0	40,5	48,1
Industrie, Verwaltung, Fachorganisationen, Wissenschaft	41,5	39,8	44,1
Alle Tätigkeitsbereiche	46,2	44,8	49,5

* Besitzer (inkl. OHG-Gesellschafter), Pächter und Verwalter; keine angestellten Filialleiter

** letzte Erhebung zum Stichtag 31.12.2014

Quelle: ABDA-Statistik

BESCHÄFTIGTE IN APOTHEKEN

Die Zahl der in öffentlichen Apotheken arbeitenden Menschen ist im Jahr 2019 auf mehr als 160.000 gestiegen. Etwa ein Drittel sind approbierte Apotheker. Zwei Drittel arbeiten als Pharmazeutisch-technische Assistenten (PTA) oder Pharmazeutisch-kaufmännische Angestellte (PKA).

	2017	2018	2019	Frauenanteil 2019
Apotheker	51.098	52.048	52.876	73,1 %
Pharmazeuten im Praktikum (PhiP)	1.693	1.612	1.641	75,4 %
Apothekerassistenten, Pharmazie-Ingenieure	5.591	5.298	4.975	96,8 %
Pharmazeutisch-technische Assistenten (inkl. Praktikanten)	65.823	66.906	68.277	96,9 %
Pharmazeutisch-kaufmännische Angestellte*	33.079	33.277	32.819	98,1 %
Arbeitsplätze insgesamt	157.284	159.141	160.588	89,1 %

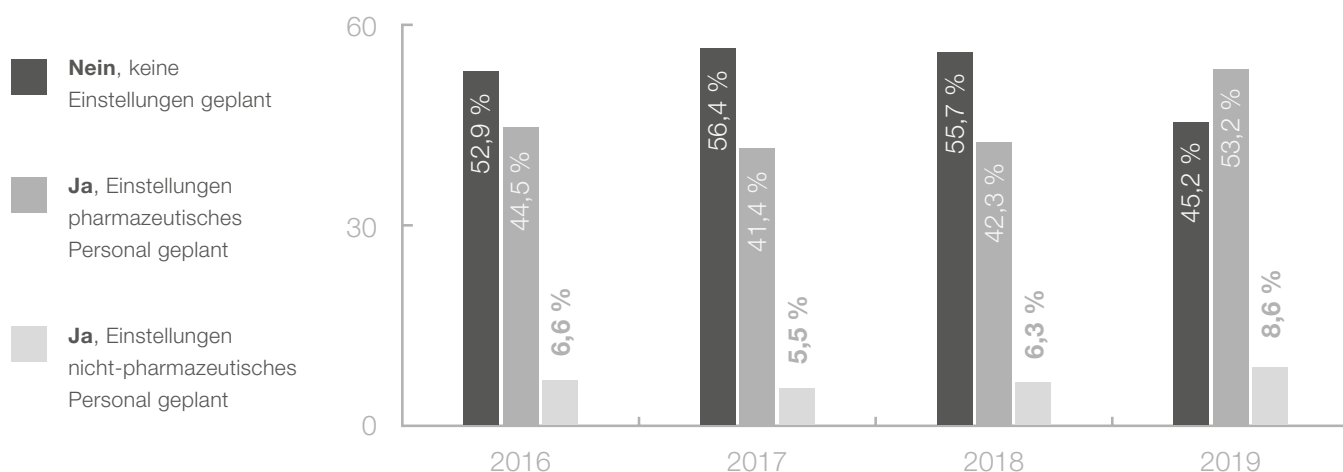
* inkl. Apothekenhelfer, -facharbeiter, -assistenten, Pharmazeutische Assistenten sowie PKA in Ausbildung
Angaben jeweils Jahresende

Quelle: ABDA-Statistik

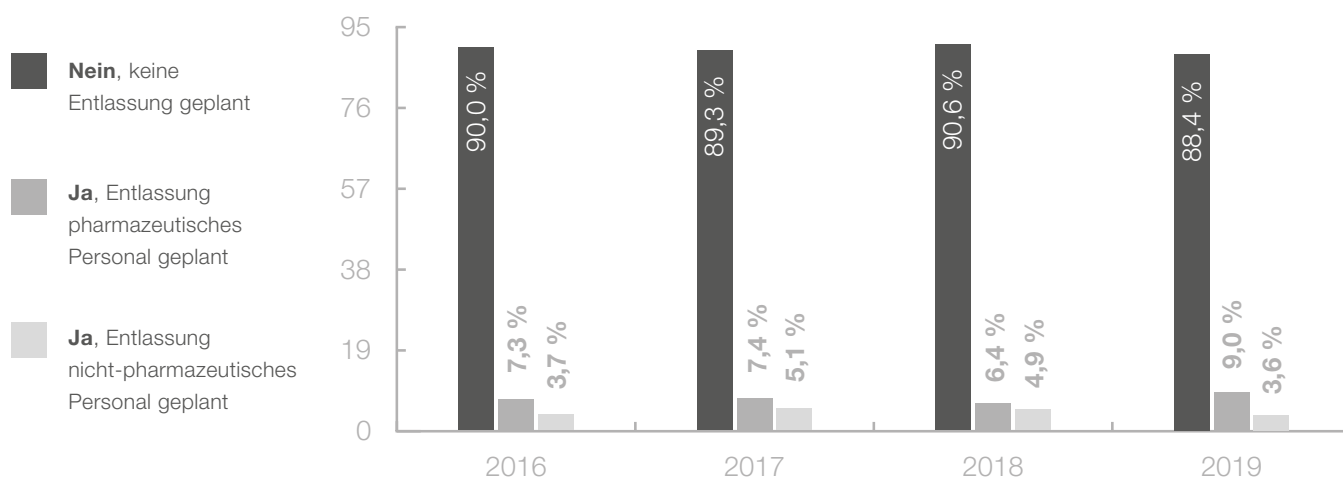
PERSONALPLANUNG

Neben den erfassbaren Beschäftigtenzahlen spielen bei der Beurteilung des Personalbedarfs auch Pläne zu Einstellungen und Entlassungen in Apotheken eine Rolle. Mehr als die Hälfte der Apothekeninhaber plant, in den nächsten zwei bis drei Jahren Fachkräfte einzustellen. Neun von zehn Inhabern planen keine Entlassungen von Mitarbeitern. Insgesamt sind Arbeitsplätze in Apotheken somit sehr sicher.

Planen Apothekeninhaber in den nächsten zwei bis drei Jahren Einstellungen?



Planen Apothekeninhaber in den nächsten zwei bis drei Jahren Entlassungen?



Quelle: Apothekenklima-Index 2019 (marpinion GmbH, Kantar TNS/Bonsai GmbH)

AUSBILDUNGSPLATZ APOTHEKE

Apotheken sind Ausbildungsplatz für rund 7.400 junge Menschen, die entweder im Rahmen einer dualen Ausbildung zur PKA, einer schulischen Ausbildung zur PTA oder im letzten Abschnitt des Pharmaziestudiums ihren praktischen Ausbildungsabschnitt dort absolvieren. Etwa die Hälfte der Apotheken bilden derzeit aus.

	2017	2018	2019
Pharmazeutisch-kaufmännische Angestellte (PKA) in Ausbildung	3.626	3.680	3.603
Pharmazeutisch-technische Assistenten (PTA) im Praktikum	2.076	2.072	2.131
Pharmazeuten im Praktikum (PhiP)	1.693	1.612	1.641
Gesamtzahl der Ausbildungsplätze	7.395	7.364	7.375

Bilden Apothekeninhaber in ihrer (Haupt-) Apotheke aktuell aus?

Nein , ich bilde aktuell niemanden aus	52,8 %
Ja , andere Ausbildungen, z. B. Schülerpraktikanten oder in anderen Berufen	26,4 %
Ja , ein oder mehrere PTA-Praktikanten	24,2 %
Ja , ein oder mehrere PKA-Auszubildende	15,4 %
Ja , ein oder mehrere PhiPs (Pharmaziepraktikanten)	13,4 %

PHARMAZIESTUDIERENDE UND APPROBATIONEN

Die Zahl der Pharmaziestudierenden und der neu approbierten Apotheker in Deutschland nimmt zu. Allerdings steigt auch der Bedarf an Pharmazeuten auf dem Arbeitsmarkt, z. B. in der Industrie oder in Krankenhäusern. An 22 Universitäten in 14 Bundesländern wird der Studiengang Pharmazie angeboten. Das Studium gliedert sich in drei Abschnitte: Grundstudium (zwei Jahre), Hauptstudium (zwei Jahre) sowie eine praktische Ausbildung (ein Jahr).

Akademisches Jahr	Studierende	Studienanfänger	Approbationen	Promotionen
2018/2019	15.986	2.833	2.281	372
2017/2018	15.894	2.775	2.233	374
2016/2017	15.682	2.766	2.202	415
2015/2016	15.548	2.752	2.025	385
2014/2015	15.268	2.748	2.079	407
2013/2014	14.632	2.708	1.947	350

Quelle: Statistisches Bundesamt (Destatis), Landesbehörden

STUDIENORTE

Bundesland	Universität	Zulassungen im Wintersemester 2018/2019	Zulassungen im Sommersemester 2019
Baden-Württemberg	Freiburg	90	0
	Heidelberg	45	0
	Tübingen	140	0
Bayern	Erlangen-Nürnberg	124	0
	München U	99	99
	Regensburg	126	0
	Würzburg	58	58
Berlin	Berlin FU	83	62
Brandenburg	—	—	—
Bremen	—	—	—
Hamburg	Hamburg	56	0
Hessen	Frankfurt/Main	90	80
	Marburg	145	95
Mecklenburg-Vorpommern	Greifswald	64	63
Niedersachsen	Braunschweig	79	70
Nordrhein-Westfalen	Bonn	82	81
	Düsseldorf	65	66
	Münster	84	76
Rheinland-Pfalz	Mainz	45	49
Saarland	Saarbrücken	32	29
Sachsen	Leipzig	48	0
Sachsen-Anhalt	Halle-Wittenberg	145	0
Schleswig-Holstein	Kiel	63	63
Thüringen	Jena	78	0
Insgesamt		1.841	891

Quelle: Stiftung für Hochschulzulassung (ZVS)

FORT- UND WEITERBILDUNG

Fortbildung trägt dazu bei, bestehendes Wissen kontinuierlich zu sichern und zu erweitern. Weiterbildung ist die berufsbegleitende Spezialisierung in einem Gebiet oder Bereich der Pharmazie. Die dreijährige Weiterbildung in einem Gebiet berechtigt zum Führen eines Fachapotheker-Titels. Nach einjähriger Weiterbildung in einem Bereich darf die entsprechende Bereichsbezeichnung geführt werden.

Fortbildungsveranstaltungen der Landesapothekerkammern (LAK) und Landesapothekerverbände (LAV)

	2017	2018	2019
Veranstaltungen	3.339	3.241	3.351
Teilnehmer	166.869	173.389	187.651

Weiterbildungsabschlüsse pro Jahr

(in Gebieten und Bereichen)

	2017	2018	2019
Anzahl Weiterbildungsabschlüsse	523	536	475

Apotheker mit abgeschlossener Weiterbildung (Ende 2019)

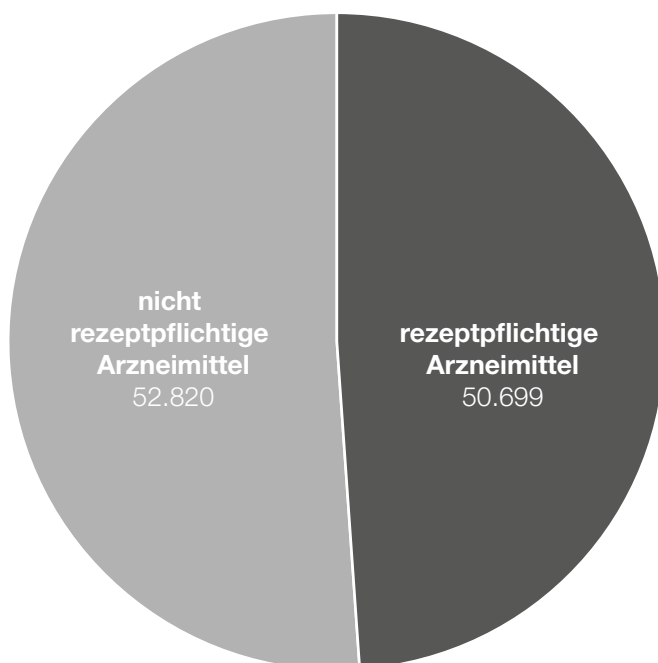
Gebiet		Bereich	
Allgemeinpharmazie	10.272	Naturheilverfahren und Homöopathie	2.281
Klinische Pharmazie	1.766	Ernährungsberatung	2.267
Pharmazeutische Analytik	819	Geriatrische Pharmazie	998
Arzneimittelinformation	705	Prävention und Gesundheitsförderung	537
Pharmazeutische Technologie	525	Onkologische Pharmazie	263
Theoretische und praktische Ausbildung	148	Infektiologie	201
Öffentliches Gesundheitswesen	130	Pflegeversorgung	62
Toxikologie und Ökologie	114		
Klinische Chemie	4		
Fachapotheker-Titel insgesamt	14.483	Bereichsbezeichnungen insgesamt	6.609

Quelle: Bundesapothekerkammer (BAK)

IN DEUTSCHLAND ZUGELASSENE ARZNEIMITTEL

In Deutschland sind über 100.000 verschiedene Arzneimittel behördlich zugelassen. Jede Packungsgröße, Wirkstärke oder Darreichungsform zählt dabei als eigenständiges Arzneimittel, auch wenn der Markenname derselbe ist. Rund die Hälfte aller Medikamente ist verschreibungspflichtig. Die amtliche Zulassung kann auf nationaler Ebene gemäß dem deutschen Arzneimittelgesetz oder auch europaweit erfolgen.

Betäubungsmittelrezeptpflichtige Arzneimittel *	1.945
Sonderrezeptpflichtige Arzneimittel (T-Rezept) **	16
Andere rezeptpflichtige Arzneimittel	48.738
Apothekenpflichtige Arzneimittel	18.518
Freiverkäufliche Arzneimittel	34.302
Verkehrsfähige Arzneimittel insgesamt	103.519



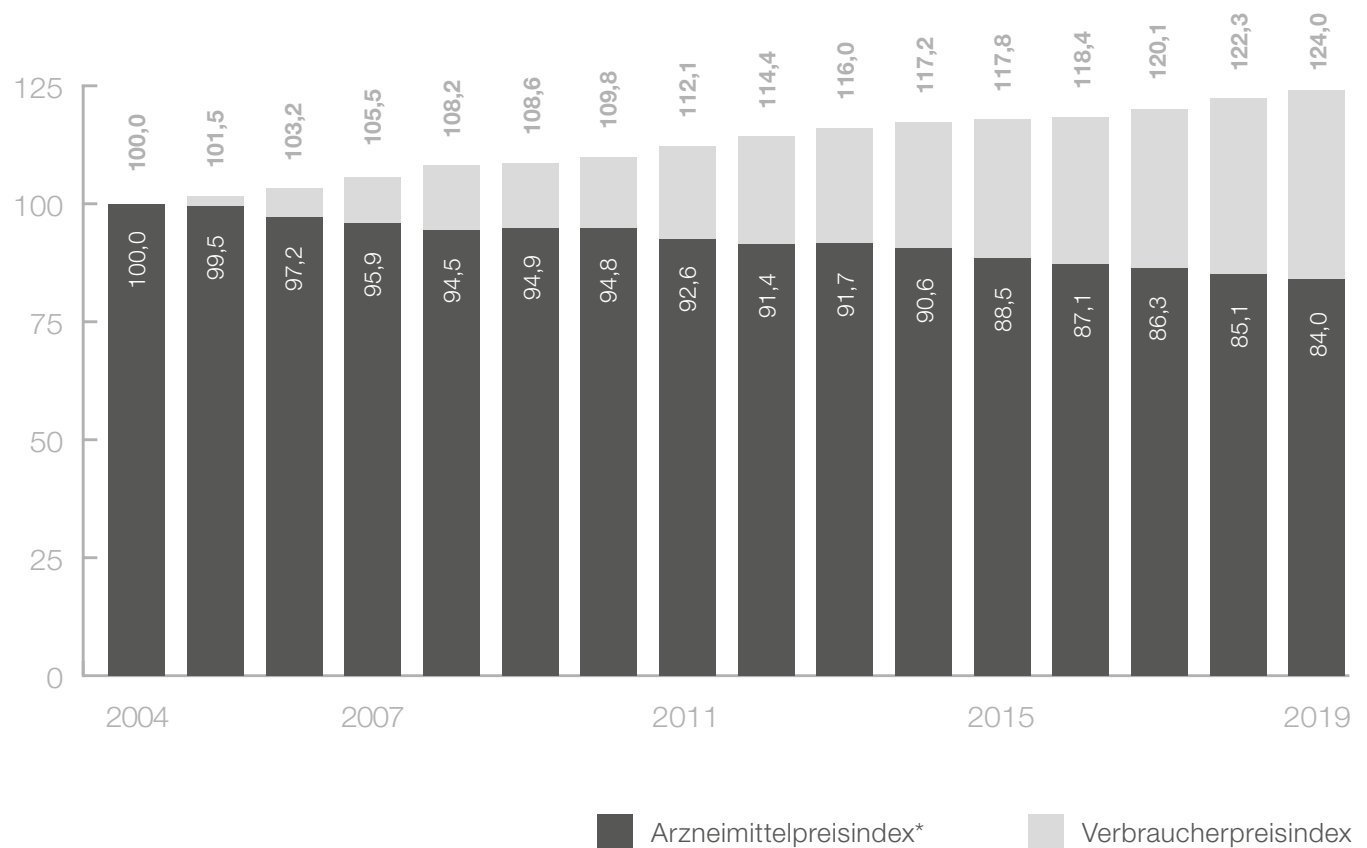
* Arzneimittel, die aufgrund ihrer Wirkweise der Betäubungsmittelverschreibungsverordnung unterliegen, z.B. starke Schmerzmittel

** Arzneimittel, die aufgrund ihres Gefährdungspotenzials nur unter ganz bestimmten Bedingungen eingesetzt werden dürfen, z.B. der Wirkstoff Thalidomid
Stand: Januar 2020

Quelle: Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)

ARZNEIMITTELPREISINDEX

Der Arzneimittelpreisindex beschreibt die durchschnittliche Preisentwicklung (inkl. MwSt.) für Arzneimittel, die zulasten der Gesetzlichen Krankenversicherung (GKV) verschrieben werden. Die Arzneimittelpreise sind seit 15 Jahren rückläufig, während die Verbraucherpreise kontinuierlich angestiegen sind.



* Apothekenabschlag, Herstellerabschläge, Rabattvertragseinsparungen und Patientenzuzahlungen sind nicht berücksichtigt.

Quelle: Wissenschaftliches Institut der AOK (WiO), Statistisches Bundesamt (Destatis)

PREISBILDUNG BEI FERTIGARZNEIMITTELN

Der Abgabepreis von rezeptpflichtigen Arzneimitteln sowie das apothekerliche Honorar richten sich nach den gesetzlichen Vorgaben der Arzneimittelpreisverordnung. Zur finanziellen Entlastung der Krankenkassen hat der Gesetzgeber Abschläge und Rabatte sowie Zuzahlungen der Versicherten vorgesehen.

Beispiel für ein verschreibungspflichtiges Fertigarzneimittel

Abgabepreis des pharmazeutischen Unternehmers (ApU)	50,00 Euro
+ Großhandelshöchstzuschlag (3,15 % auf ApU + 0,70 Euro)	2,28 Euro
= Apothekeneinkaufspreis (AEP)	52,28 Euro
+ Apothekenzuschlag (3 % auf AEP + 8,35 Euro)	9,92 Euro
+ Notdienstzuschlag (0,21 Euro)	0,21 Euro
= Netto-Apothekenverkaufspreis (Netto-AVP)	62,41 Euro
+ Mehrwertsteuer (19 % auf Netto-AVP)	11,86 Euro
= Apothekenverkaufspreis (AVP)	74,27 Euro
– Gesetzliche Zuzahlung des Versicherten (10 % vom AVP)	7,43 Euro
– Gesetzlicher Apothekenabschlag (1,77 Euro)	1,77 Euro
– Gesetzlicher Herstellerabschlag* (7 % vom ApU)	3,50 Euro
= effektive Ausgaben der GKV**	61,57 Euro

* Der Herstellerabschlag für nicht-festbetragsgebundene Arzneimittel beträgt 7 Prozent bei patentgeschützten Originalen und 16 Prozent bei Generika. Für festbetragsgebundene Generika gelten hingegen 10 Prozent. Liegt der Arzneimittelpreis 30 Prozent unterhalb des Festbetrags, entfällt der Herstellerabschlag (§ 130a SGB V).

** Eventuelle Rabattverträge, die kostensenkend für die GKV wirken, sind unberücksichtigt.

PREISBILDUNG BEI STANDARDREZEPTUREN

Bei Standardrezepturen richtet sich der Abgabepreis nach den gesetzlichen Vorgaben der Arzneimittelpreisverordnung (AMPreisV) – ähnlich wie bei industriell hergestellten, rezeptpflichtigen Medikamenten. Zu- und Abschläge sind dort genau definiert. Die Vergütungsregeln für Standardrezepturen wurden 2017 angepasst.

Beispiel für eine verschreibungspflichtige Salbe (100 g)

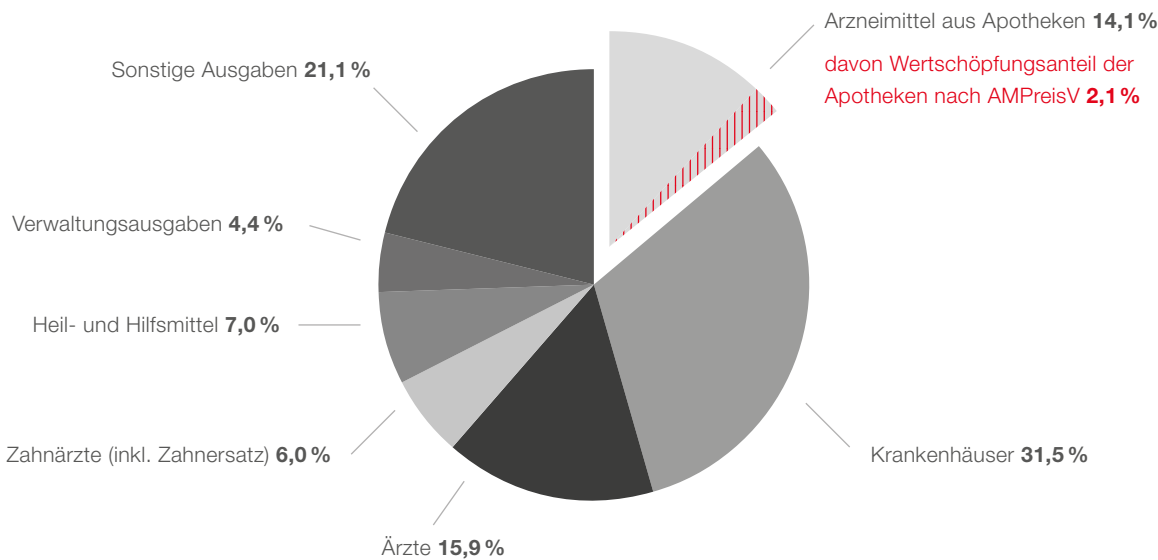
Apothekeneinkaufspreis (AEP) für Wirkstoff (1 g Pulver), Grundlage (99 g Salbengrundlage) und Gefäß (1 Spenderdose für 100 g)	5,00 Euro
+ Festzuschlag (90 % auf AEP)	4,50 Euro
+ Rezepturzuschlag für Herstellung (6,00 Euro bei Anfertigung von Salben bis 200 g)	6,00 Euro
+ Fixentgelt	8,35 Euro
= Netto-Apothekenverkaufspreis (Netto-AVP)	23,85 Euro
+ Mehrwertsteuer (19 % auf Netto-AVP)	4,53 Euro
= Apothekenverkaufspreis (AVP)	28,38 Euro
– Gesetzliche Zuzahlung des Versicherten (10 % vom AVP, mindestens aber 5 Euro)	5,00 Euro
– Gesetzlicher Apothekenabschlag (1,77 Euro)	1,77 Euro
= effektive Ausgaben der GKV	21,61 Euro

AUFTEILUNG DER GKV-GESAMTAUSGABEN

Von den über 250 Milliarden Euro, die die Gesetzliche Krankenversicherung (GKV) im Jahr 2019 ausgab, entfielen die größten Anteile auf Krankenhäuser und Ärzte. Der Arzneimittelbereich (inkl. Apotheken) stand mit 14,1 Prozent an dritter Stelle. Mit nur noch 2,1 Prozentpunkten sind die Kosten für Apotheken und ihre Leistungen im System weiter rückläufig und betragen weniger als die Hälfte der GKV-Verwaltungsausgaben (4,4 Prozent).

	Gesamtausgaben der GKV (Mrd. EUR)	davon in % Ärzte	Zahnärzte (inkl. Zahnersatz)	Heil- und Hilfsmittel	Krankenhäuser	Verwaltungsausgaben	Sonstige Ausgaben	Arzneimittel*	davon Wertschöpfungsanteil der Apotheken nach AMPPreisV
2019**	251,94	15,9	6,0	7,0	31,5	4,4	21,1	14,1	2,1
2018	239,27	16,1	6,1	6,7	31,6	4,8	20,4	14,4	2,2
2017	230,39	16,2	6,1	6,4	31,8	4,7	20,2	14,6	2,3
2016	222,73	16,1	6,2	6,4	32,1	4,9	19,8	14,5	2,3
2015	213,67	16,1	6,3	6,4	32,2	4,9	19,6	14,6	2,3
2014	205,54	16,0	6,3	6,4	32,7	4,9	19,2	14,5	2,3
2013	194,49	16,2	6,5	6,2	33,0	5,1	19,1	13,9	2,4
2012	184,25	15,3	6,4	6,2	33,5	5,2	19,1	14,3	2,3
2011	179,61	15,4	6,5	6,2	33,4	5,3	18,7	14,6	2,3
2010	175,99	15,4	6,5	6,0	33,0	5,4	18,1	15,6	2,5
2009	170,78	15,5	6,6	6,0	32,5	5,2	18,2	16,0	2,6

GKV-Gesamtausgaben 2019**: 251,94 Mrd. EUR

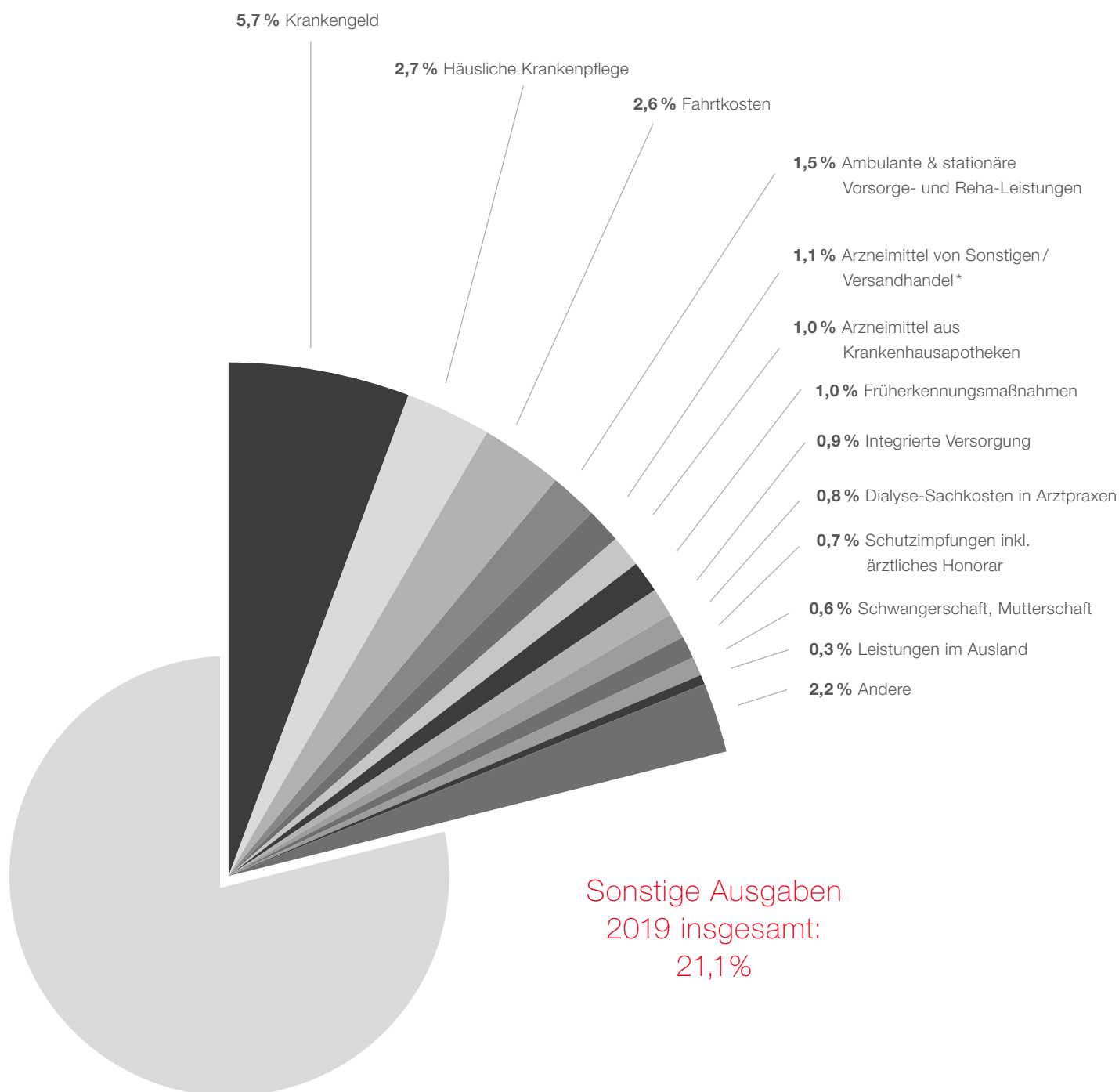


* aus öffentlichen Apotheken (ohne ausländischen Versandhandel und Sonstige)
** vorläufig

Quelle: Bundesministerium für Gesundheit (BMG), ABDA-Statistik

SONSTIGE AUSGABEN DER KRANKENKASSEN

Zu den sonstigen Ausgaben der GKV gehören unter anderem das Krankengeld, die häusliche Krankenpflege und Fahrtkosten. „Arzneimittel von Sonstigen/Versandhandel“ meint ausländische Versandapotheken oder Gesundheitsämter. Auch „Schutzimpfungen inkl. ärztliches Honorar“ sind Bestandteil der sonstigen Ausgaben.



* 1,1 % entsprechen 2,70 Mrd. €, wovon 427 Mio. € auf den ausländischen Versandhandel entfallen (siehe Kapitel Versandhandel). Arzneimittel aus Krankenhausapotheken waren in den Vorjahren bei den Sonstigen enthalten und werden jetzt gesondert ausgewiesen.

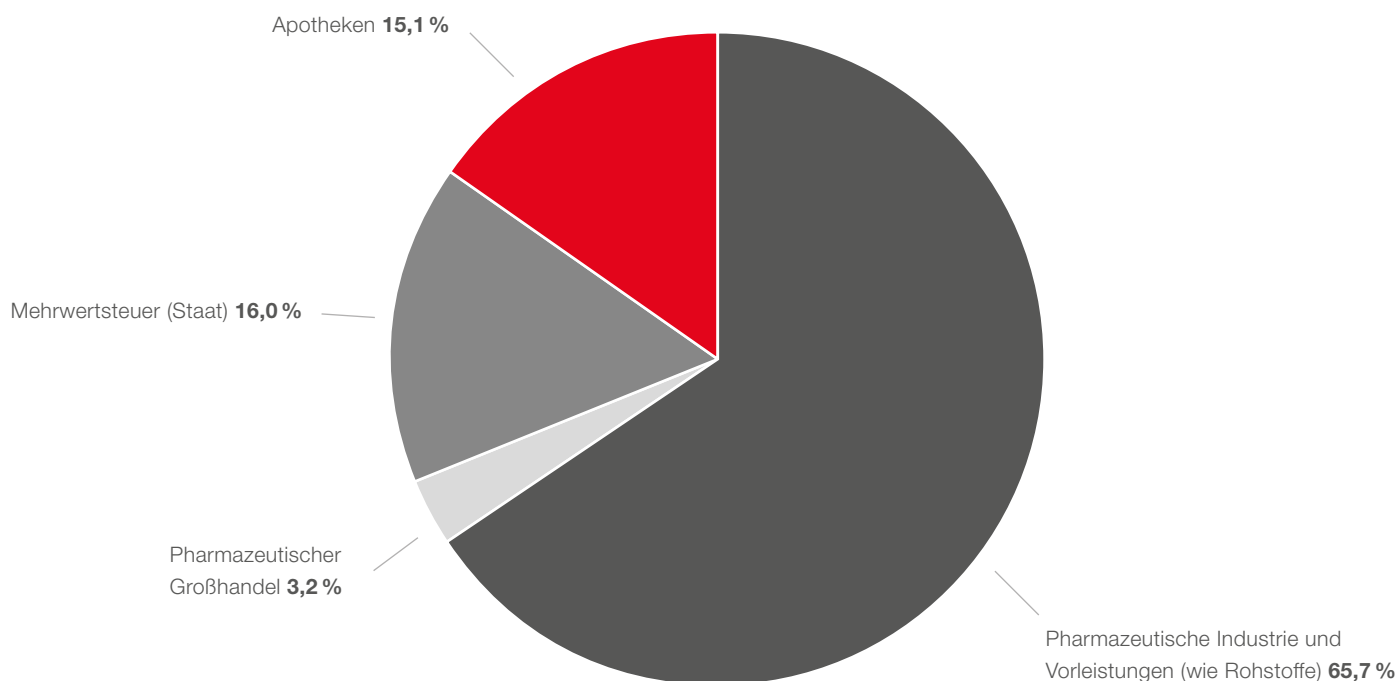
Quelle: Bundesministerium für Gesundheit (BMG), ABDA-Statistik

GKV-AUSGABEN FÜR ARZNEIMITTEL

Rund zwei Drittel der Ausgaben der Gesetzlichen Krankenversicherung (GKV) für Arzneimittel entfallen auf die Pharmazeutische Industrie. Die Ausgaben für die 19-prozentige Mehrwertsteuer auf Arzneimittel lagen 2019 noch über den Ausgaben für die Leistungen der Apotheken.

	2017		2018		2019*	
	in Mrd. EUR		in Mrd. EUR		in Mrd. EUR	
Pharmazeutische Industrie und Vorleistungen (wie Rohstoffe)	21,92	65,2 %	22,46	65,3 %	23,29	65,7 %
Pharmazeutischer Großhandel	1,11	3,3 %	1,10	3,2 %	1,13	3,2 %
Mehrwertsteuer (Staat)	5,37	16,0 %	5,49	16,0 %	5,66	16,0 %
Apotheken	5,21	15,5 %	5,33	15,5 %	5,35	15,1 %
GKV-Ausgaben für Arzneimittel insgesamt**	33,61	100,0 %	34,38	100,0 %	35,43	100,0 %

GKV-Ausgaben für Arzneimittel 2019: 35,43 Mrd. EUR



* vorläufig

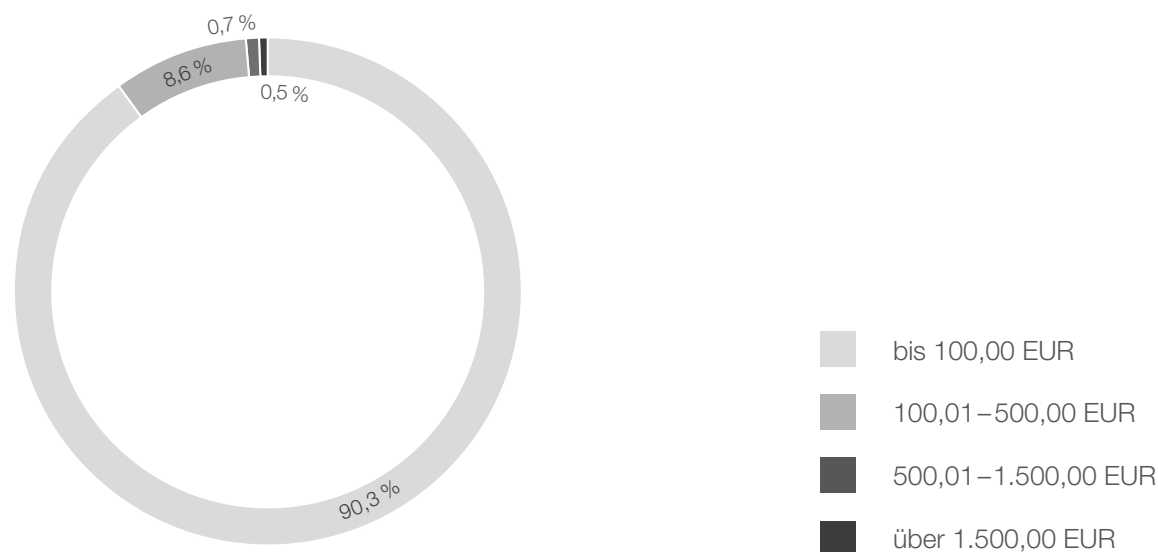
** Fertigarzneimittel, Rezepturen und Verbandstoffe aus öffentlichen Apotheken (ohne ausländischen Versandhandel und Sonstige)

Quelle: Bundesministerium für Gesundheit (BMG), ABDA-Statistik

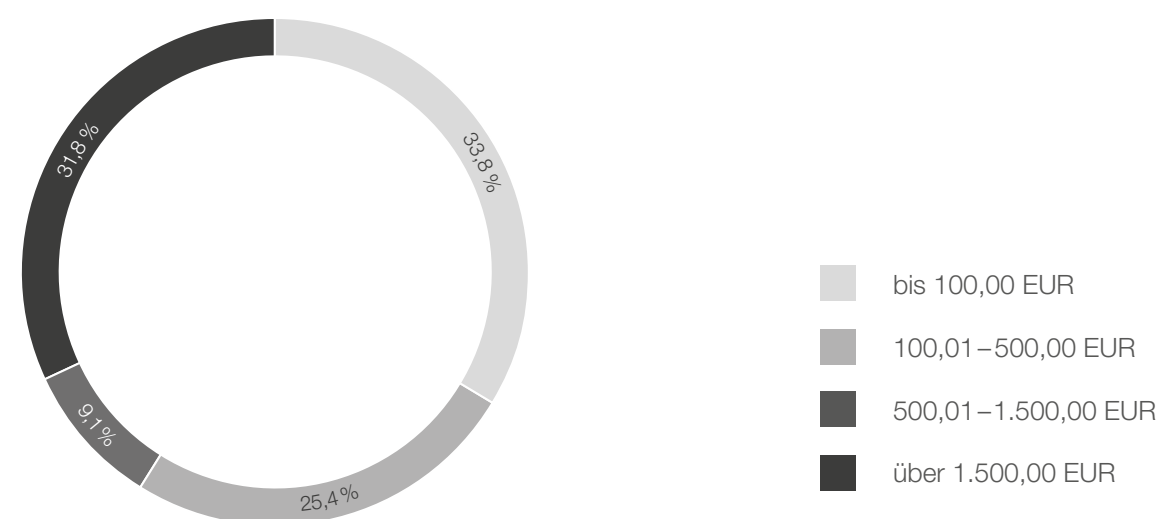
ARZNEIMITTEL NACH PREISKLASSEN

Der Apothekenverkaufspreis (AVP) jedes rezeptpflichtigen Arzneimittels ergibt sich per Gesetz durch die Arzneimittelpreisverordnung (AMPreisV) auf Basis des jeweiligen Abgabepreises des pharmazeutischen Unternehmers (ApU). Bei neun von zehn Medikamenten liegt dieser Betrag bei maximal 100 Euro. Trotz geringer Packungszahlen machen höherpreisige, innovative Arzneimittel einen wachsenden Anteil am Gesamtumsatz aus.

Absatzanteil von verschreibungspflichtigen GKV-Fertigarzneimitteln



Umsatzanteil von verschreibungspflichtigen GKV-Fertigarzneimitteln



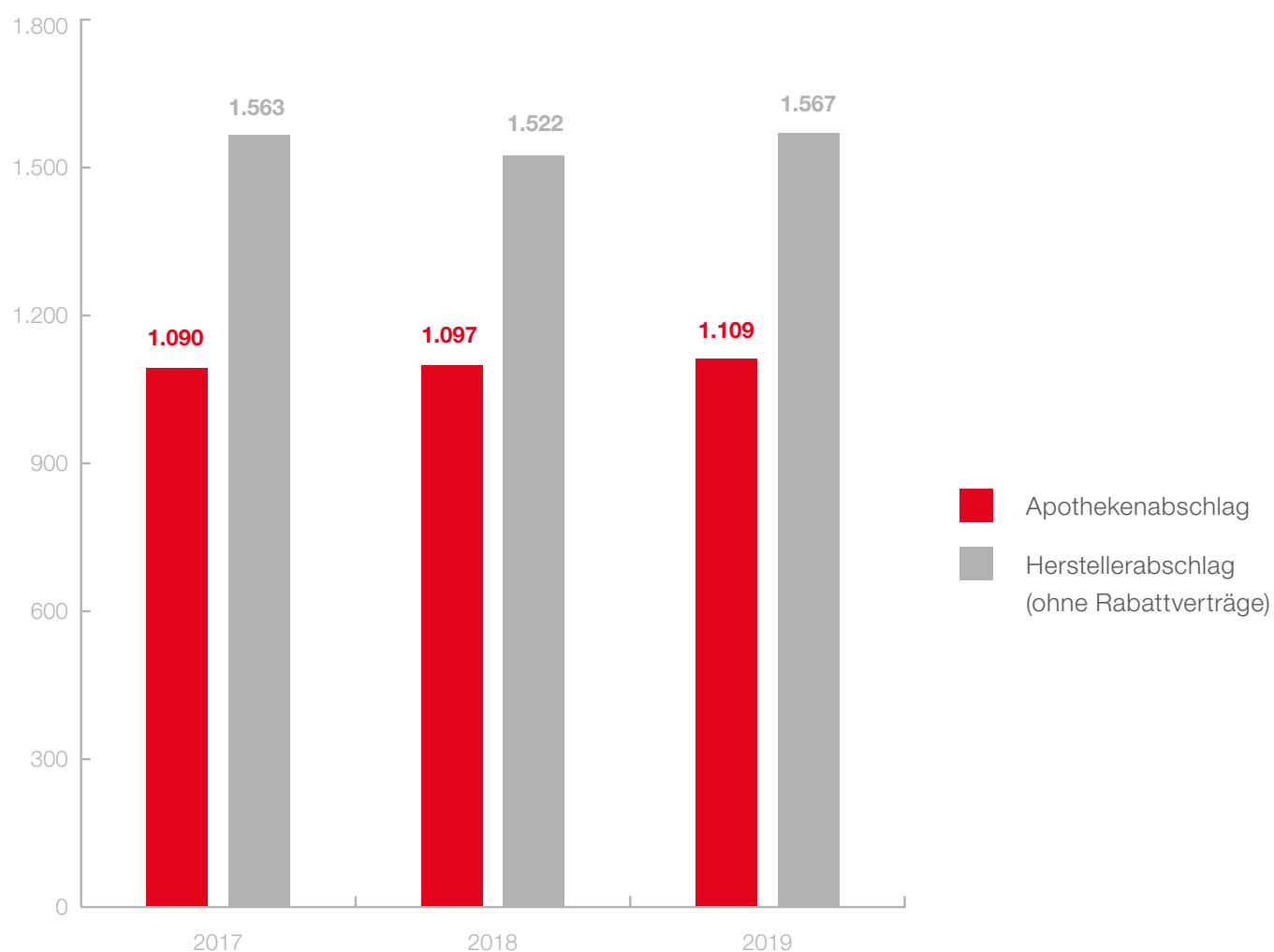
* Preisklassen beziehen sich auf Apothekenverkaufspreise
Auswertung für das Jahr 2018

Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

APOTHEKEN- UND HERSTELLERABSCHLAG

Der Gesetzgeber hat im Laufe der Jahre verschiedene Instrumente eingeführt, um die Ausgaben der Gesetzlichen Krankenversicherung (GKV) für Arzneimittel zu begrenzen. Apotheken müssen der GKV ebenso wie Arzneimittelhersteller Abschläge bei der Abgabe von rezeptpflichtigen Arzneimitteln gewähren. Der Apothekenabschlag liegt derzeit bei 1,77 Euro (inkl. MwSt.). Dieser Betrag muss für jede zulasten der GKV abgegebene Packung vom Apothekenhonorar an die Krankenkasse zurückerstattet werden. Der Abschlag summiert sich auf mehr als eine Milliarde Euro pro Jahr.

in Mio. EUR



Quelle: Deutscher Apothekerverband e. V. (DAV)

RABATTVERTRÄGE

Krankenkassen können mit Arzneimittelherstellern seit 2007 Rabattverträge für die preisgünstigere Abgabe von Arzneimitteln abschließen. Mittlerweile gibt es mehr als 30.000 kassenspezifische Rabattverträge, die vorschreiben, welcher Versicherte welches Präparat von welchem Hersteller erhalten kann. Die Berücksichtigung der wachsenden Zahl dieser Verträge bei der Patientenversorgung bedeutet für die Apotheken einen hohen administrativen Aufwand, für die Krankenkassen aber Einsparungen in Milliardenhöhe.

4,9 Mrd. EUR

Einsparungen der GKV aus Rabattverträgen im Jahr 2019

30.400

Anzahl der Rabattverträge*

18.800

Anzahl der rabattierten Arzneimittel (Pharmazentralnummern)
Ende 2019

213

Zahl der beteiligten pharmazeutischen Unternehmen*

21 %

Anteil der rabattierten verschreibungspflichtigen Arzneimittel,
die Ende 2019 zuzahlungsbefreit oder -ermäßigt waren

Rabattarzneimittel: Verträge und Einsparungen der GKV im Vergleich

	2017	2018	2019
Zahl der Rabattverträge zum Jahresende	27.300	28.000	30.400*
Einsparungen der GKV im Gesamtjahr	4,0 Mrd. Euro	4,5 Mrd. Euro	4,9 Mrd. EUR

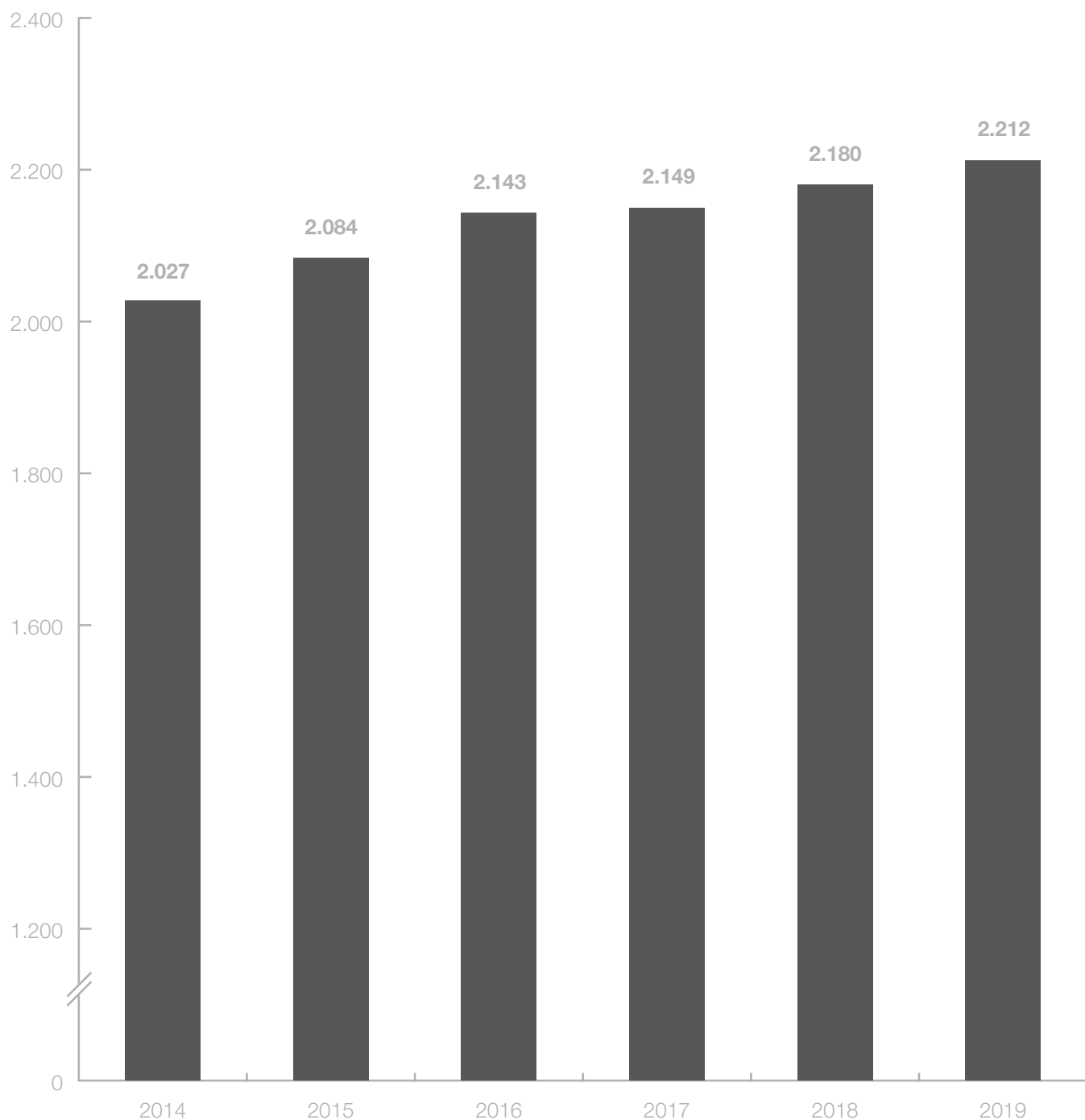
* September 2019

Quelle: ABDA, Pro Generika e. V., Bundesministerium für Gesundheit (BMG), IQVIA Commercial GmbH & Co. OHG

ZUZAHLUNGEN DER PATIENTEN

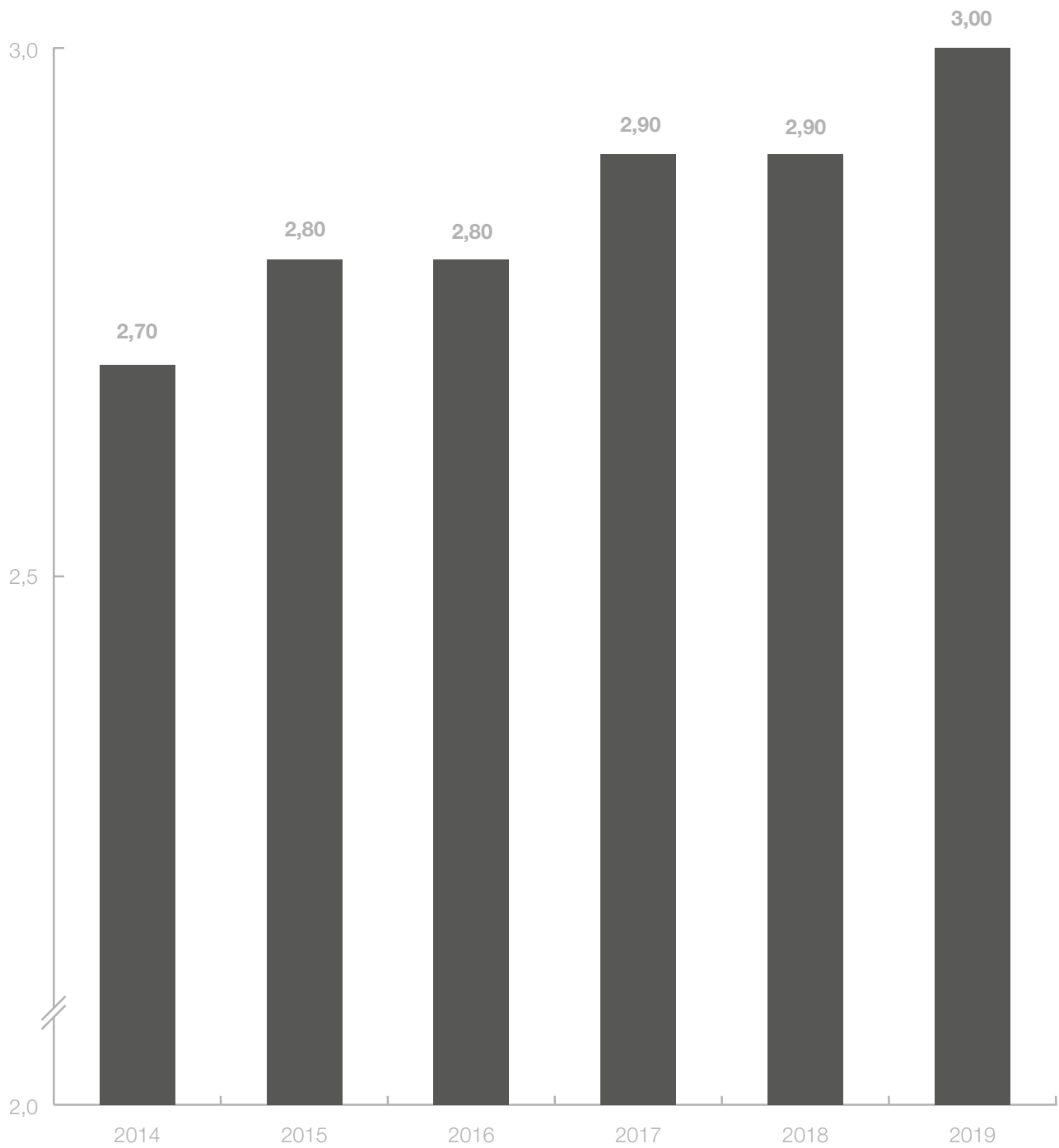
Gesetzlich krankenversicherte Patienten müssen bei bestimmten Leistungen ihrer Krankenkasse zuzahlen. Bei verordneten Arzneimitteln sind das zehn Prozent des Arzneimittelpreises, mindestens aber fünf und höchstens zehn Euro. Der Durchschnitt von 3,00 Euro ergibt sich, weil manche Medikamente zuzahlungsfrei und manche Versicherte zuzahlungsbefreit sind. Die Krankenkassen sparen durch die Zuzahlungen, die von Apotheken eingezogen werden müssen, über zwei Milliarden Euro pro Jahr, Tendenz steigend.

Zuzahlungen der Patienten zu Arzneimitteln in Mio. EUR



Quelle: Deutscher Apothekerverband e. V. (DAV)

Durchschnittliche Zuzahlung pro Packung in EUR



Quelle: Deutscher Apothekerverband e. V. (DAV)

ZUZAHLUNGSBEFREIUNGEN

Eine Härtefallregelung in § 62 SGB V sieht vor, dass gesetzlich Krankenversicherte maximal zwei Prozent ihres Jahresbruttoeinkommens für Zuzahlungen aufbringen müssen. Bei chronisch kranken Menschen liegt die Grenze bei einem Prozent. Von den rund 73 Millionen gesetzlich krankenversicherten Menschen in Deutschland ist daher etwa jeder Zwölfte von weiteren Zuzahlungen befreit. Die Quote ist seit Jahren rückläufig.

Zuzahlungsbefreiungen	2013	2014	2015	2016	2017	2018
Chronisch kranke Patienten in Mio.	6,5	6,4	6,2	6,0	5,9	5,8
Übrige Patienten in Mio.	0,4	0,4	0,3	0,3	0,3	0,3
Zuzahlungsbefreite Personen insgesamt in Mio.	6,9	6,8	6,5	6,3	6,2	6,1
Anteil Zuzahlungsbefreiter an allen GKV-Versicherten	9,9 %	9,6 %	9,2 %	8,8 %	8,6 %	8,4 %

LEITLINIEN UND ARBEITSHILFEN

Die Leitlinien der Bundesapothekerkammer, einschließlich ihrer Kommentare und Arbeitshilfen, sind Empfehlungen zur Qualitätssicherung für apothekerliches Handeln in charakteristischen Situationen. Sie berücksichtigen die gültigen Gesetze und Verordnungen und orientieren sich am Stand von Wissenschaft und Technik, entbinden jedoch nicht von der heilberuflichen Verantwortung des Einzelnen. Entsprechende Materialien gibt es zu folgenden Themen und Tätigkeiten in der Apotheke:

- 1.** Arzneimittelinformation
- 2.** Arzneimittelrisiken
- 3.** Asthma
- 4.** Blutdruckmessung
- 5.** Blutuntersuchungen
- 6.** Darreichungsformen
- 7.** Diabetes
- 8.** Ernährungsberatung
- 9.** Heimversorgung
- 10.** Hygienemanagement
- 11.** Krankenhausversorgung
- 12.** Manuelle Neuverpackung
- 13.** Medikationsanalyse
- 14.** Opioidsubstitution
- 15.** Parenteralherstellung
- 16.** Prüfung Ausgangsstoffe / Primärpackmittel
- 17.** Prüfung Fertigarzneimittel
- 18.** Rezeptbelieferung
- 19.** Rezeptur / Defektur
- 20.** Selbstmedikation

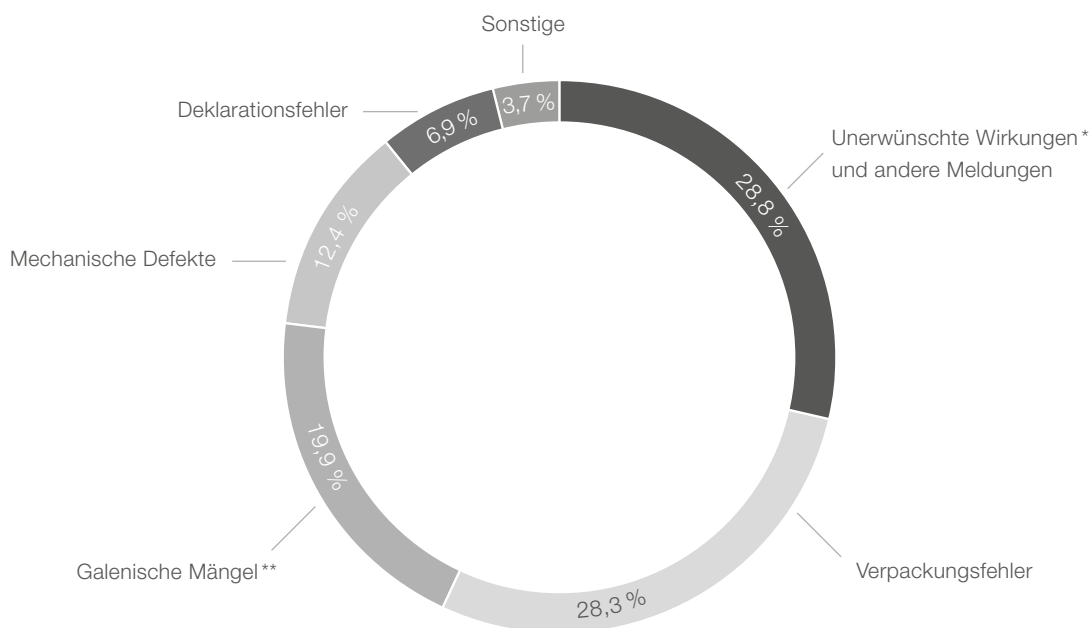
Materialien unter: www.abda.de/fuer-apotheker/qualitaetssicherung/leitlinien/leitlinien-und-arbeitshilfen/

Quelle: Bundesapothekerkammer (BAK)

AMK: MELDUNGEN VON ARZNEIMITTELRISIKEN

Apotheker prüfen Arzneimittel auf ihre Qualität und melden Qualitätsmängel an die Arzneimittelkommission der Deutschen Apotheker (AMK). Sie erfasst und bewertet gemeldete Arzneimittelrisiken und gibt nötigenfalls Warnmeldungen heraus, die ein wichtiges Instrument des Verbraucherschutzes darstellen. Die Zahl der Meldungen nimmt zu.

Gründe von Meldungen an die Arzneimittelkommission der Deutschen Apotheker (AMK)



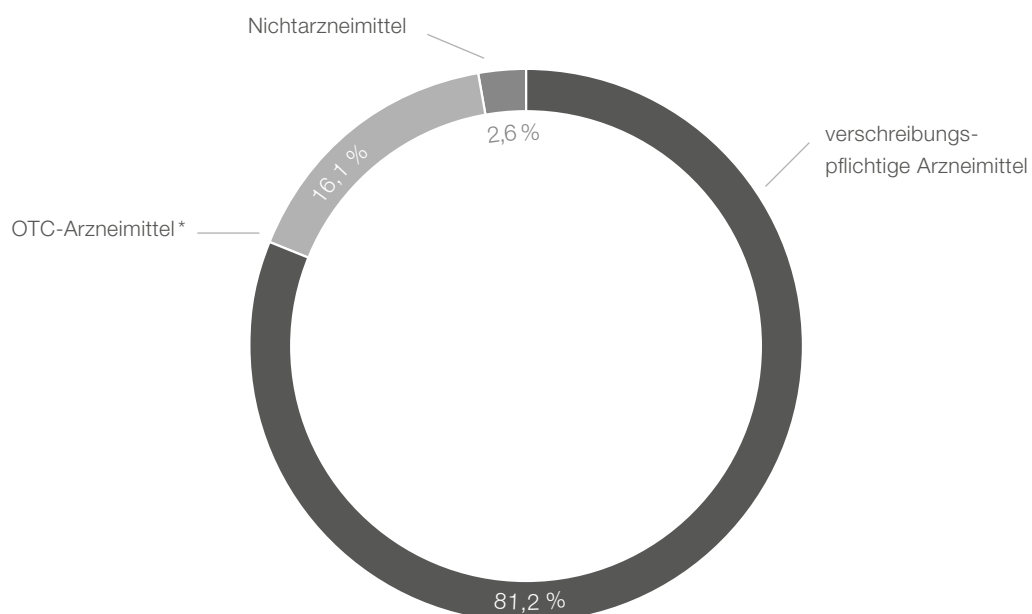
	2017	2018	2019		
	absolut	absolut	absolut	Anteil	Veränderung zum Vorjahr
Unerwünschte Wirkungen* und andere Meldungen	2.702	2.959	3.110	28,8 %	5,1 %
Verpackungsfehler	2.780	2.883	3.046	28,3 %	5,7 %
Galenische Mängel**	1.494	1.403	2.141	19,9 %	52,6 %
Mechanische Defekte	1.095	1.269	1.335	12,4 %	5,2 %
Deklarationsfehler	623	628	748	6,9 %	19,1 %
Sonstige	390	344	402	3,7 %	16,9 %
Insgesamt	9.084	9.486	10.782	100,0 %	13,7 %

* Meldungen von Verdachtsfällen zu Arzneimitteln und anderen Produktgruppen

** Herstellungs- / technologische Mängel

Quelle: Arzneimittelkommission der Deutschen Apotheker (AMK)

Risiken nach Arzneimittelgruppen



2019	absolut	Anteil
verschreibungspflichtige Arzneimittel	8.758	81,2 %
OTC-Arzneimittel*	1.740	16,1 %
Nichtarzneimittel	284	2,6 %
Insgesamt	10.782	100,0 %

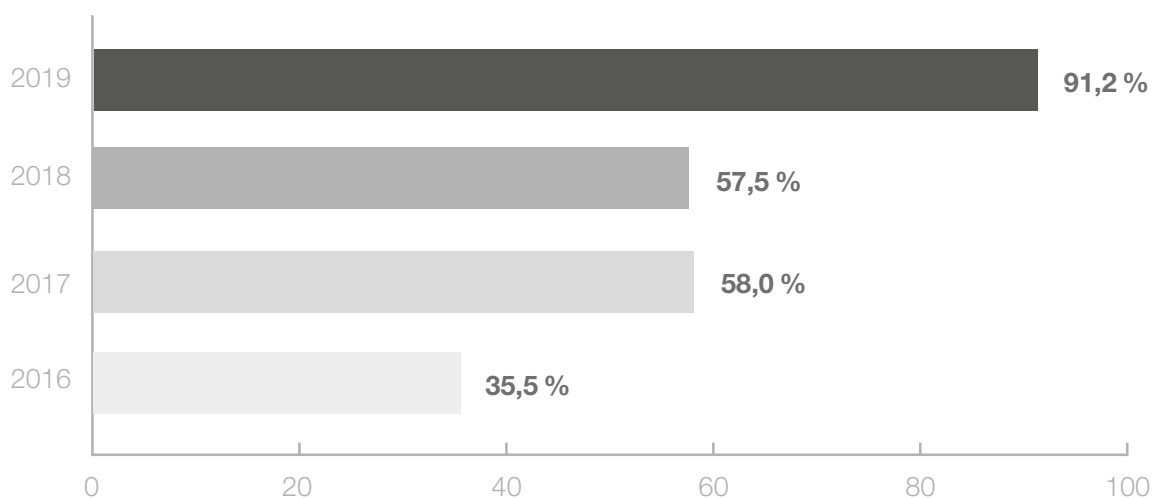
* OTC = Over-the-Counter = Über den Handverkaufstisch = rezeptfreie Arzneimittel

Quelle: Arzneimittelkommission der Deutschen Apotheker (AMK)

MANAGEMENT VON LIEFERENGPÄSSEN

Lieferengpässe sind ein Risiko für die qualitativ hochwertige Arzneimittelversorgung, betreffen unterschiedliche Wirkstoffe und gehören zu den größten Ärgernissen im Apothekenalltag der vergangenen Jahre – Tendenz steigend. Die Mehrheit der Apothekeninhaber gibt an, dass mehr als zehn Prozent der Arbeitszeit der Beschäftigten dafür aufgewendet wird, um Ersatzpräparate zu beschaffen. Allein im Jahr 2019 mussten die Apotheker eine „Abweichende Abgabe“ wegen „Nichtverfügbarkeit von Rabattarzneimitteln“ bei 18,0 Millionen Packungen vornehmen – doppelt so häufig wie im Vorjahr.

Anteil der Apothekeninhaber, die Lieferengpässe zu den größten Ärgernissen im Berufsalltag zählen.



Anteil der Teamarbeitszeit in Apotheken für das Management von Lieferengpässen

2019

Weniger als 1 Prozent	1,2 %
1 bis 5 Prozent	11,2 %
6 bis 10 Prozent	25,4 %
11 bis 15 Prozent	24,0 %
16 bis 20 Prozent	20,4 %
Mehr als 20 Prozent	17,8 %

Nichtverfügbare Arzneimittelpackungen	2017	2018	2019
Anzahl Packungen aller abgegebenen GKV-Fertigarzneimittel	648.100.000	651.000.000	651.600.000
Anzahl Packungen mit Sonderkennzeichen „Nichtverfügbarkeit“	4.700.000	9.300.000	18.000.000

Häufigste Lieferengpässe nach Wirkstoffen 2019		Laienverständliche Bezeichnung (für die Hauptindikation)	Anzahl Packungen mit „Nichtverfügbarkeit“
1	Candesartan	Blutdrucksenker	1.750.000
2	Allopurinol	Arzneistoff zur Behandlung der Gicht	820.000
3	Valsartan	Blutdrucksenker	780.000
4	Venlafaxin	Antidepressivum	690.000
5	Diclofenac	Schmerzmittel	670.000
6	Metamizol-Natrium	Schmerzmittel	560.000
7	Etoricoxib	Schmerzmittel	470.000
8	Candesartan und Diuretika	Blutdrucksenker	470.000
9	Tamsulosin	Arzneistoff zur Behandlung der Prostatavergrößerung	370.000
10	Ramipril	Blutdrucksenker	360.000
Alle Sonstigen			11.100.000
Insgesamt			18.000.000

Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

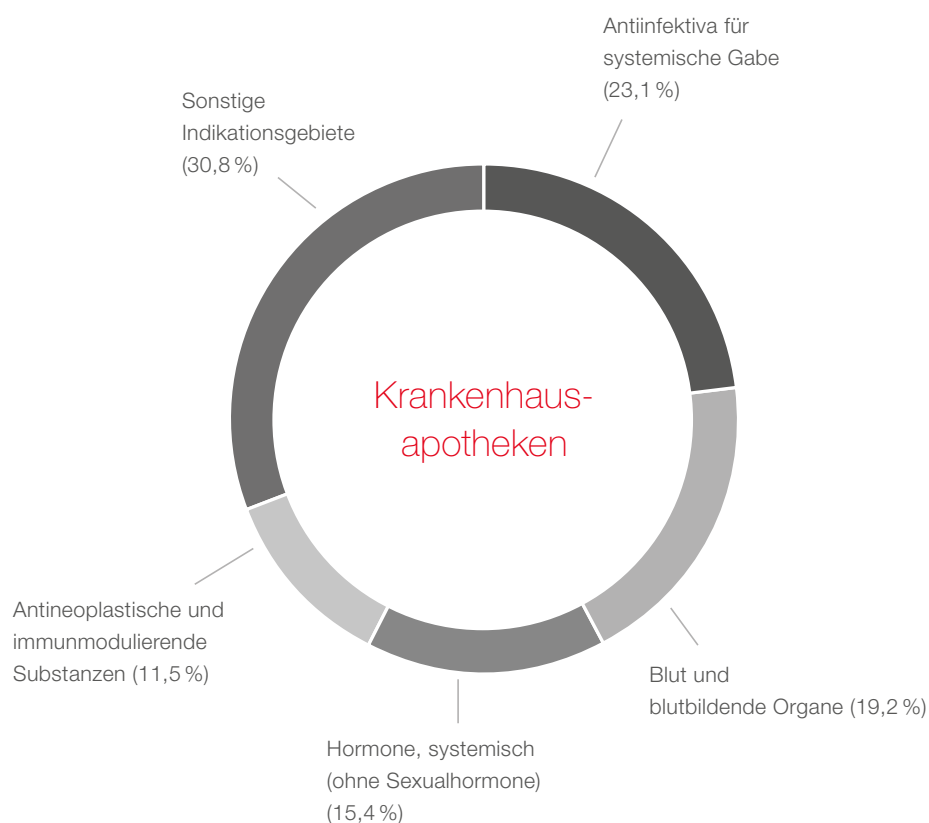
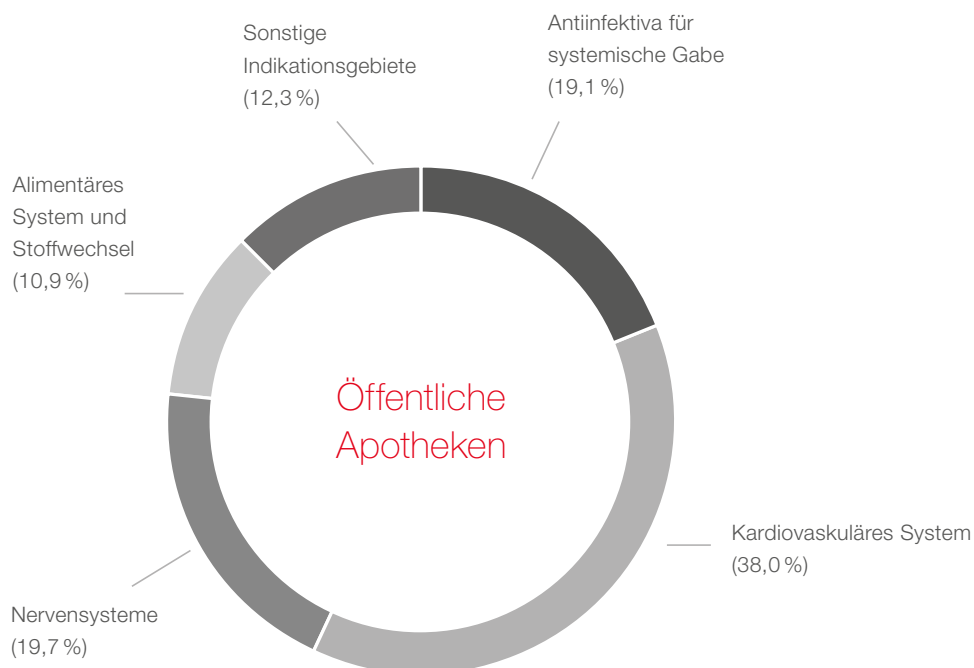
KONSEQUENZEN VON LIEFERENGPÄSSEN

Lieferengpässe haben sich laut Umfragen nicht nur zu einem der größten Ärgernisse im Apothekenalltag entwickelt. Sie führen trotz aller Bemühungen der Apotheken vor Ort auch in vielen Fällen zu einer Verschlechterung der Arzneimitteltherapie von Patienten, da fehlende Präparate nicht gleichwertig ersetzt werden können. Das bestätigt eine Referenzapotheken-Umfrage der Arzneimittelkommission der Deutschen Apotheker (AMK) zu Reichweite und Auswirkungen von Engpässen.

Wie häufig sind in den letzten drei Monaten Versorgungsengpässe bei Arzneimitteln in Ihrer Apotheke aufgetreten, die Ihrer Ansicht nach gesundheitliche Folgen für die Patienten hatten oder gehabt haben könn(t)en?

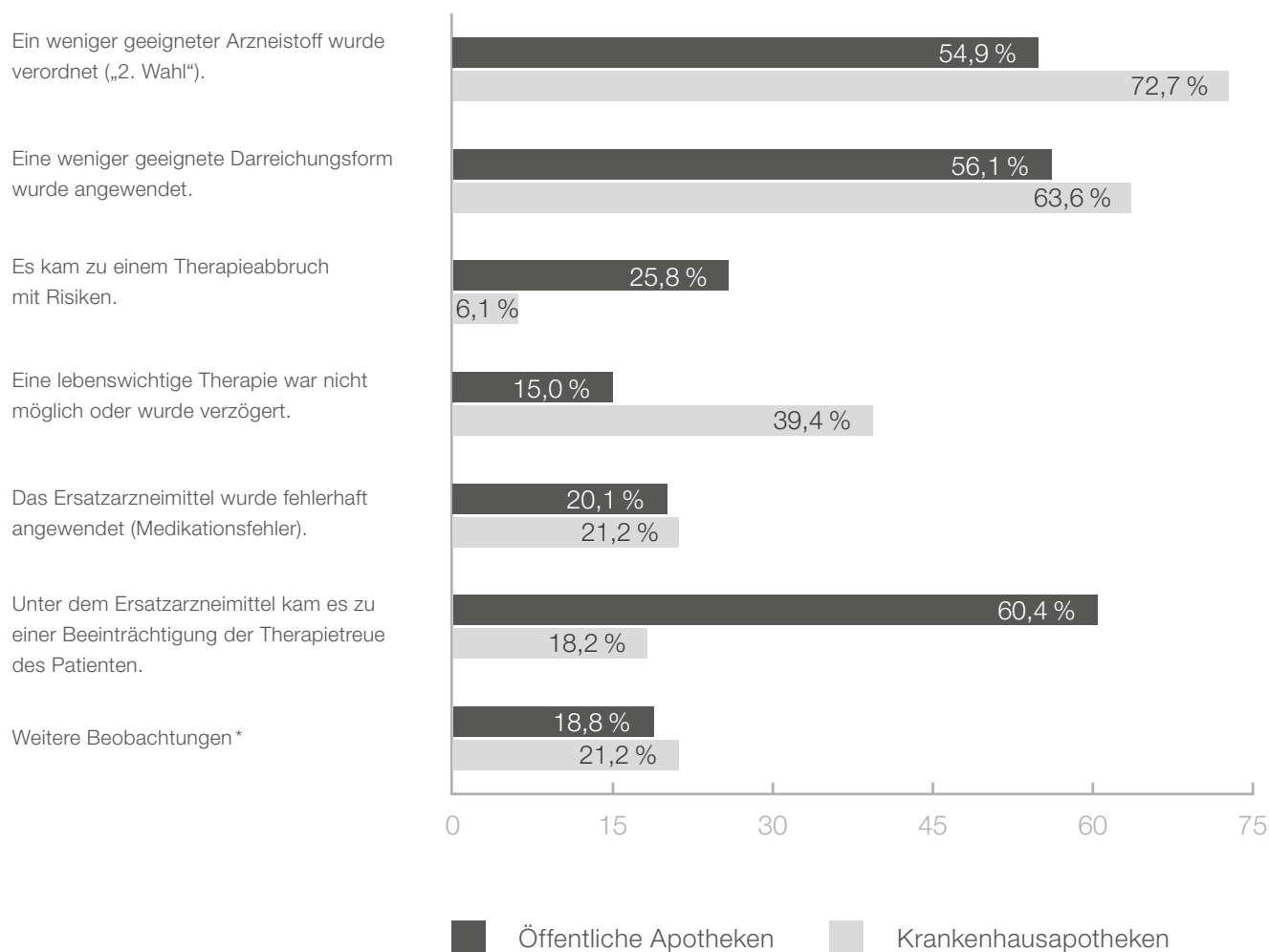
	Öffentliche Apotheken	Krankenhausapotheken
nie	11,4 %	19,4 %
< 5 mal	27,6 %	25,0 %
5 – 10 mal	28,2 %	33,4 %
11 – 15 mal	10,4 %	2,8 %
> 15 mal	22,4 %	19,4 %
	100 %	100 %

Quelle: Arzneimittelkommission der Deutschen Apotheker (AMK) 2017



Quelle: Arzneimittelkommission der Deutschen Apotheker (AMK) 2017

Welche Beobachtung(en) haben Sie in Ihrer Apotheke in den letzten drei Monaten bei aufgetretenen Liefer- und Versorgungsengpässen gemacht (Mehrfachantworten sind möglich)?



* erhöhter Zeit- und Beratungsaufwand, erhöhte Verunsicherung des Patienten u.a.

Quelle: Arzneimittelkommission der Deutschen Apotheker (AMK) 2017

QUALITÄTSSICHERUNG BEI REZEPTUREN

Das Zentrallaboratorium Deutscher Apotheker (ZL) in Eschborn trägt durch seine Ringversuche zur Qualitätssicherung bei Rezepturen bei. Alle Apotheken können daran teilnehmen, indem sie vom ZL spezifizierte Rezepturen anfertigen, einschicken und auf Wirkstoffidentität, -gehalt und -verteilung sowie weitere Prüfparameter wie pH-Wert, Partikelgröße, Dichte etc. überprüfen lassen. Der Trend geht seit Jahren eindeutig nach oben: Mehr als jede dritte Apotheke nimmt inzwischen mindestens einmal pro Jahr an dieser freiwilligen Qualitätsprüfung teil.

Ringversuche des Zentrallaboratoriums Deutscher Apotheker (ZL)

Jahr	Teilnehmerzahl (untersuchte Rezepturen)	Apothekenzahl*	Prozentuale Teilnahme (bezogen auf die Gesamtapothekenzahl)
2019	8.899	6.862	35,3
2018	8.945	6.684	33,8
2017	8.600	6.437	32,0
2016	7.733	6.019	29,5
2015	7.674	6.086	29,5
2014	8.079	5.706	27,4
2013	6.578	4.955	23,5
2012	5.877	4.191	19,6
2011	4.845	3.490	16,1
2010	4.738	3.286	15,0
2009	3.956	2.897	13,2

Anmerkung: Veränderte Zuordnungssystematik im Vergleich zur Vorjahrespublikation (inkl. Spezial- und Kapsel-Ringversuche)

* Öffentliche Apotheken und Krankenhausapotheken (Teilnehmeranzahl beinhaltet Mehrfach-Teilnahmen einzelner Apotheken)

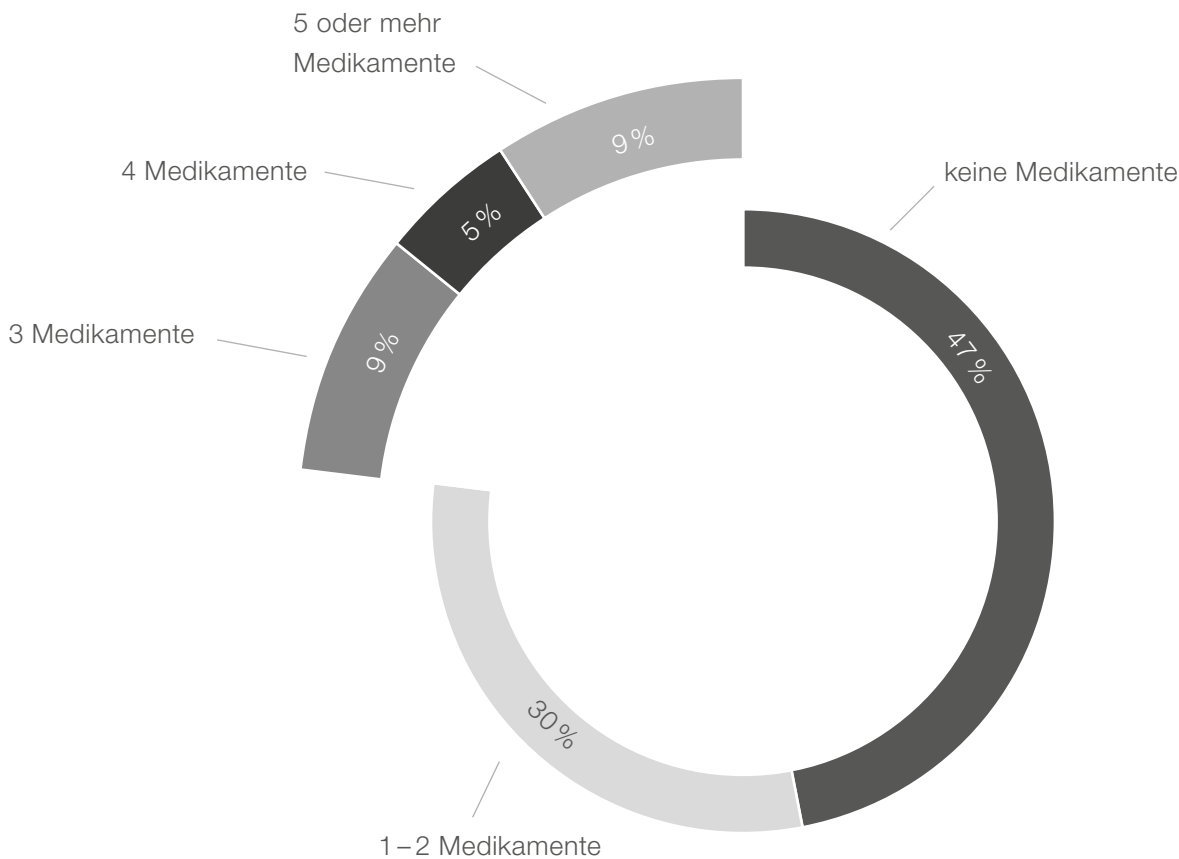
Quelle: Zentrallaboratorium Deutscher Apotheker e. V. (ZL)

HERAUSFORDERUNG POLYMEDIKATION

Polymedikation (Synonym: Multimedikation) liegt vor, wenn ein Patient parallel mehrere systemisch wirkende Medikamente dauerhaft einnimmt. Je nach Definition geht man von mindestens drei oder fünf solcher Arzneimittel aus. Etwa jeder vierte Bundesbürger nimmt permanent drei oder mehr Arzneimittel ein. Um den Risiken der Polymedikation zu begegnen, gibt es verschiedene Initiativen für ein Medikationsmanagement, wie z. B. ARMIN („Arzneimittelinitiative Sachsen-Thüringen“) oder PRIMA („Primärsystem-Integration des Medikationsplans mit Akzeptanzuntersuchung“).

Jeder Vierte ist von Polymedikation betroffen

23 % aller erwachsenen Bundesbürger (15 Millionen) nehmen dauerhaft drei oder mehr Medikamente ein.



Patienten mit Polymedikation

Probleme mit Polymedikation	
Ja	40 %
Nein	60 %

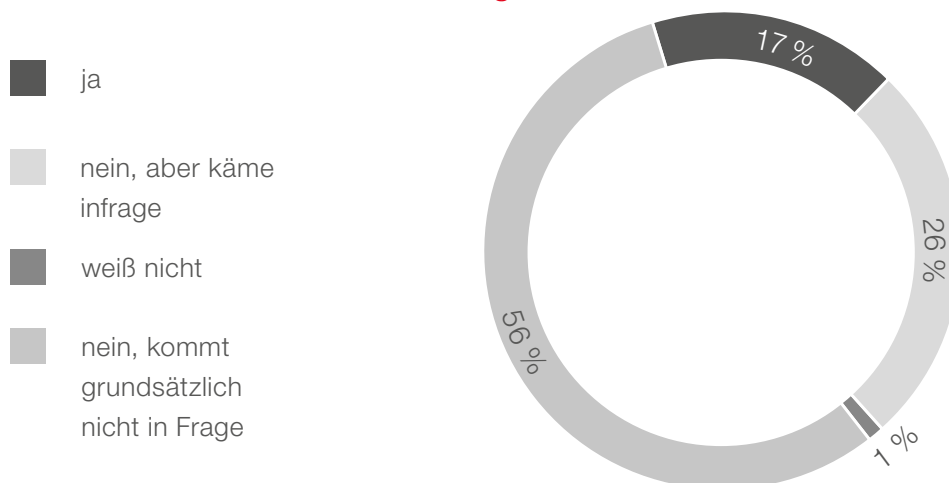
Art der Medikamente	
nur rezeptpflichtige Medikamente	71 %
auch rezeptfreie Medikamente	29 %

Quelle: Forsa Gesellschaft für Sozialforschung und statistische Analysen mbH (Erhebung 2015)

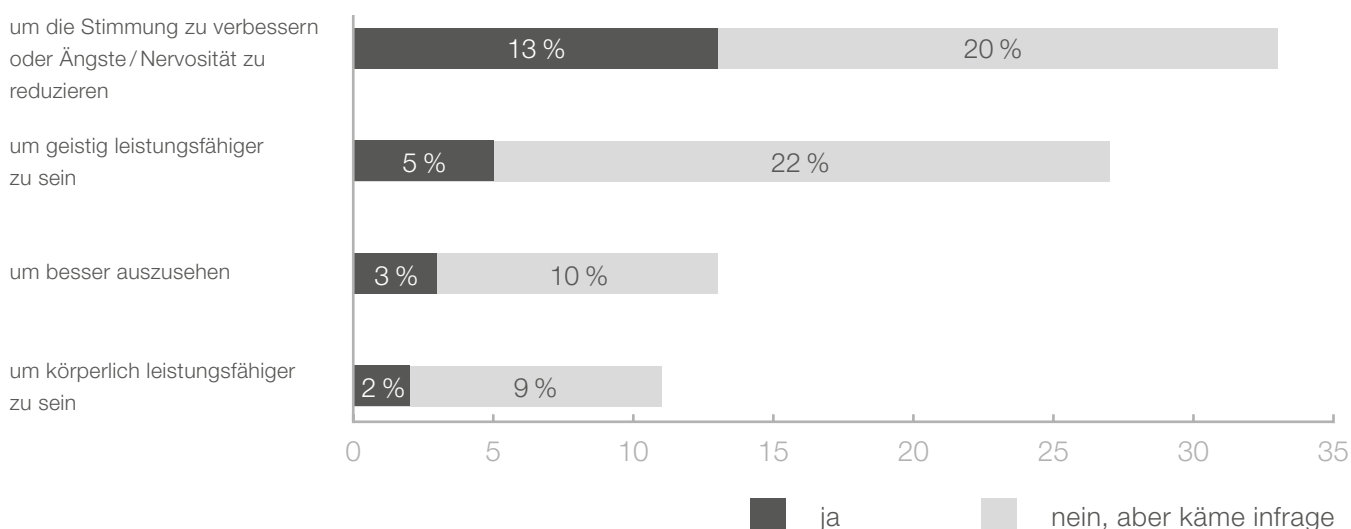
RISIKO ARZNEIMITTELMISSBRAUCH

Etwa 4 bis 5 Prozent aller verordneten Arzneimittel in Deutschland wird ein Missbrauchs- oder Abhängigkeitspotenzial zugeschrieben. Die Gesamtzahl der Betroffenen wird auf 1,4 bis 1,5 Millionen geschätzt. Am häufigsten ist die Abhängigkeit von Schlaf- und Beruhigungsmitteln. Bei Substanzen, die eine körperliche Abhängigkeit hervorrufen können, muss zwischen einem Missbrauch und einer Abhängigkeit unterschieden werden. Bei Substanzen, die keine körperliche Abhängigkeit zur Folge haben, ist nur ein Missbrauch möglich. Bezogen auf das Gesamtsortiment enthalten 10 bis 12 Prozent der in der Selbstmedikation abgegebenen Packungen Wirkstoffe, bei denen es ein Missbrauchspotenzial gibt.

Erfahrung mit der Einnahme verschreibungspflichtiger Medikamente ohne medizinische Notwendigkeit *



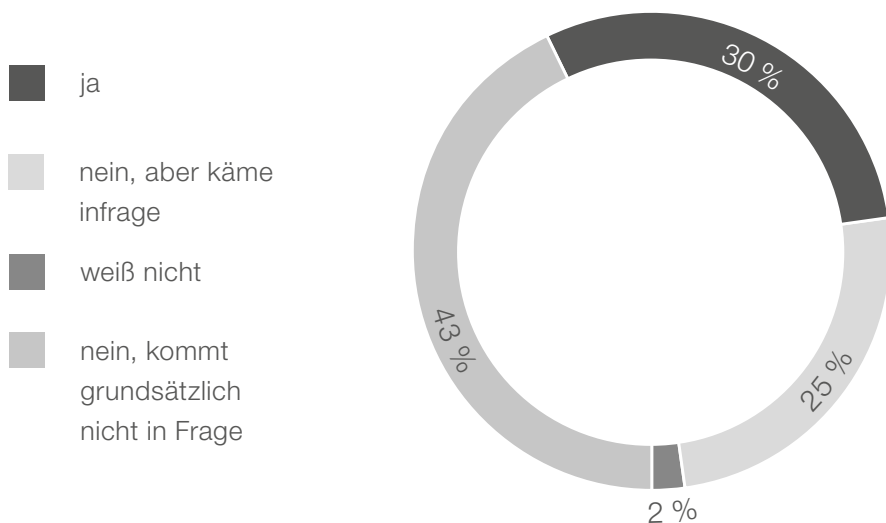
Bereitschaft zur Einnahme verschreibungspflichtiger Medikamente ohne medizinische Notwendigkeit *



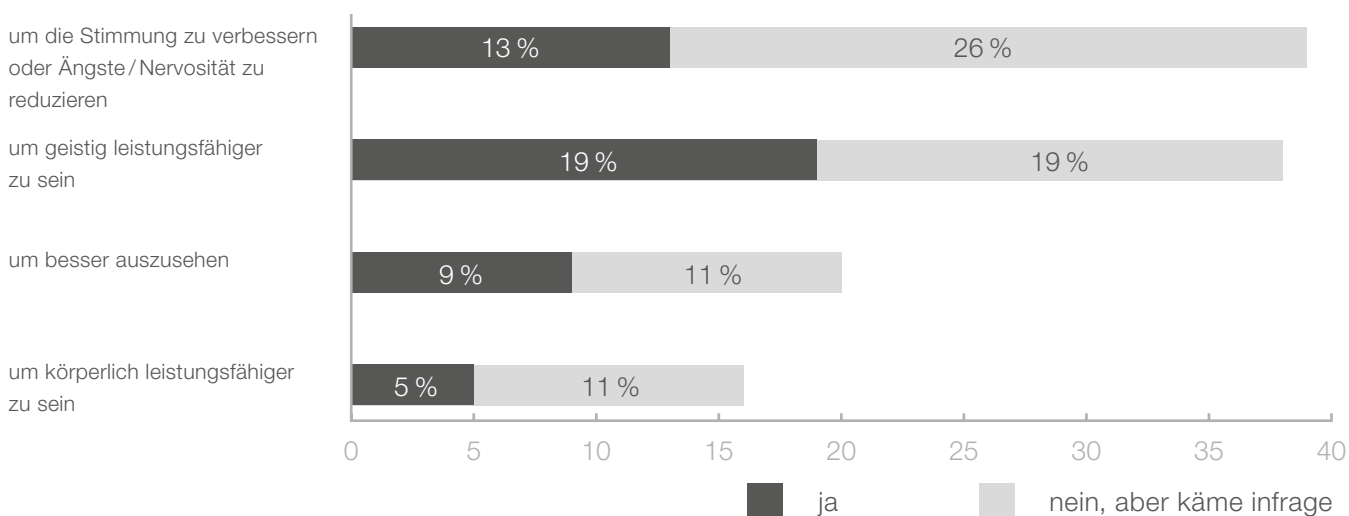
* Umfrage von Forsa im Auftrag der ABDA unter 5.008 Deutschen im Alter von 16 bis 70 Jahren. Der Erhebungszeitraum erstreckte sich auf die Zeit vom 15. Dezember 2017 bis 5. Januar 2018.

Quelle: Bundesapothekerkammer, Deutsche Hauptstelle für Suchtfragen (DHS), Forsa Gesellschaft für Sozialforschung und statistische Analysen mbH

Erfahrung mit der Einnahme **nicht** verschreibungspflichtiger Medikamente ohne medizinische Notwendigkeit *



Bereitschaft zur Einnahme **nicht** verschreibungspflichtiger Medikamente ohne medizinische Notwendigkeit *



* Umfrage von Forsa im Auftrag der ABDA unter 5.008 Deutschen im Alter von 16 bis 70 Jahren. Der Erhebungszeitraum erstreckte sich auf die Zeit vom 15. Dezember 2017 bis 5. Januar 2018.

Quelle: Bundesapothekerkammer, Deutsche Hauptstelle für Suchtfragen (DHS), Forsa Gesellschaft für Sozialforschung und statistische Analyse mbH

SECURPHARM

Die Europäische Fälschungsschutzrichtlinie ist im Jahr 2019 in Kraft getreten. In Deutschland ist dieser Schutzschild gegen Arzneimittelplagiate unter dem Namen „securPharm“ bekannt. Während die pharmazeutischen Unternehmen jede einzelne Packung von rezeptpflichtigen Medikamenten in einer Herstellerdatenbank hochladen, buchen die Apotheken jede Packung bei der Abgabe an den Patienten aus einer korrespondierenden Apothekendatenbank wieder aus. Da jede Packung mit Seriennummer und Erstöffnungsschutz ein Unikat ist, würde eine zweite Ausbuchung einen Fälschungsverdachtsalarm auslösen, der eingehend untersucht würde. Insofern macht „securPharm“ die Arzneimittel aus deutschen Apotheken noch sicherer als bisher.

securPharm-System und Nutzung in Zahlen

Akteure	
Pharmazeutische Unternehmen	386
Pharmazeutische Großhändler	945
Öffentliche Apotheken	19.075
Krankenhausapotheken	362



6,2 Mio.

Transaktionen pro Tag



62.404

Serialisierungspflichtige
Produkte



1,05 Mrd.

Hochgeladene Packungsdaten

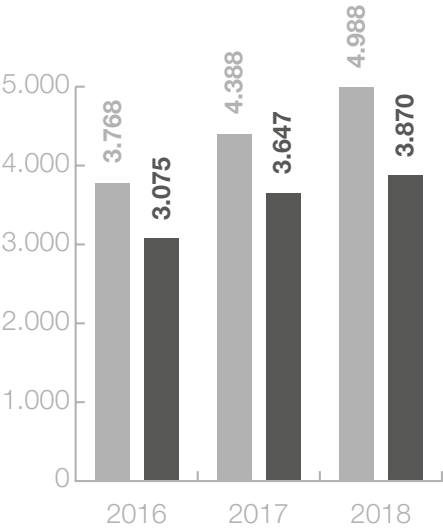
Stand: 31. 12. 2019

Quelle: securPharm e.V.

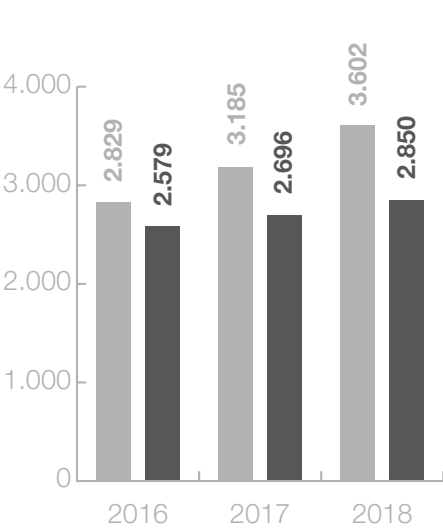
ARZNEIMITTEL FÜR SCHWERE ERKRANKUNGEN

Bei den innovativen Fertigarzneimitteln spielen in jüngerer Vergangenheit vor allem Onkologika (gegen Krebserkrankungen) und Immunsuppressiva (gegen körpereigene Abstoßungsreaktionen) eine wichtige Rolle. Den Kosten steht der jeweilige therapeutische Nutzen gegenüber. Neben Fertigarzneimitteln werden in der onkologischen Therapie auch individuell hergestellte Spezialrezepturen (Zytostatika) eingesetzt. Darüber hinaus gibt es auch Parenterale Lösungen, zur intravenösen Verabreichung u. a. mit monoklonalen Antikörpern. Die Herstellung aller dieser Spezialrezepturen unterliegt besonderen technischen Anforderungen, die bundesweit von etwa 300 Apotheken mit einem speziellen Reinraumlabor gemäß § 35a Apothekenbetriebsordnung erfüllt werden.

Immunsuppressiva



Onkologika



Umsatz in Mio. EUR
 Absatz in Tsd. Packungen

In öffentlichen Apotheken zulasten der GKV abgegebene Fertigarzneimittel.

Zytostatika

	2016		2017		2018	
	Verordnungen (Mio.)	Umsatz (Mio. EUR)	Verordnungen (Mio.)	Umsatz (Mio. EUR)	Verordnungen (Mio.)	Umsatz (Mio. EUR)
Zytostatika-Zubereitungen	2,4	1.245	2,3	1.163	2,2	1.022
Parenterale Lösungen	1,2	2.388	1,4	2.773	1,6	3.105
darunter: mit monoklonalen Antikörpern	0,8	2.199	0,9	2.576	1,0	2.896

In öffentlichen Apotheken zulasten der GKV angefertigte Spezialrezepturen.

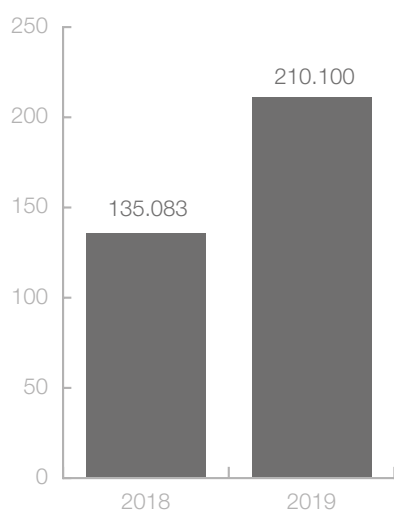
Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI), Arzneiverordnungsreport (AVR)

MEDIZINISCHES CANNABIS

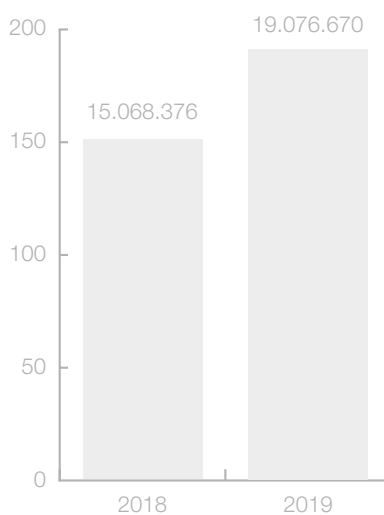
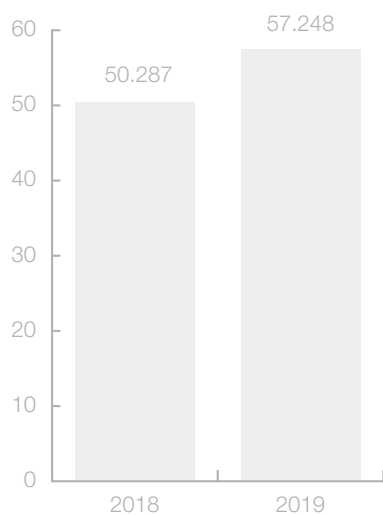
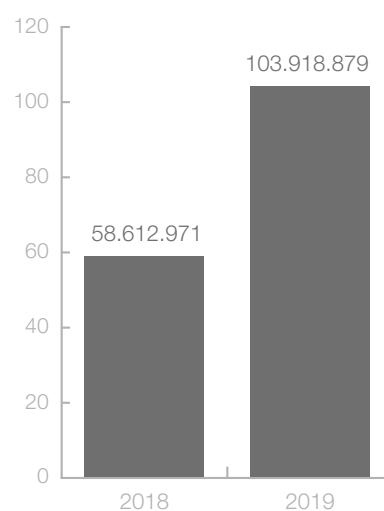
Seit dem 10. März 2017 dürfen Ärzte im Rahmen ihrer Therapiefreiheit im Einzelfall medizinisches Cannabis verordnen. Jede Apotheke kann entsprechende Rezepturarzneimittel herstellen und abgeben. Cannabis kann in verschiedenen Formen verordnet werden, zum Beispiel als Blüten oder als isolierter Hauptwirkstoff Dronabinol, auch als „THC“ bekannt. Über die Dosis und die Anwendungsform entscheidet der Arzt. Apotheker geben ihren Patienten bei der Abgabe des Rezepturarzneimittels entsprechende Anweisungen mit. Wenn eine Genehmigung vorliegt, übernehmen die Krankenkassen die Kosten für ärztlich verordnete Rezepturarzneimittel.

Cannabis-Verordnungen für GKV-Versicherte

Verordnungen



Umsatz in EUR



■ Cannabis-haltige Zubereitungen
und unverarbeitete Cannabis-Blüten

■ Cannabis-haltige Fertigarzneimittel

Anmerkung: Die genaue Zahl der Verordnungen liegt für 2017 aufgrund von Änderungen in der Erhebungsbasis nicht vor. Die Ausgaben der GKV lagen in diesem Jahr bei ca. 30 Mio. Euro. Laut Berechnungen des Deutschen Arzneiprüfungsinstituts (DAPI) wurden 2017 insgesamt 79.004 Abgabeeinheiten verordnet, davon 34.780 Fertigarzneimittel und 44.224 Zubereitungen/Blüten.

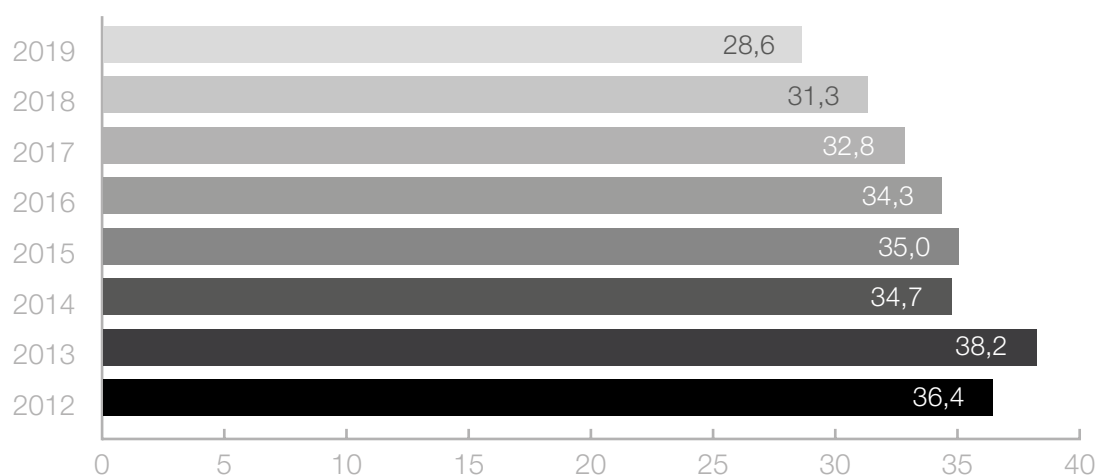
Quelle: GKV-Spitzenverband

ANTIBIOTIKA

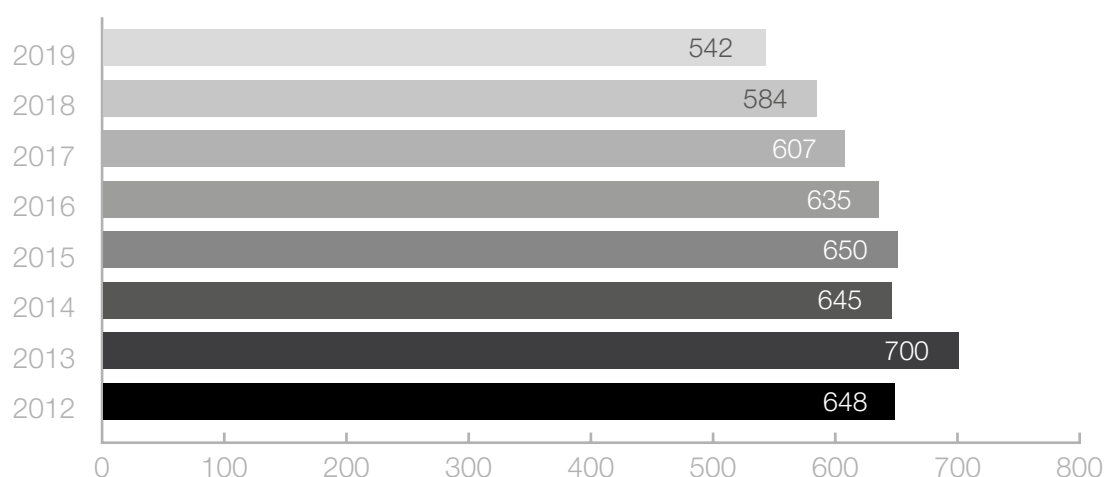
Antibiotika sind unerlässlich zur Therapie bakterieller Infektionen. Falscher bzw. zu häufiger Einsatz begünstigt aber die Entstehung resistenter Bakterienstämme, gegen die bestimmte Antibiotika wirkungslos werden. Zum richtigen Umgang mit Antibiotika gehört unter anderem, dass Antibiotika nur nach ärztlicher Verordnung eingenommen werden. Der Einsatz von Antibiotika ist in Deutschland seit 2013 rückläufig.

Orale Antibiotika

abgegebene Packungen in Mio.



Umsatz in Mio.



In öffentlichen Apotheken zulasten der GKV abgegebene orale Antibiotika. Verordnungen von Zahnärzten sind unberücksichtigt.

Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

ANTIDIABETIKA UND BLUTZUCKERTESTSTREIFEN

In Deutschland sind derzeit etwa 7 Millionen Menschen an Diabetes mellitus erkrankt. Etwa 95 Prozent leiden an Diabetes Typ 2. Der Verlauf und die Prognose einer Diabetes-Erkrankung hängen entscheidend vom Verhalten des jeweiligen Patienten ab. Diabetiker werden in den öffentlichen Apotheken mit Medikamenten versorgt und auf Wunsch dauerhaft begleitet. Dazu gehört nicht nur die Abgabe von Arzneimitteln, sondern auch die Versorgung mit Blutzuckermessgeräten und die Abgabe von dazugehörigen Blutzuckerteststreifen. Die Apothekerverbände schließen dazu Versorgungsverträge auf Bundes- und Landesebene mit Krankenkassen ab.

Wirkstoffe, die vorrangig zur Behandlung von Diabetes eingesetzt werden*

2019	Absatz pro 1.000 GKV-Versicherte	Umsatz pro 1.000 GKV-Versicherte
Orale Antidiabetika	235	13.600 €
Insuline	156	18.600 €
Sonstige subkutane** Antidiabetika	14	4.300 €
Alle Antidiabetika	404	36.500 €

Blutzuckerteststreifen***

	2017	2018	2019
Abgegebene Packungen in Mio.	23,8	22,4	20,6
Stückzahlen in Mio.	1.235	1.158	1.062
Umsatz in Mio. EUR (inkl. MwSt.)	630,5	584,9	533,5

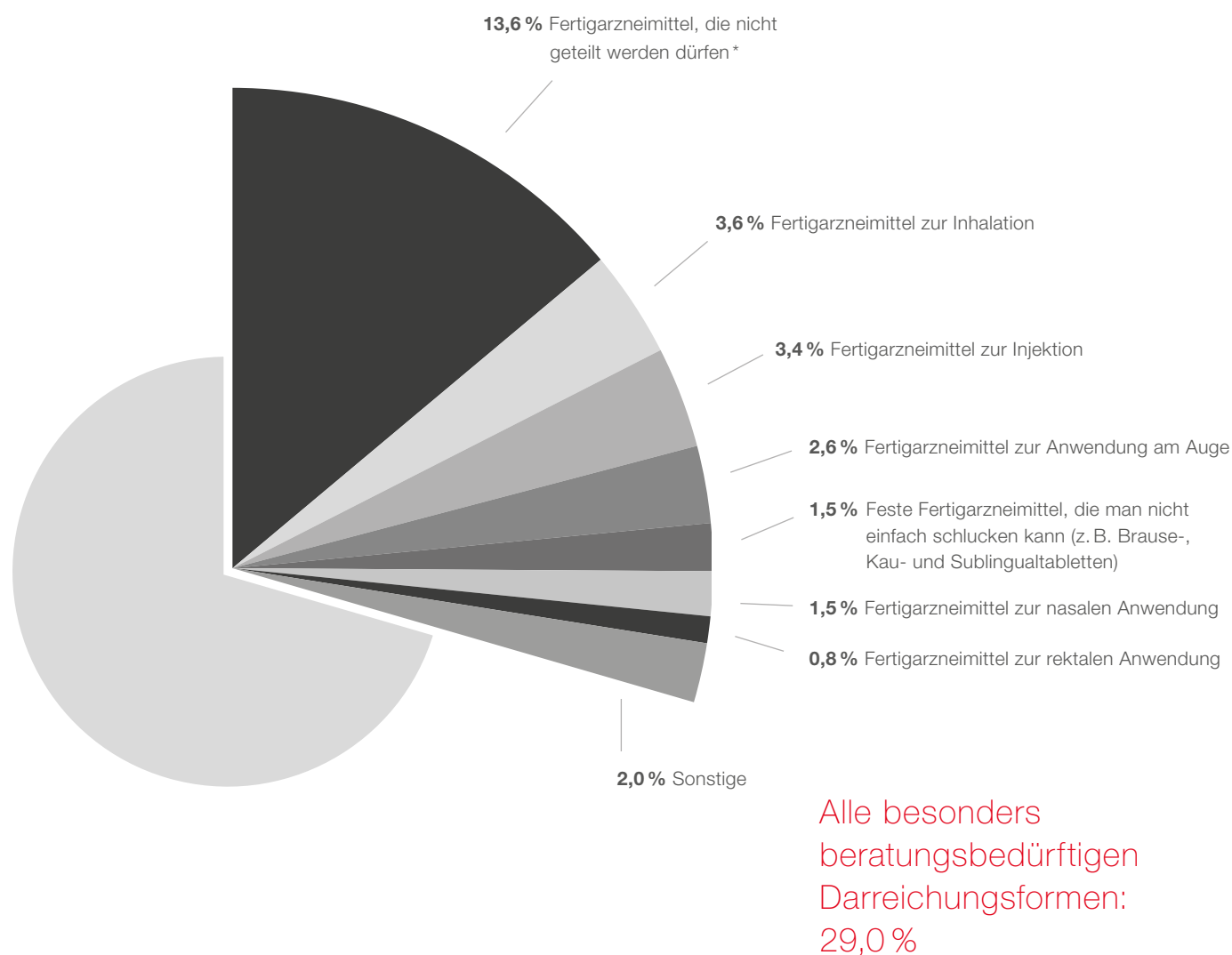
* In öffentlichen Apotheken zulasten der GKV abgegebene Antidiabetika.

** zur Injektion unter die Haut

*** In öffentlichen Apotheken zulasten der GKV abgegebene Blutzuckerteststreifen (exklusive Sprechstundenbedarf).

BERATUNGSINTENSIVE ARZNEIMITTEL

Pro Jahr geben die Apotheken schätzungsweise etwa 200 Millionen Arzneimittel ab, die – unabhängig vom Wirkstoff – allein wegen ihrer Darreichungsform besonders beratungsintensiv sind. Das sind 29 Prozent aller zulasten der Gesetzlichen Krankenversicherung abgegebenen Fertigarzneimittel (gesamt: rund 650 Mio.). Die Beratung und Abgabe sind z. B. dann aufwendig, wenn bei einem Asthmaspray die Anwendung des Inhalators demonstriert werden muss.



* Darreichungsformen wie magensaftresistente Medikamente oder Retard-Arzneimittel, die nicht ohne Rücksprache mit dem Arzt bzw. Apotheker geteilt werden sollten

Auswertung für das Jahr 2018

Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

ARZNEIMITTEL MIT SPEZIFISCHEN ANFORDERUNGEN

Für bestimmte Arzneimittelgruppen gelten besondere Auflagen. Beispielsweise erfordern Betäubungsmittel (starke Schmerzmittel) ein besonderes Rezept und eine besondere Dokumentation, um Missbrauch oder unerwünschte Wirkungen zu vermeiden. Dasselbe gilt für Thalidomid-haltige Arzneimittel (T-Rezept). Auch für temperaturempfindliche Arzneimittel gelten besondere Vorgaben, um ihre Haltbarkeit sicherzustellen.

Absatz in Packungen	
Betäubungsmittel (Fertigarzneimittel)	10,6 Mio.
Betäubungsmittel (Rezepturen)	7,1 Mio.
Auf T-Rezept verordnete Arzneimittel	81.000
Blutprodukte nach Transfusionsgesetz	323.000
Kühlartikel (Lagertemperatur max. 8 °C)	19,2 Mio.
Kühlkettenpflichtige Arzneimittel*	8,8 Mio.

* müssen innerhalb der gesamten Lieferkette sowie bei der Lagerung ohne Unterbrechung zwischen 2 °C und 8 °C gekühlt werden (z.B. Impfstoffe)

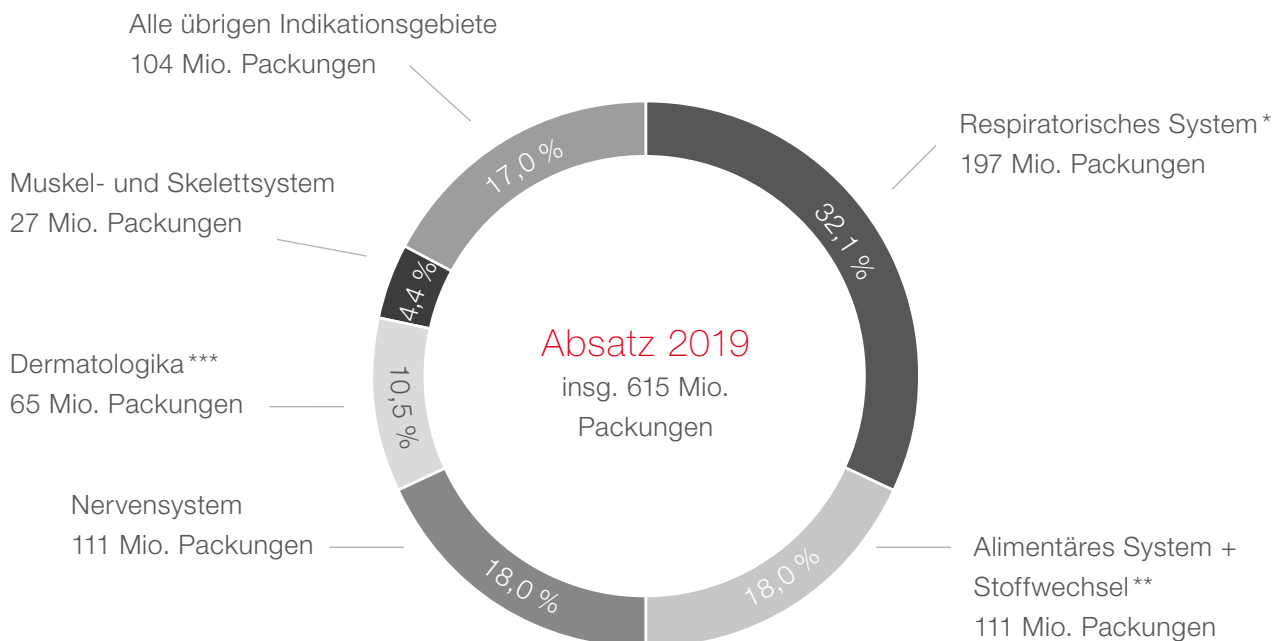
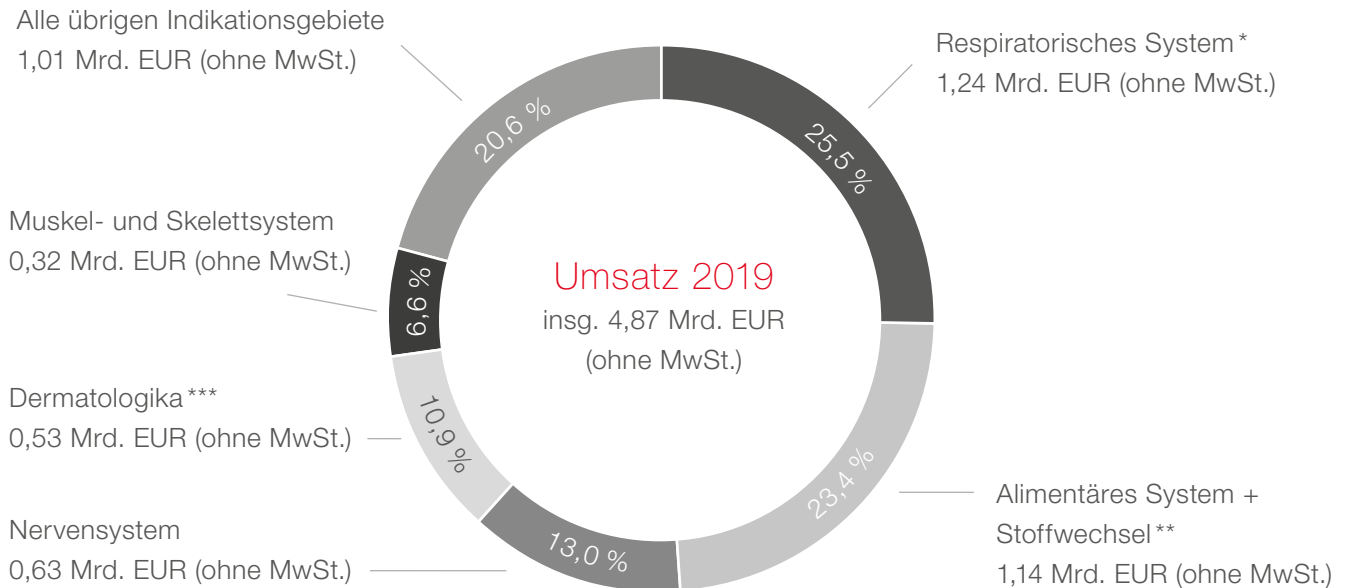
In öffentlichen Apotheken zulasten der GKV abgegebene Fertigarzneimittel, Rezepturen und Impfstoffe

Auswertung für das Jahr 2018

Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

OTC-ARZNEIMITTEL: FÜHRENDE INDIKATIONSGBIETE

Bei OTC-Präparaten (OTC = Over-the-Counter = über den Handverkaufstisch) handelt es sich um rezeptfreie – apothekenpflichtige oder freiverkäufliche – Arzneimittel, die vorrangig im Bereich der Selbstmedikation abgegeben werden. Die Beratung in der Apotheke ist besonders wichtig, da dort die Eigendiagnose des Patienten hinterfragt werden kann. Durch Erkältungswellen oder Pollenallergien kann es im Laufe des Jahres zu erheblichen Bedarfschwankungen kommen.



* unter anderem Atemwegserkrankungen

** vor allem Magen-Darm-Erkrankungen

*** Mittel gegen Hauterkrankungen

Quelle: Insight Health GmbH & Co. KG

REZEPTFREIE ARZNEIMITTEL: BESONDERE THERAPIERICHTUNGEN

Zu den besonderen Therapierichtungen im Arzneimittelgesetz (AMG) gehören Pflanzliche, Homöopathische und Anthroposophische Arzneimittel. Die rezeptfreien Medikamente (inkl. Gesundheitsmittel) werden durchaus häufig in Apotheken nachgefragt.

Umsatzentwicklung

in Mio. EUR (ohne MwSt.)

	2017	2018	2019
Pflanzliche Arzneimittel	986	989	986
Homöopathische Arzneimittel	392	380	368
Anthroposophische Arzneimittel	88	90	92

Absatzentwicklung

in Mio. Packungen

	2017	2018	2019
Pflanzliche Arzneimittel	103	101	98
Homöopathische Arzneimittel	37	35	33
Anthroposophische Arzneimittel	9	9	9

GRÜNES REZEPT

Mit dem Grünen Rezept können Ärzte ihren Patienten rezeptfreie Arzneimittel empfehlen, die sie dann in der Apotheke selbst bezahlen. Allerdings enthält das Formular auch den Hinweis, dass man das Grüne Rezept bei vielen Krankenkassen zur Erstattung im Rahmen einer Satzungsleistung einreichen kann. In jedem Fall dient das Grüne Rezept dem Patienten als Merkhilfe bezüglich Name, Wirkstoff und Darreichungsform.

Verordnungen 2019 in Mio.

Rezeptfreie Arzneimittel auf grünem Rezept

45,4

TOP 10 Arzneimittelgruppen:

23,8

Auswurfmittel ohne antiinfektive Komponente (R05C)	6,5
topische Schnupfenmittel (R01A)	3,4
Schmerzmittel (N02B)	2,4
Halsschmerzmittel (R02A)	2,3
Antithrombosemittel (B01C) *	2,1
Mittel gegen Verstopfung (A06A)	1,6
Mikroorganismen gegen Diarrhoe (A07F)	1,5
Husten- und Erkältungsmittel (R05F)	1,5
Dermatologische Antimykotika (D01A)	1,4
Systemische Antihistamine (R06A)	1,2

* Thrombozytenaggregationshemmer

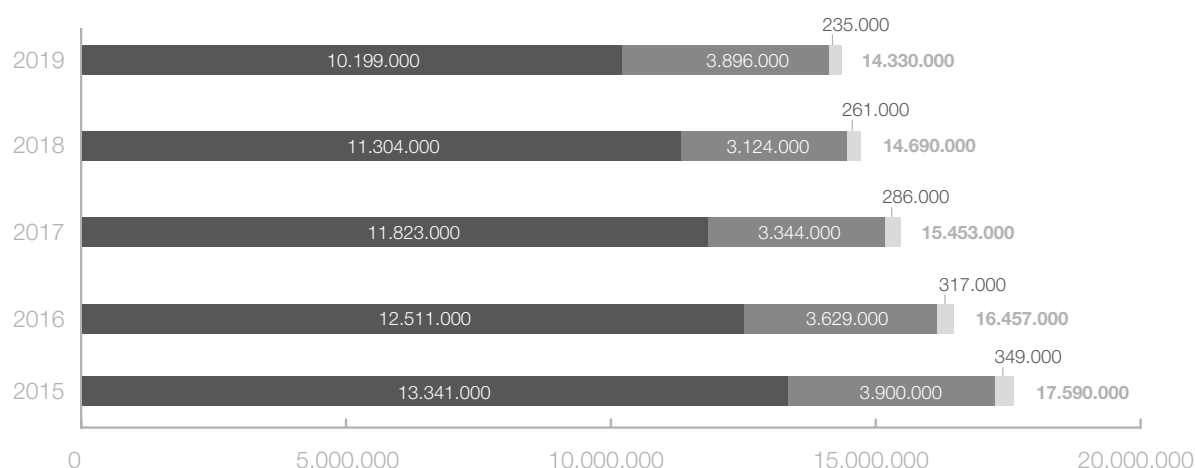
Quelle: IQVIA Commercial GmbH & Co. OHG (IMS Diagnosis Monitor)

VERSORGUNG MIT VERHÜTUNGSMITTELN

Seit 15. März 2015 sind Notfallverhütungsmittel (Notfallkontrazeptiva, „Pille danach“) rezeptfrei in der Apotheke erhältlich. Der Gesetzgeber wollte Frauen den Zugang zu diesem Verhütungsmittel erleichtern. Dementsprechend sind die Absatzzahlen in der Selbstmedikation angestiegen, während es einen deutlichen Rückgang ärztlicher Verordnungen gegeben hat. Wie bei anderen Kontrazeptiva auch, haben Frauen bis zur Vollendung des 22. Lebensjahres einen Anspruch auf die Kostenerstattung durch ihre gesetzliche Krankenkasse, müssen sich das Medikament dafür aber von einem Arzt auf einem rosa Rezept verordnen lassen.

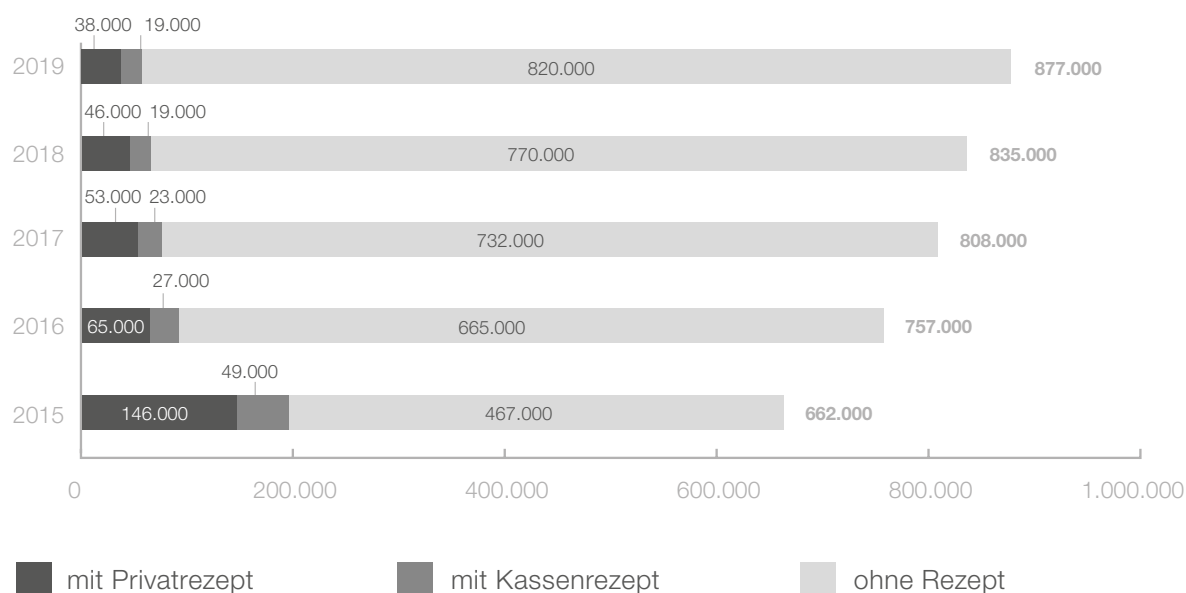
Absatz von Kontrazeptiva in öffentlichen Apotheken

abgegebene Packungen (ohne Notfallkontrazeptiva)



Absatz von Notfallkontrazeptiva in öffentlichen Apotheken

abgegebene Packungen



Quelle: Insight Health GmbH & Co. KG

HILFSMITTELVERSORGUNG

Neben Sanitätshäusern können auch Apotheken die Versicherten der Gesetzlichen Krankenversicherung (GKV) mit Hilfsmitteln versorgen. Das erfordert zumeist die Teilnahme der Apotheke an einem Versorgungsvertrag zwischen Krankenkasse und Apothekerverband. Voraussetzung dafür ist die sogenannte Präqualifizierung, die je nach Hilfsmittelgruppe schon vorab alle notwendigen Voraussetzungen für die Versorgung bestätigt. Rund 18.000 Apotheken besitzen mindestens eine produktgruppenspezifische Präqualifizierung.

GKV-Hilfsmittelumsatz * in öffentlichen Apotheken

in Mio. EUR

Applikationshilfen (z. B. Insulin-Pens)	264
Inkontinenzhilfen (z. B. Bettbeutel)	119
Hilfsmittel zur Kompressionstherapie (z. B. Kompressionsstrümpfe)	97
Messgeräte für Körperzustände / -funktionen (z. B. Lanzetten und Blutdruckmessgeräte)	48
Inhalations- und Atemtherapiegeräte (z. B. Vernebler)	42
Zum Verbrauch bestimmte Pflegehilfsmittel (z. B. Handschuhe und Mundschutze)	28
Absauggeräte (z. B. Milchpumpen)	20
Sehhilfen (z. B. Augenpflaster)	19
Bandagen	10
Stomaartikel	7
Orthesen/Schienen	6
übrige Produktgruppen	17
Insgesamt	677 Mio. EUR (inkl. MwSt.)

* Einzelverordnungen und Sprechstundenbedarf zu Apothekenverkaufspreisen
Auswertung für das Jahr 2018

Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

IMPFSTOFFE

Die Gesetzliche Krankenversicherung (GKV) gibt mehr als eine Milliarde Euro pro Jahr (inkl. MwSt.) für Impfstoffe aus. Sie werden in der Regel als Sprechstundenbedarf auf einem rosa Rezept verordnet. Grippewellen und Empfehlungen der Ständigen Impfkommission sind für saisonale oder mehrjährige Veränderungen verantwortlich.

	2017	2018	2019
GKV-Ausgaben für Impfstoffe (in Mio. EUR)	1.205	1.290	1.503
Impfstoffpackungen* (in Mio.)	5,1	5,2	6,1

Aufteilung der Impfstoffe im Jahr 2018**	Umsatz in Mio. EUR (inkl. MwSt.)	Absatz in Mio. Impfdosen
Influenza (Grippe)	163	13,4
Pertussis (Keuchhusten)***	341	7,6
Pneumokokken	189	3,5
FSME (Frühsommer Meningoenzephalitis)	148	4,1
Masern****	133	2,0
Rotavirus	62	1,3
Meningokokken	35	0,9
Hepatitis	50	0,9
HPV (Humane Papillomaviren)	111	0,7
Sonstige	52	2,0
Insgesamt	1.284	36,4

* eine Packung enthält in der Regel mehrere Impfdosen

** Zahlen für das Jahr 2019 lagen bis Redaktionsschluss nicht vor.

*** inkl. Kombinationsimpfstoffe mit Diphtherie, Tetanus etc.

**** inkl. Kombinationsimpfstoffe mit Mumps, Röteln, Windpocken

In den Zahlen ist nur der Impfstoffbezug über öffentliche Apotheken berücksichtigt.

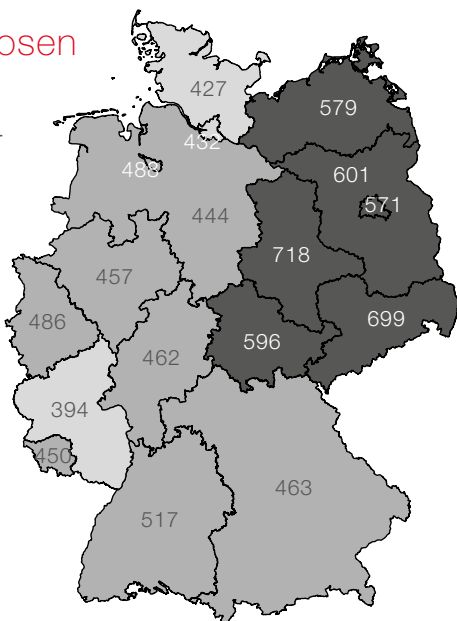
Quelle: Deutscher Apothekerverband e. V. (DAV), Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

Beim Impfen gibt es regionale und saisonale Unterschiede. Die höheren Zahlen in den neuen Bundesländern gehen vor allem auf die stärkere Durchimpfung von Influenza zurück. Bei Masern liegen einzelne ost- und westdeutsche Länder vorn. Bei FSME lässt sich der Schwerpunkt in Süddeutschland mit der dortigen Verbreitung der Zecken im Sommer erklären.

Zulasten der GKV abgegebene Impfdosen pro 1.000 GKV-Versicherte

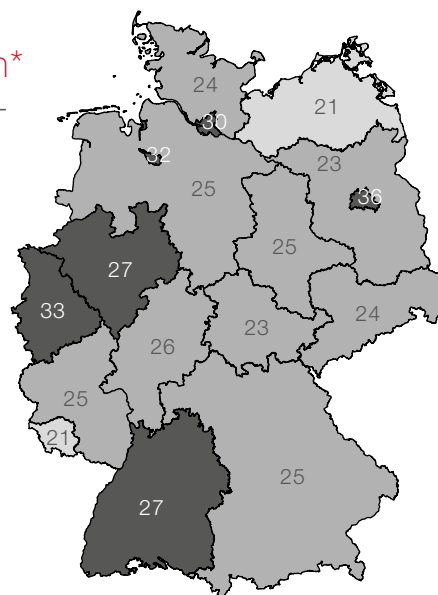
Impfstoffdosen gesamt

Bundesdurchschnitt: 480



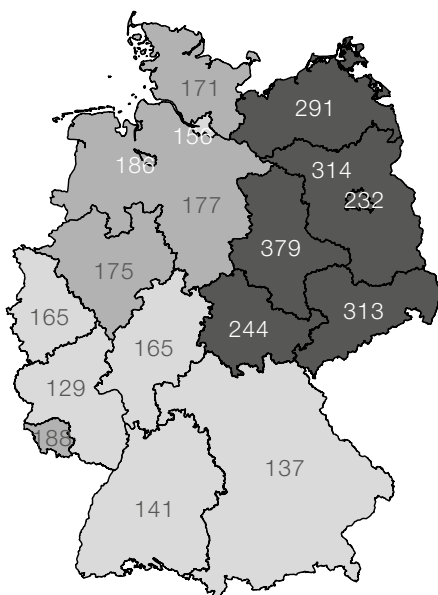
Masern-Impfdosen*

Bundesdurchschnitt: 24



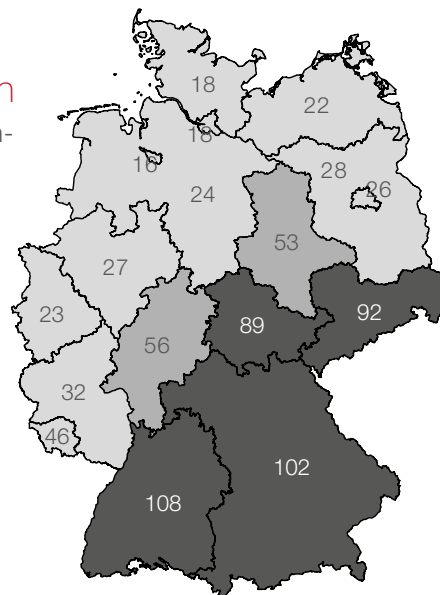
Influenza-Impfdosen

Bundesdurchschnitt: 184



FSME-Impfdosen

Bundesdurchschnitt: 54



* inkl. Kombinationsimpfstoffe mit Mumps, Röteln, Windpocken

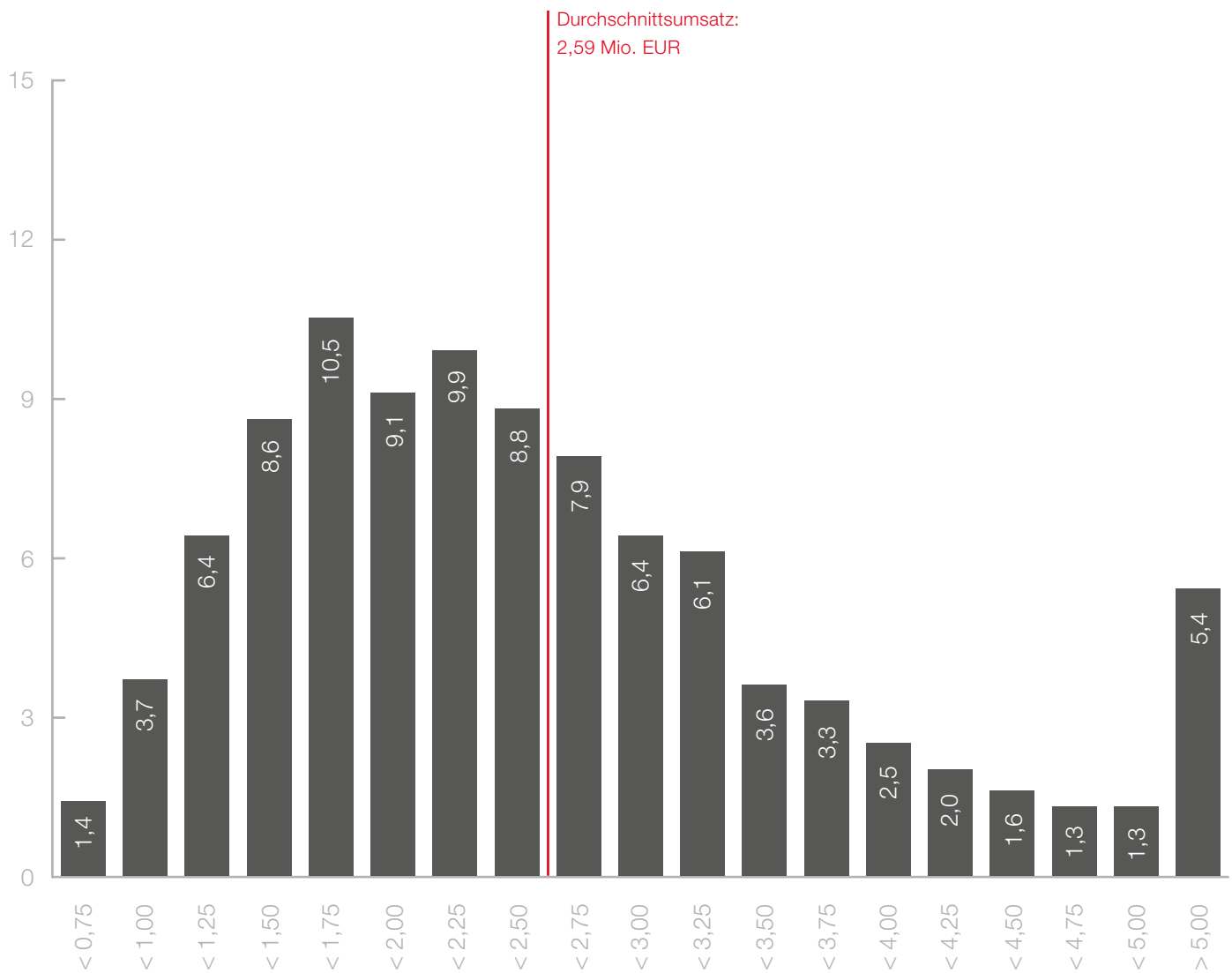
In den Zahlen ist nur der Impfstoffbezug über öffentliche Apotheken berücksichtigt.
Auswertungen für das Jahr 2018

Quelle: Deutsches Arzneiprüfungsinstitut e. V. (DAPI)

APOTHEKEN NACH UMSATZKLASSEN

Der durchschnittliche Netto-Umsatz einer Apotheke in Deutschland liegt bei ca. 2,59 Millionen Euro pro Jahr (ohne MwSt.). Allerdings gibt es eine sehr breite Streuung. Rund 60 Prozent der Apotheken erreichen den durchschnittlichen Umsatz nicht, während einzelne große Apotheken weit oberhalb des Durchschnitts liegen.

Anteil der Apotheken in Prozent



Umsatz in Mio. EUR (ohne MwSt.)

BETRIEBSWIRTSCHAFTLICHES ERGEBNIS DER DURCHSCHNITTLICHEN APOTHEKE

Drei Viertel des durchschnittlichen Umsatzes einer Apotheke von 2,59 Millionen Euro pro Jahr werden für den Wareneinsatz aufgewandt. Vom verbleibenden Rohertrag müssen Personal- und sonstige Kosten abgezogen werden. Der Gewinn vor Steuern lag 2019 im Schnitt bei 148.000 Euro. Dieser Betrag ist aber nicht einem Bruttogehalt gleichzusetzen, da der Apothekeninhaber als selbständiger Freiberufler davon nicht nur Steuern abführen, sondern auch Investitionen in die Apotheke tätigen und seine komplette Altersvorsorge bestreiten muss.

	2017	2018	2019
Nettoumsatz* in Tsd. EUR	2.315	2.381	2.587
– Wareneinsatz	1.760	1.815	1.991
= Rohertrag	555	567	596
– Personalkosten	247	256	272
– Sonstige steuerlich abzugsfähige Kosten	170	173	181
= steuerliches Betriebsergebnis (Gewinn vor Steuern)**	143	144	148
davon Teilbetriebsergebnis GKV***	84	83	84
davon Zuschüsse des Nacht- und Notdienstfonds	6	6	6

* ohne Umsatzsteuer und GKV-Abschläge

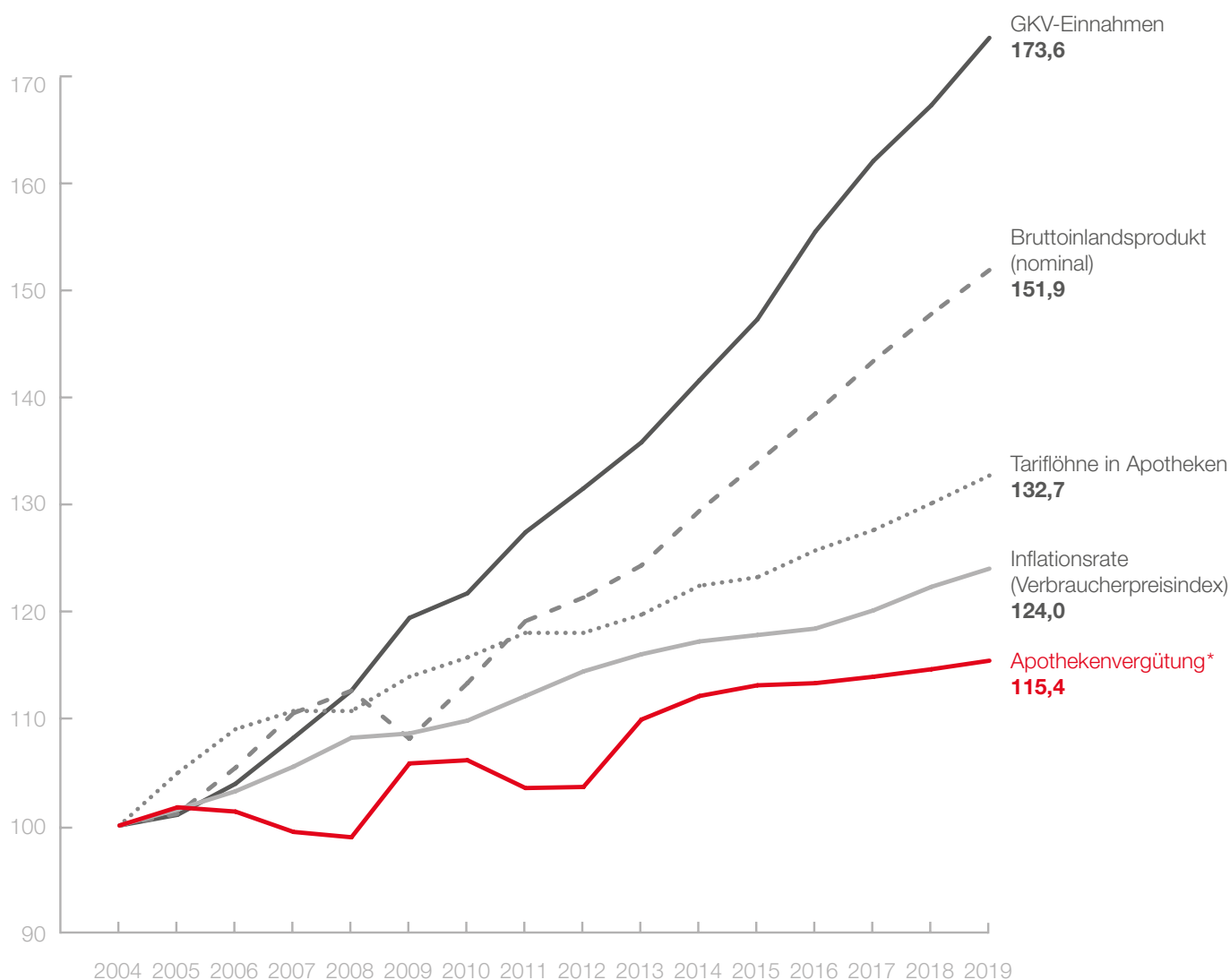
** inkl. Zuschüsse des Nacht- und Notdienstfonds

*** Die Kostenzuteilung erfolgte nach der hälftigen Umsatz-/Absatzmethode.

ENTWICKLUNG DER APOTHEKENVERGÜTUNG

Im Jahr 2004 wurde das Apothekenhonorar auf 8,10 Euro pro rezeptpflichtigem Arzneimittel festgelegt. 2013 wurde es erstmalig nach zehn Jahren auf 8,35 Euro erhöht. Hinzu kommt ein Zuschlag von drei Prozent des Apothekeneinkaufspreises sowie ein Zuschlag von 0,21 Euro zur Förderung des Nacht- und Notdienstes. Bei Arzneimitteln zulasten der GKV verringert der Apothekenabschlag von derzeit 1,77 Euro (inkl. MwSt.) das effektive Apothekenhonorar. Die Sachkosten (z. B. Energiekosten) und Personalkosten (z. B. Tariflöhne) sind deutlich stärker gestiegen als die Vergütung.

Index (2004 = 100)



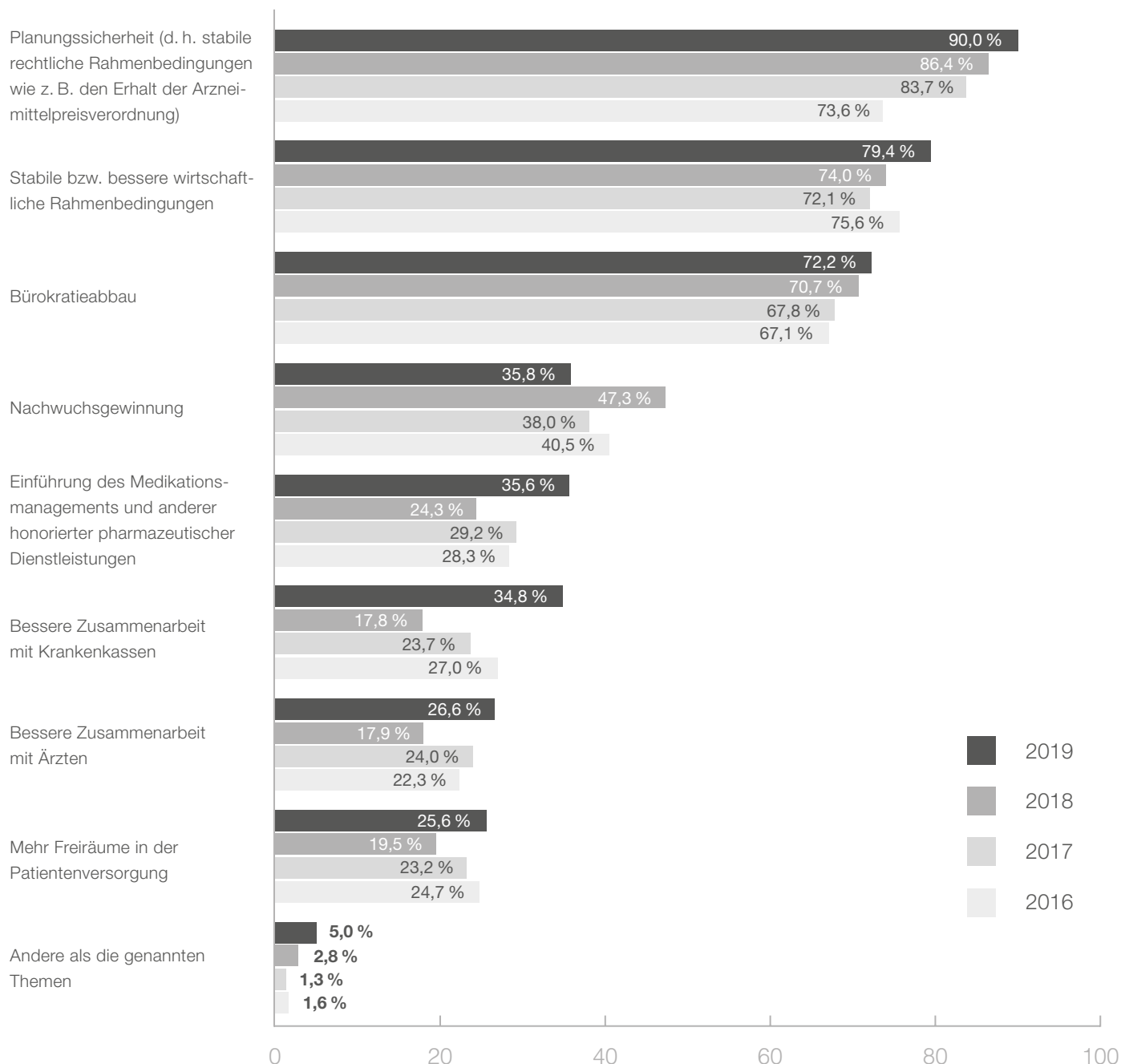
* Apothekenvergütung pro rezeptpflichtiger Arzneimittelpackung gemäß § 1 AMPreisV i. V. m. § 130 SGB V

Quelle: Bundesministerium für Gesundheit (BMG), Statistisches Bundesamt (Destatis), ADEXA, ABDA-Statistik

ZUKUNFTSERWARTUNGEN DER APOTHEKEN

Neben der retrospektiven Betrachtung der betriebswirtschaftlichen Ergebnisse sind auch die Zukunftserwartungen maßgeblich für die Bewertung der Gesamtsituation der Apotheken. Das Branchenklima hat sich in den letzten Jahren auch wegen ungelöster ordnungspolitischer Fragen eingetrübt.

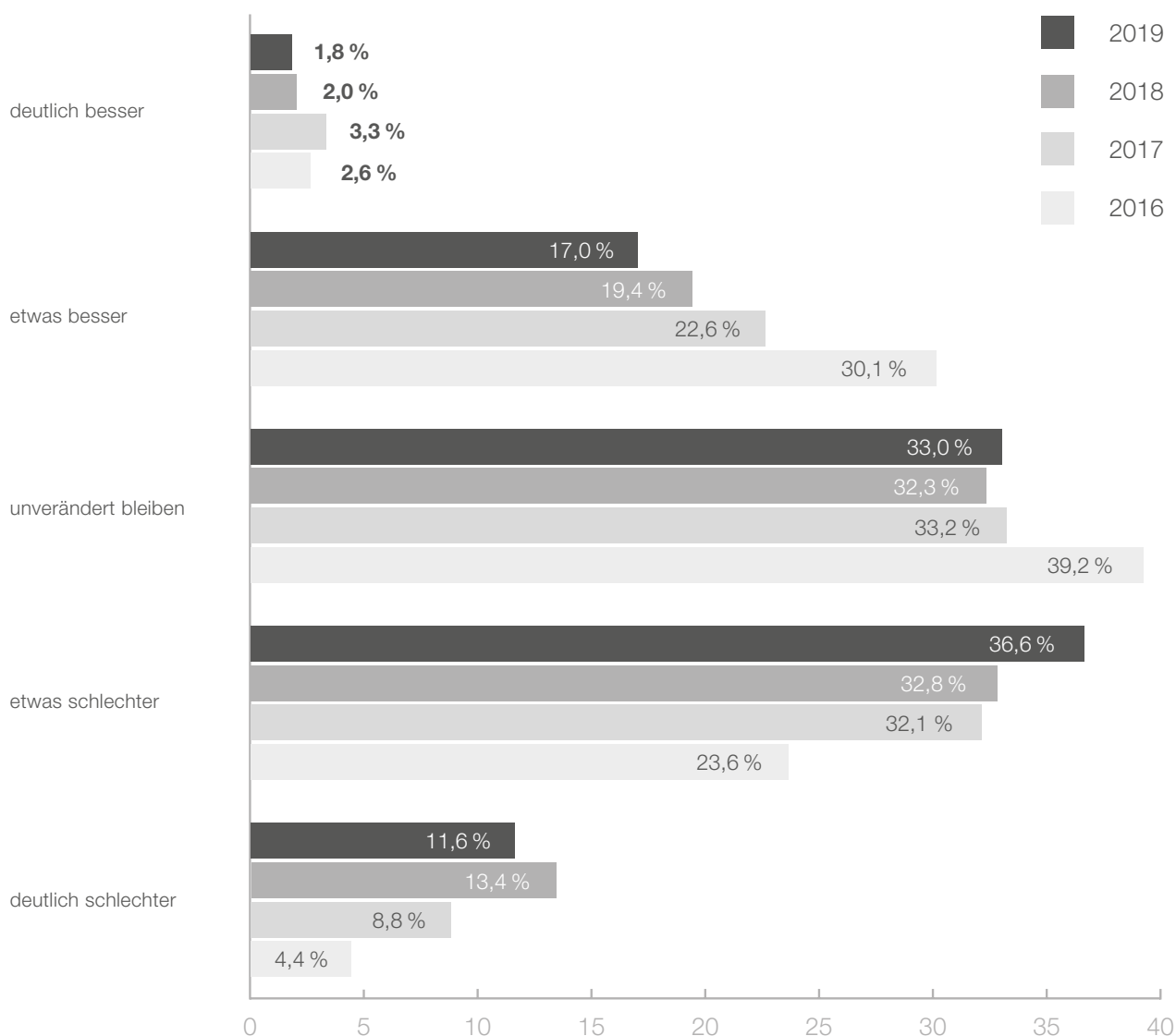
Einschätzung der Apothekeninhaber zu den wichtigsten gesundheitspolitischen Herausforderungen der nächsten zwei bis drei Jahre



Quelle: Apothekenklima-Index 2019 (marpinion GmbH, Kantar TNS/Bonsai GmbH)

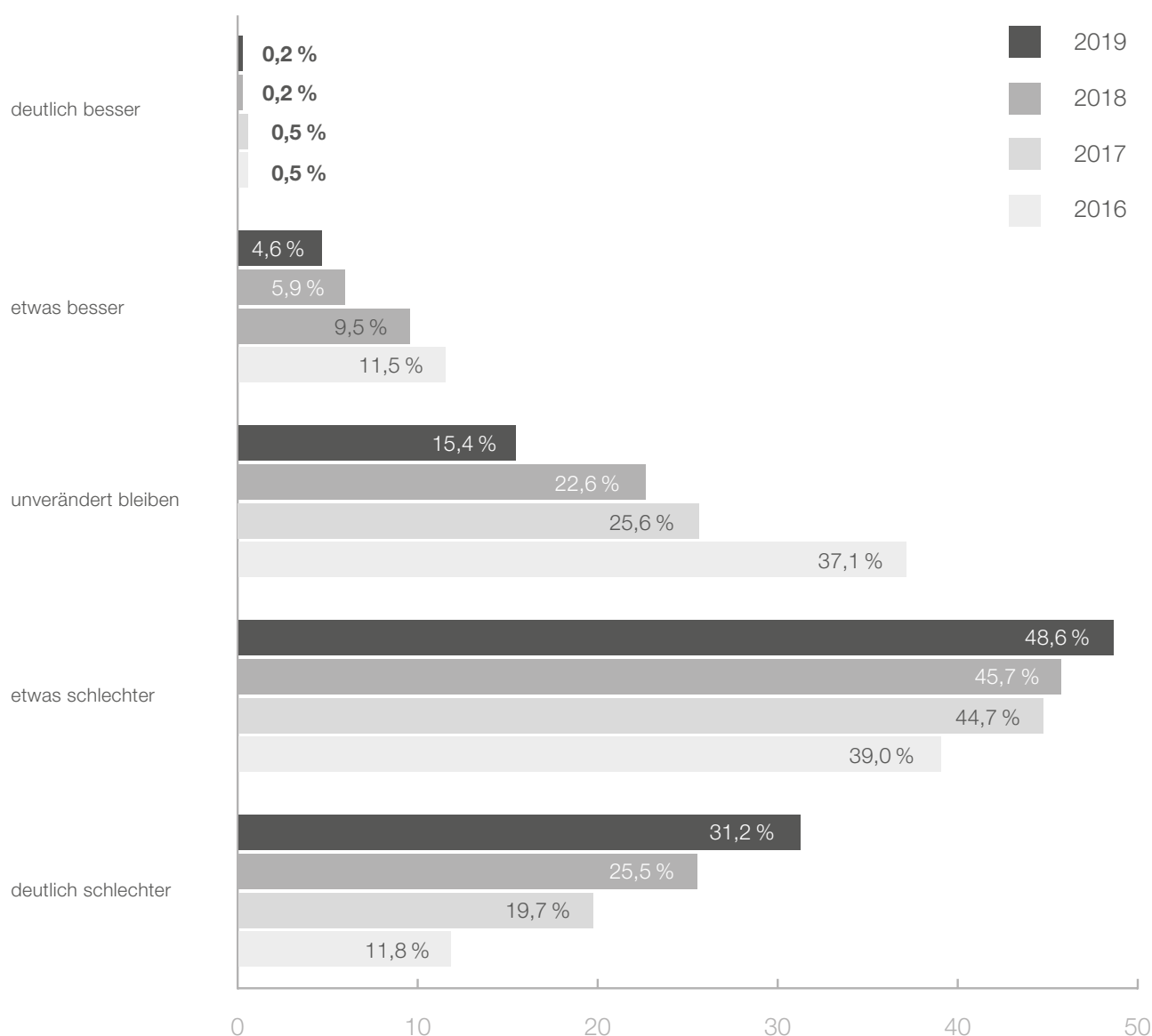
Auch weil sich die Apothekenvergütung längerfristig unterhalb der Inflationsrate entwickelt hat, haben sich die Erwartungen der Apothekeninhaber trotz der im Durchschnitt relativ stabilen betriebswirtschaftlichen Ergebnisse der Apotheken in den letzten Jahren sukzessive verschlechtert. Das gilt sowohl für die Erwartung des eigenen Betriebes als auch für die Erwartungen der eigenen Branche. Grund dafür ist vor allem die fehlende Planungssicherheit.

Wirtschaftliche Erwartung von Inhabern für den eigenen Betrieb in den nächsten zwei bis drei Jahren



Quelle: Apothekenklima-Index 2019 (marpinion GmbH, Kantar TNS/Bonsai GmbH)

Wirtschaftliche Erwartung von Inhabern für die Branche „Apotheken“ in den nächsten zwei bis drei Jahren



Quelle: Apothekenklima-Index 2019 (marpinion GmbH, Kantar TNS/Bonsai GmbH)

APOTHEKENBETRIEB UND INVESTITIONEN

Für den Betrieb einer öffentlichen Apotheke müssen zahlreiche Bedingungen erfüllt werden, die im Apothekengesetz (ApoG) und in der Apothekenbetriebsordnung (ApBetrO) aufgeführt sind. Sie erfordern umfängliche Investitionen. Die Mindestanforderungen werden von vielen Apotheken im Sinne von Qualitätsmanagement, Patientenfreundlichkeit und Alltagstauglichkeit weit übertroffen. Das erfordert jedoch umfangreiche Investitionen.

Betriebserlaubnis

- » approbierter Apotheker
- » persönliche Leitung
- » eigene Verantwortung

Betriebsräume

- » mindestens 110 Quadratmeter Grundfläche
- » Offizin, Labor, Lagerraum, Nachtdienstzimmer

Arzneimittel

- » rezept- und apothekenpflichtige Arzneimittel als Güter besonderer Art
- » Fertigarzneimittel, Rezepturen und Betäubungsmittel
- » Vorrat für mindestens eine Woche Durchschnittsbedarf

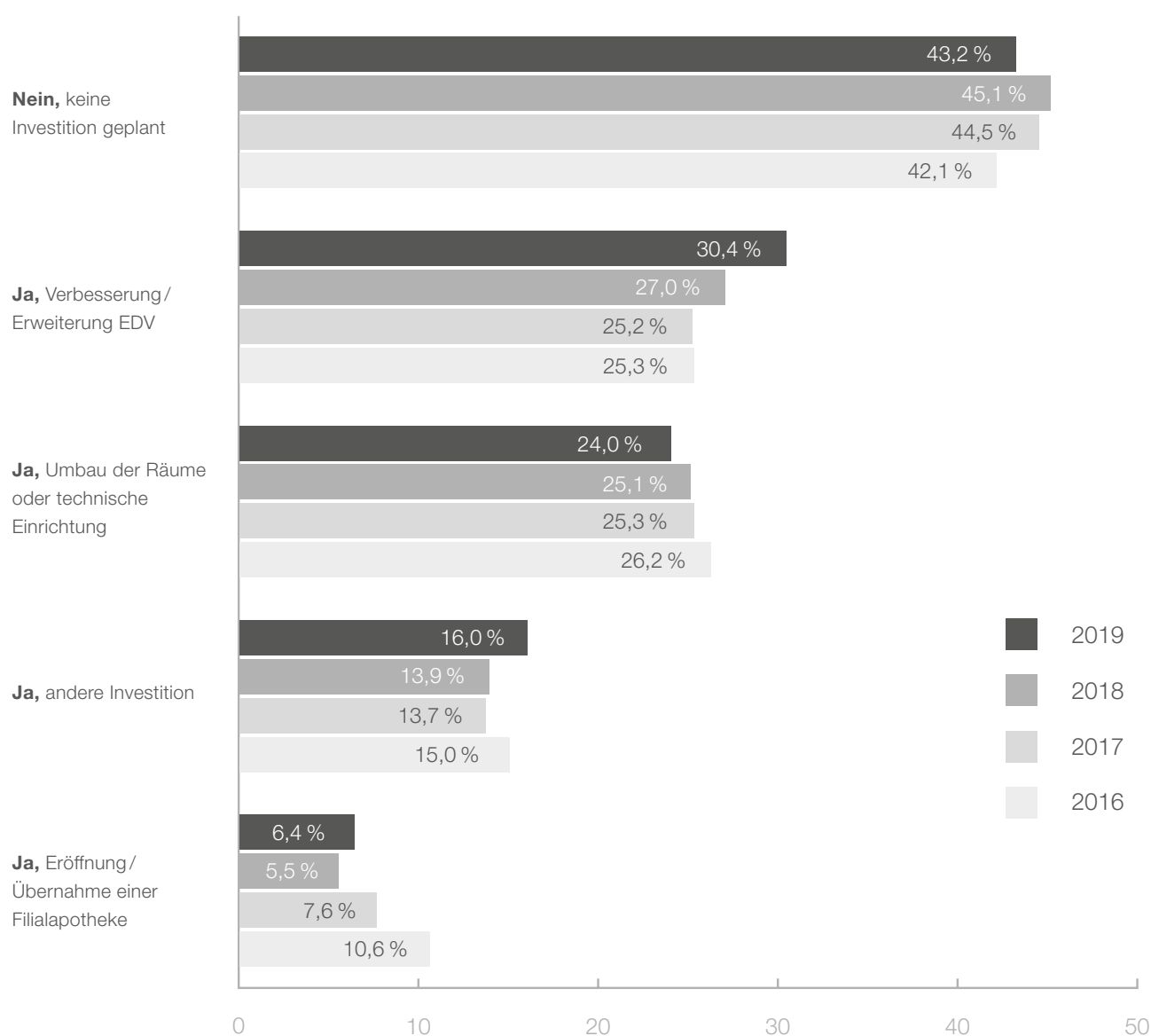
Qualitätsmanagement

- » pharmazeutisches Personal u. a. PTA, Pharmazieingenieure, Apotheker
- » verpflichtendes QMS-System für Abläufe in der Apotheke
- » Leitlinien der Bundesapothekerkammer und Zertifizierung (Kammerzertifikat, TÜV etc.) als Orientierung

Dienstbereitschaft

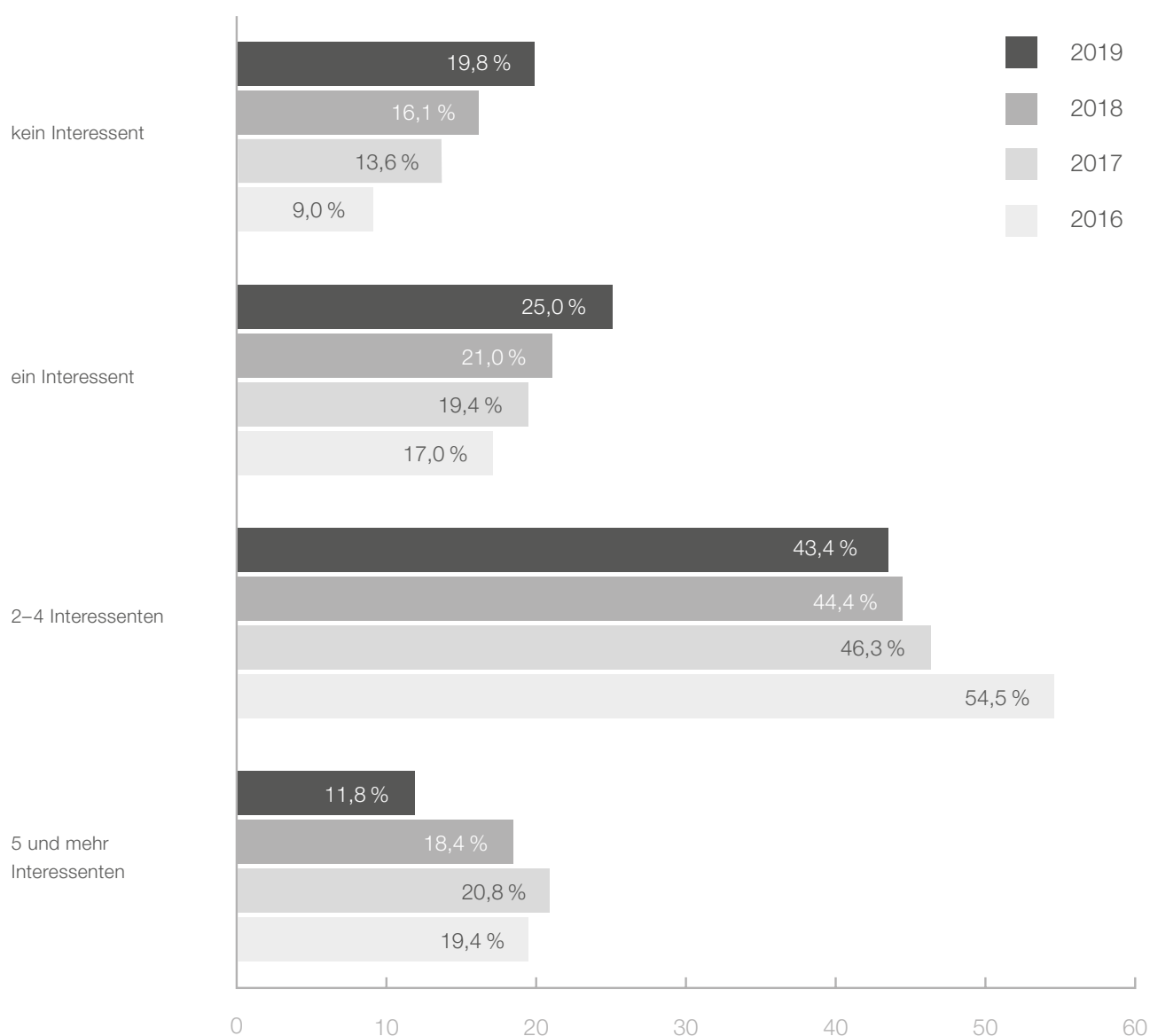
- » ordnungsgemäße Arzneimittelversorgung der Bevölkerung
 - » Pflicht zur ständigen Dienstbereitschaft, turnusgemäße Befreiung durch die Apothekerkammern
 - » Hinweis auf nächstgelegene dienstbereite Apotheke an jeder Apotheke
-

Investitionsplanung der Apotheken



Quelle: Apothekenklima-Index 2019 (marpinion GmbH, Kantar TNS/Bonsai GmbH)

Einschätzung der Inhaber, wie viele Interessenten im Falle eines Verkaufs ihrer Apotheke zu erwarten wären

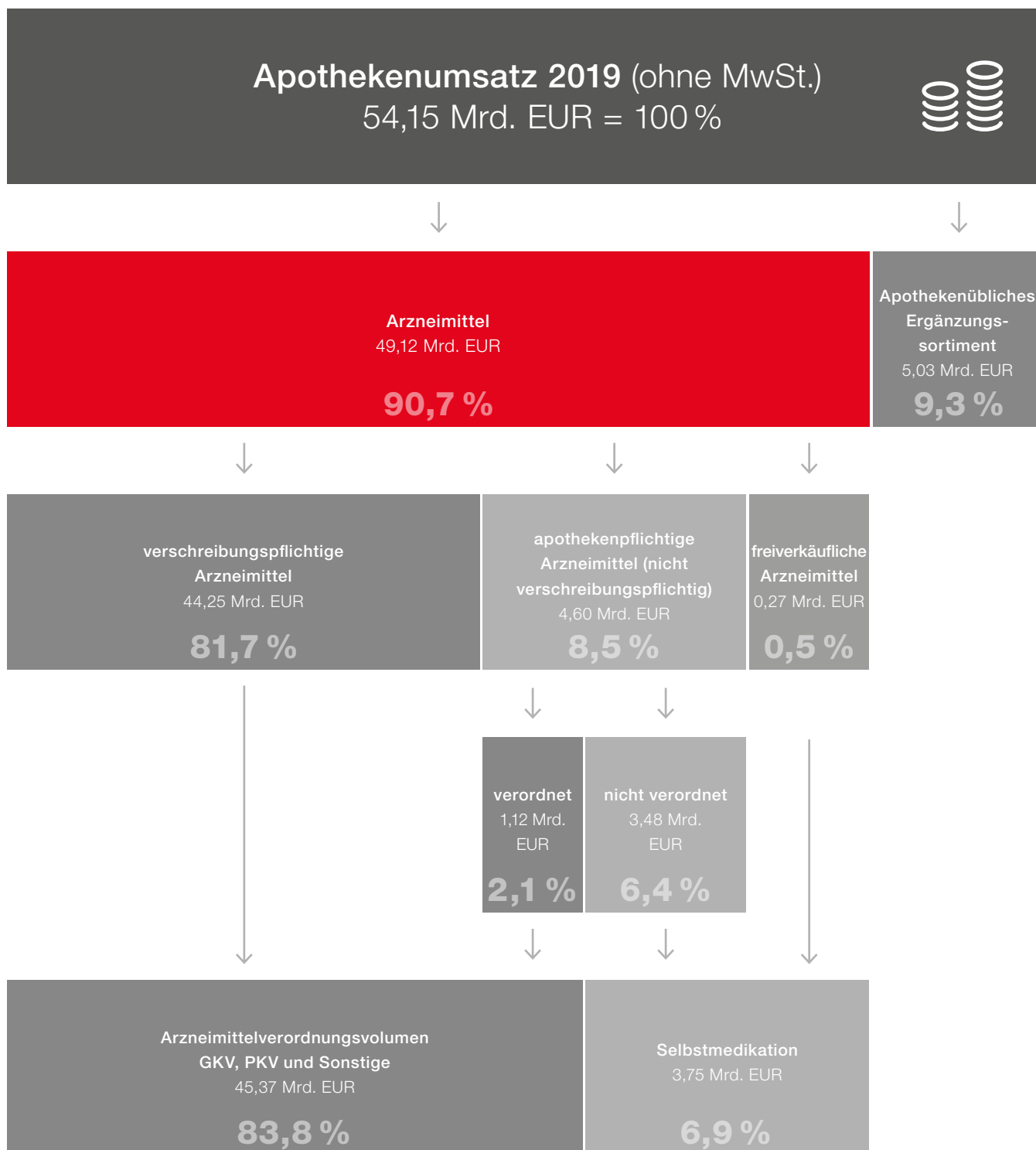


Quelle: Apothekenklima-Index 2019 (marpinion GmbH, Kantar TNS/Bonsai GmbH)

UMSATZSTRUKTUR UND ABGEGEBENE PACKUNGEN

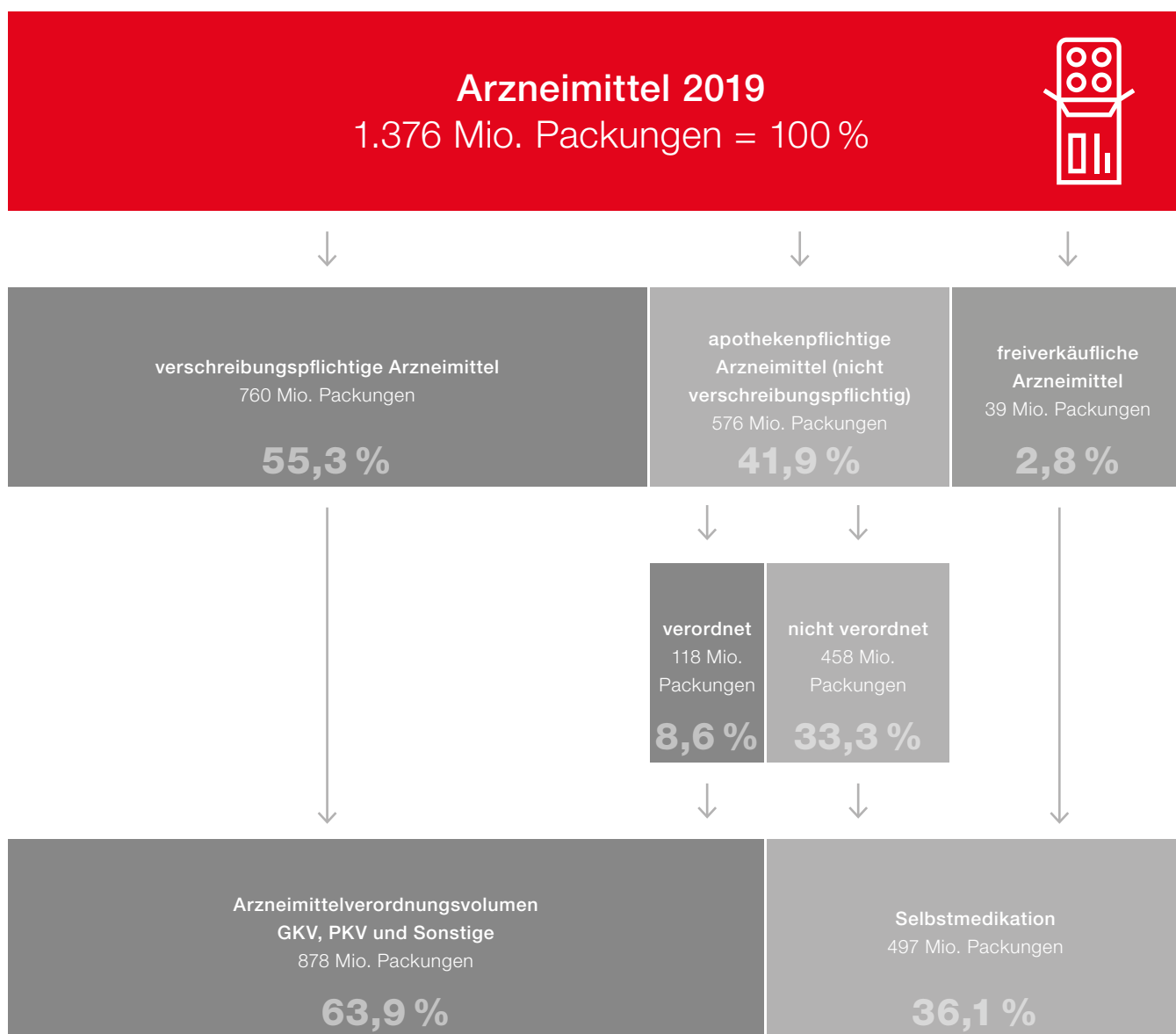
91 Prozent des Umsatzes der Apotheken entfallen auf die Abgabe von Arzneimitteln, die übrigen Anteile auf das apothekenübliche Ergänzungssortiment. Rund 82 Prozent des Umsatzes resultieren aus verschreibungspflichtigen Arzneimitteln, die ein Arzt oder Zahnarzt verordnet hat.

GEMESSEN IN UMSATZWERTEN




Quelle: Insight Health GmbH & Co. KG, ABDA-Statistik

GEMESSEN IN PACKUNGSZAHLEN



Quelle: Insight Health GmbH & Co. KG, ABDA-Statistik

Umsatz und Absatz

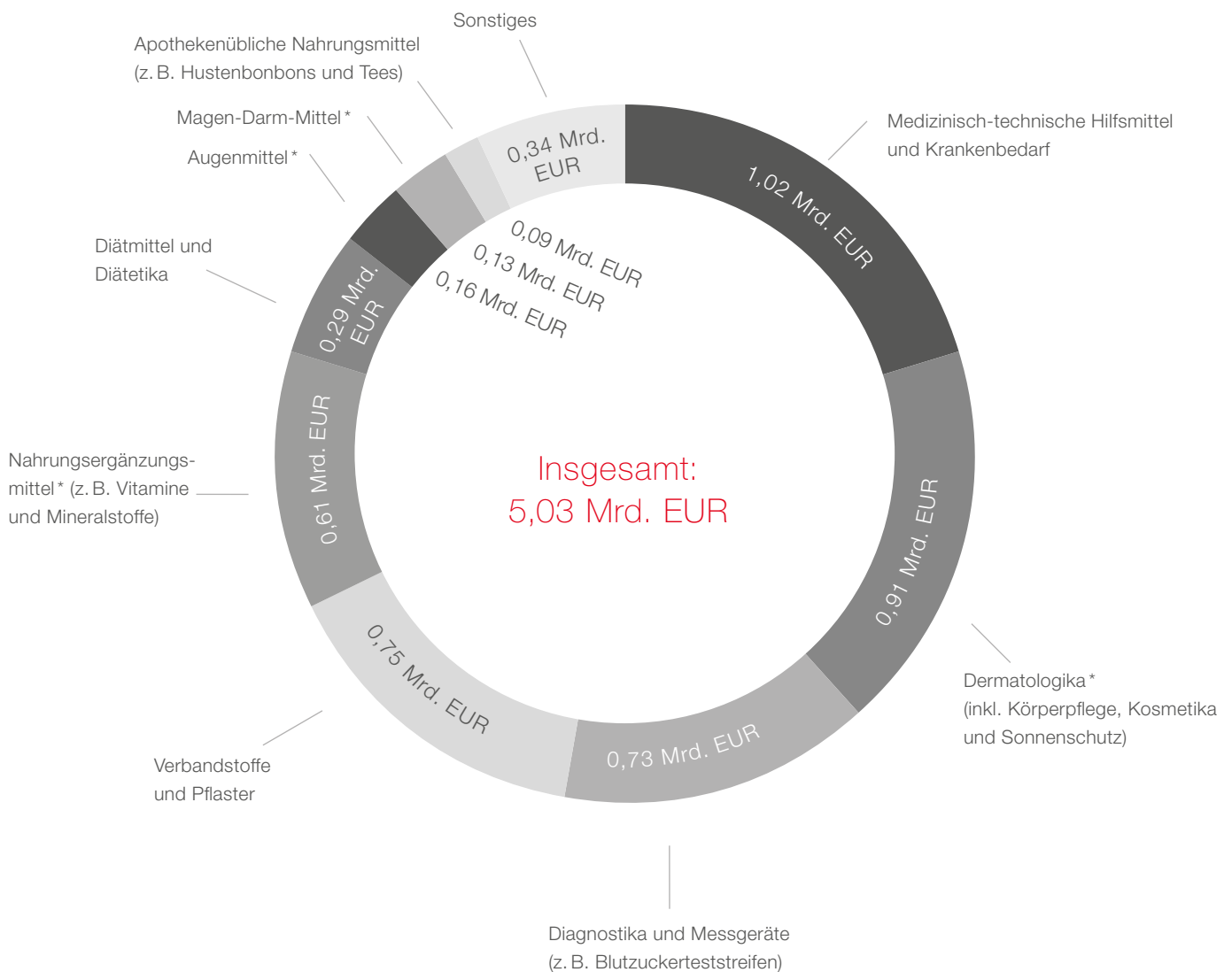
in Mrd. EUR 	2017	2018	2019
Apothekenumsatz (ohne MwSt.)	49,05	50,76	54,15
verschreibungspflichtige Arzneimittel	39,37	41,04	44,25
apothekenpflichtige Arzneimittel (nicht verschreibungspflichtig)	4,55	4,57	4,60
verordnet	1,12	1,12	1,12
nicht verordnet	3,43	3,46	3,48
freiverkäufliche Arzneimittel	0,26	0,27	0,27
Arzneimittelverordnungsvolumen GKV, PKV und Sonstige	40,48	42,16	45,37
Selbstmedikation	3,69	3,72	3,75
Apothekenübliches Ergänzungssortiment	4,88	4,87	5,03

in Mio. Packungen 	2017	2018	2019
Arzneimittel	1.373	1.363	1.376
verschreibungspflichtige Arzneimittel	741	740	760
apothekenpflichtige Arzneimittel (nicht verschreibungspflichtig)	595	584	576
verordnet	123	121	118
nicht verordnet	469	463	458
freiverkäufliche Arzneimittel	41	40	39
Arzneimittelverordnungsvolumen GKV, PKV und Sonstige	864	861	878
Selbstmedikation	509	503	497

APOTHEKENÜBLICHES ERGÄNZUNGSSORTIMENT

Zum Ergänzungssortiment gehören alle Nicht-Arzneimittel, die in der Apotheke abgegeben und verkauft werden. Dies können bestimmte Hilfsmittel, Blutzuckerteststreifen, Nahrungsergänzungsmittel, Vitamine und Mineralstoffe sein, aber auch Kosmetika und Sonnenschutz. Sie tragen mit 9,3 Prozent zum Gesamtumsatz bei.

Umsatz 2019 (ohne MwSt.)



* soweit nicht als Arzneimittel klassifiziert

Quelle: Insight Health GmbH & Co. KG

FACHSPRACHENPRÜFUNG FÜR AUSLÄNDISCHE APOTHEKER

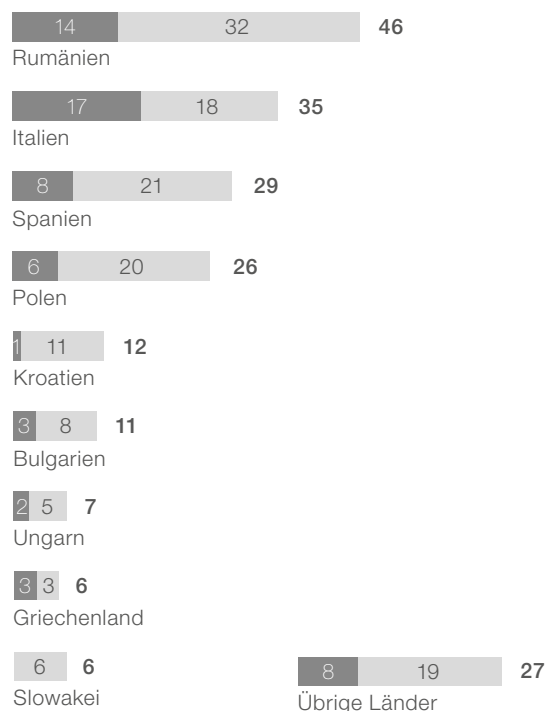
Auch im Bereich der Arzneimittelversorgung gibt es Arbeitsmigration. Nicht deutschsprachige Apotheker, die in Deutschland die Approbation als Apotheker beantragen, müssen Kenntnisse der deutschen Umgangssprache und der Fachsprache haben. Basierend auf dem Gemeinsamen Europäischen Referenzrahmen für Sprachen (GER) müssen sie im Rahmen einer dreiteiligen Prüfung Fachsprachenkenntnisse nachweisen. Fast alle Apothekerkammern der Länder sind von ihrer Landesbehörde mit der Durchführung der Fachsprachenprüfung beauftragt worden.

Zahl der Prüfungen und Bestehensquote

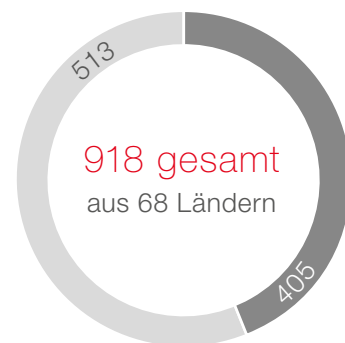
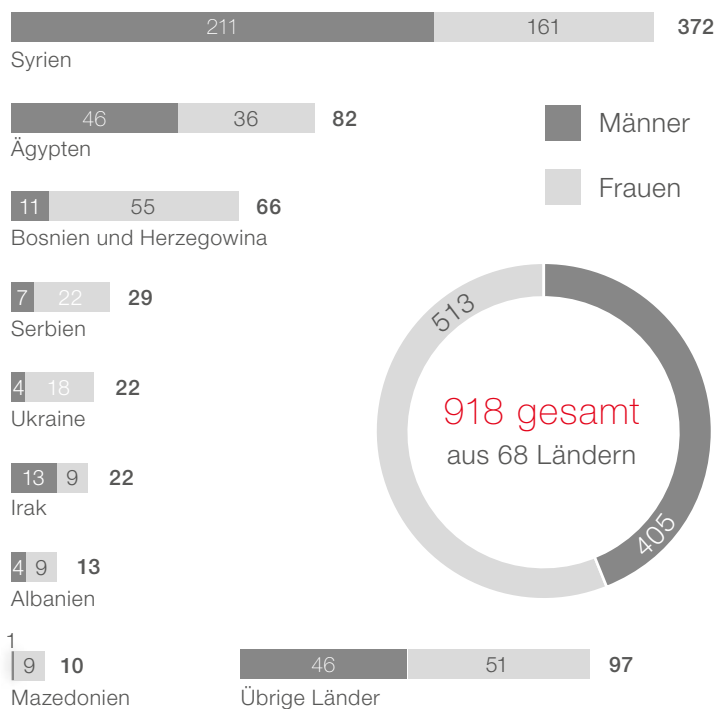


Zahl der Prüfungskandidaten, Geschlechterverhältnis und Herkunftsländer 2019

Europäisches Ausland (EU, EWR, Schweiz)



Drittstaaten



Quelle: Bundesapothekerkammer (BAK)

APOTHEKENDICHTE IM EUROPÄISCHEN VERGLEICH

Mit 23 Apotheken pro 100.000 Einwohner liegt Deutschland im unteren Drittel des europäischen Vergleichsfeld. Die 27 Mitgliedsstaaten der Europäischen Union weisen eine durchschnittliche Apothekendichte von 32 Apotheken pro 100.000 Einwohner auf.

	Apotheken je 100.000 Einwohner	Anzahl der Apotheken*
Griechenland	88	9.500
Zypern	62	524
Malta	49	221
Spanien	47	22.071
Litauen	47	1.317
Bulgarien	46	3.282
Rumänien	44	8.620
Lettland	43	840
Belgien	42	4.841
Irland	38	1.876
Estland	37	494
Slowakei	37	1.994
Polen	36	13.497
Italien	32	19.331
EU-Durchschnitt	32	—
Frankreich	31	20.966
Portugal	28	2.922
Kroatien	28	1.181
Tschechische Republik	24	2.551
Ungarn	23	2.304
Deutschland	23	19.075
Slowenien	16	339
Österreich	16	1.380
Luxemburg	15	94
Finnland	15	815
Schweden	14	1.422
Niederlande	12	1.996
Dänemark	8	492

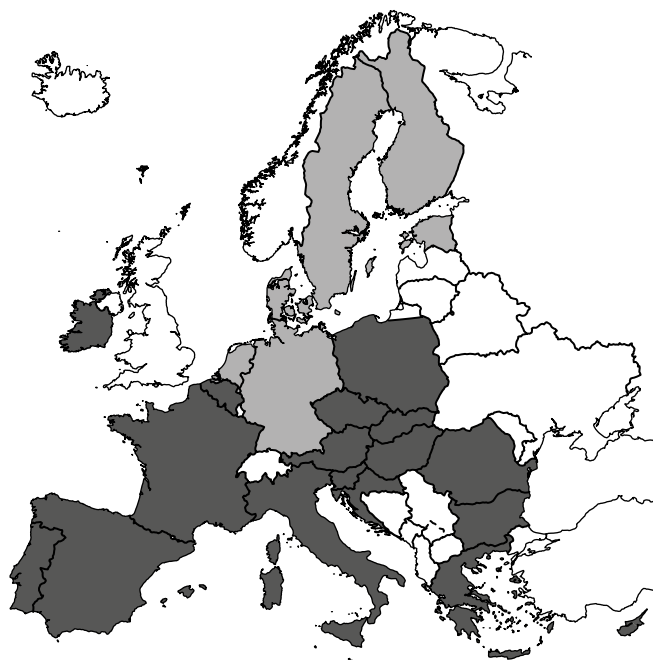
* letztes verfügbares Jahr

Quelle: ABDA-Statistik, Zusammenschluss der Apotheker in der Europäischen Union (ZAEU), nationale Apothekerverbände, Europäische Kommission (EC)

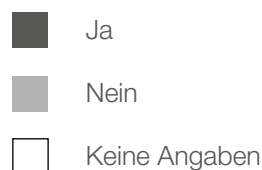
APOTHEKENRECHTLICHE REGELUNGEN IN EUROPA

Die Gesundheitssysteme in der Europäischen Union sind unterschiedlich organisiert. Entsprechend unterscheiden sich auch die ordnungspolitischen Regeln für die Arzneimittelversorgung von Mitgliedsstaat zu Mitgliedsstaat. Nur eine Minderheit der Staaten hat den Versandhandel mit verschreibungspflichtigen Arzneimitteln erlaubt, in einigen ist der Fremdbesitz von Apotheken (durch Nicht-Apotheker, Kapitalgesellschaften) möglich.

Versandhandelsverbot für verschreibungspflichtige Arzneimittel



Fremdbesitzverbot



Quelle: Zusammenschluss der Apotheker in der Europäischen Union (ZAEU)

Land	Rx-Versandhandelsverbot	Fremdbesitzverbot
Belgien	✓	×
Bulgarien	✓	×
Dänemark	×	✓
Deutschland	×	✓
Estland	×	✓
Finnland	×	✓
Frankreich	✓	✓
Griechenland	✓	×
Irland	✓	×
Italien	✓	×
Kroatien	✓	×
Lettland	k. A.	k. A.
Litauen	k. A.	k. A.
Luxemburg	k. A.	✓
Malta	×	×
Niederlande	×	×
Österreich	✓	✓
Polen	✓	✓
Portugal	✓	×
Rumänien	✓	×
Schweden	×	×
Slowakei	✓	×
Slowenien	✓	✓
Spanien	✓	✓
Tschechische Republik	✓	×
Ungarn	✓	✓
Zypern	✓	✓

MEHRWERTSTEUER AUF ARZNEIMITTEL

Der Mehrwertsteuersatz auf Arzneimittel ist in den 27 Mitgliedsstaaten der Europäischen Union sehr unterschiedlich. Deutschland hat – nach Dänemark und Bulgarien – einen der höchsten Steuersätze. Im Gegensatz dazu haben Malta, Irland und Schweden zumindest bestimmte Arzneimittel komplett von der Mehrwertsteuer befreit.

		Steuersatz für Arzneimittel 2019	Allgemeiner MwSt.-Satz 2019
Dänemark		25,0	25,0
Bulgarien		20,0	20,0
Deutschland		19,0	19,0
Lettland		12,0	21,0
Finnland		10,0	24,0
Italien		10,0	22,0
Tschechische Republik		10,0	21,0
Österreich		10,0	20,0
Slowakei		10,0	20,0
Slowenien		9,5	22,0
Niederlande		9,0	21,0
Estland		9,0	20,0
Rumänien		9,0	19,0
Polen		8,0	23,0
Griechenland		6,0	24,0
Portugal		6,0	23,0
Belgien		6,0	21,0
Ungarn		5,0	27,0
Kroatien	Arzneimittel im Rahmen des Nationalen Gesundheitsdienstes; nicht verschreibungspflichtige Arzneimittel	5,0 25,0	25,0
Litauen	erstattungsfähige Arzneimittel; nicht erstattungsfähige Arzneimittel	5,0 21,0	21,0
Zypern		5,0	19,0
Spanien		4,0	21,0
Luxemburg		3,0	17,0
Frankreich	erstattungsfähige Arzneimittel; nicht erstattungsfähige Arzneimittel	2,1 10,0	20,0
Schweden	verschreibungspflichtige Arzneimittel; nicht verschreibungspflichtige Arzneimittel	0,0 25,0	25,0
Irland	Arzneimittel zur oralen Anwendung; Arzneimittel zur nicht-oralen Anwendung	0,0 23,0	23,0
Malta		0,0	18,0

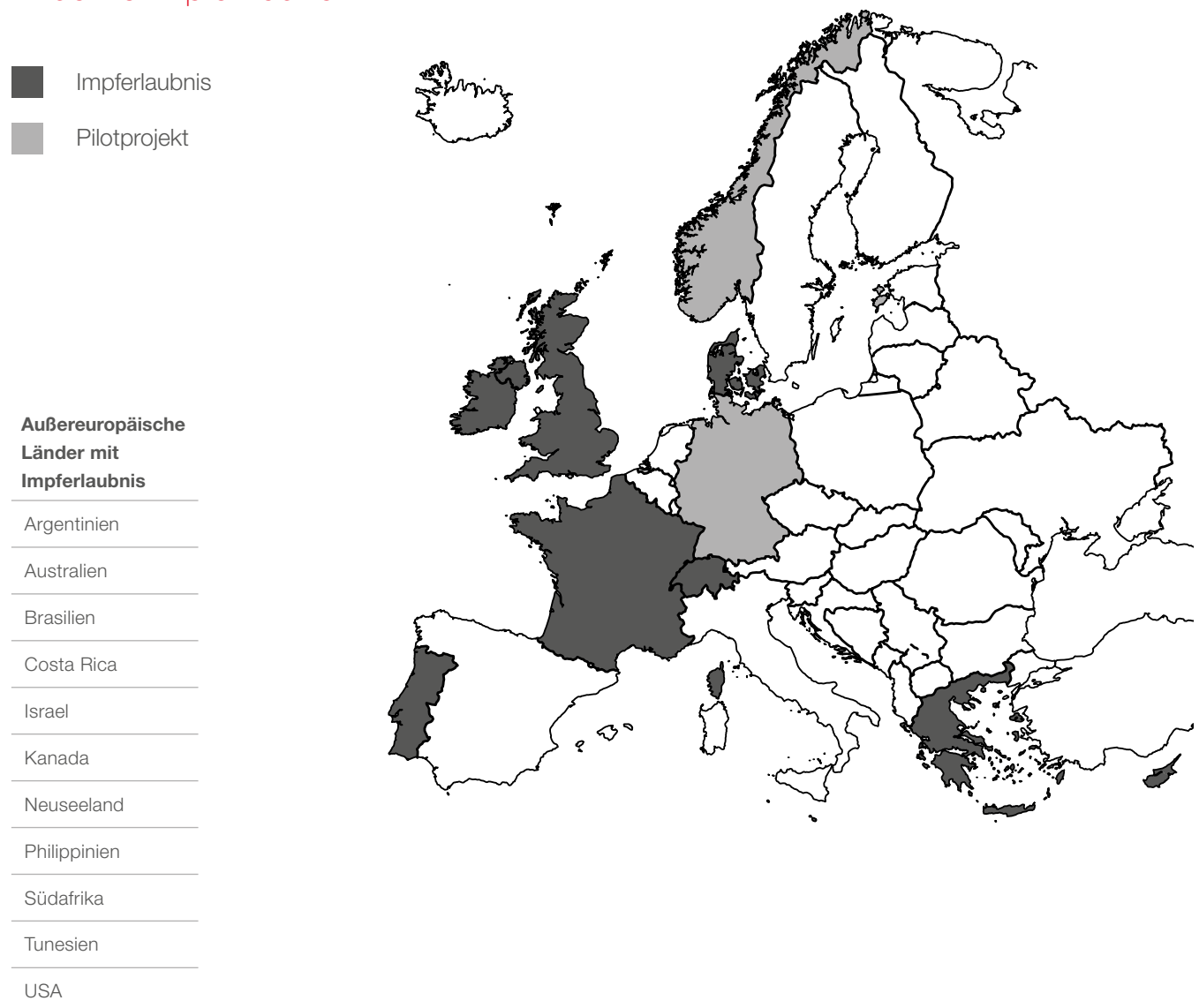
Bis Redaktionsschluss lag die Veröffentlichung der Europäischen Kommission für 2020 nicht vor.

Quelle: Europäische Kommission (EC)

LÄNDERVERGLEICH: IMPFEN IN APOTHEKEN

Weltweit dürfen Apothekerinnen und Apotheker in mindestens 20 Ländern in Apotheken gegen Grippe (Influenza) impfen, darunter Frankreich, Großbritannien und die USA. Ziel sind die Erhöhung der Impfquote und die Sicherstellung einer Grundversorgung in Regionen mit schwacher Gesundheitsinfrastruktur. In Deutschland sind seit dem 1. März 2020 Pilotprojekte zur Gripeschutzimpfung in Apotheken erlaubt.

Länder, in denen Apotheker
in öffentlichen Apotheken gegen
Influenza impfen dürfen



Anmerkung: In der Schweiz gilt die Impferlaubnis in 21 der 26 Kantone

Quelle: ABDA – Bundesvereinigung Deutscher Apothekerverbände e. V.

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Regulation

Zulassung Human

NAVIGATION

[Beratung](#)[Klinische Prüfung](#)[Zulassung Human](#)[Erlaubnisse](#)[Zulassungsverfahren](#)[Folgeverfahren](#)[TSE-Konformität](#)[Tierversuchersatzmethoden](#)[WHO-Zertifikate](#)[Produktinformation](#)[Schulungsmaterial](#)[Blutkomponenten](#)[Parallelhandel](#)[Zulassung Veterinär](#)[Genehmigungen](#)[Chargenprüfung Human](#)[Chargenprüfung Veterinär](#)[Inspektionen](#)[Referenzmaterial](#)[Elektronische Einreichung](#)[Gebühren](#)[Prüflabor IVD](#)[Meldung an das PEI](#)[Qualitätsmanagement](#)

Parallelhandel

Pharmazeutische Unternehmer vermarkten ihre Arzneimittel in vielen Fällen sowohl in Deutschland als auch in anderen Mitgliedstaaten der Europäischen Union ([EU](#)) bzw. des Europäischen Wirtschaftsraumes ([EWR](#)). Sie besitzen folglich auch in vielen dieser Mitgliedstaaten eine separate nationale Zulassung. Beim Parallelhandel sind Parallelimport und Parallelvertrieb voneinander abzugrenzen.

Parallelimport

Bei einem Parallelimport kauft ein (in der Regel auf den Pharmasektor spezialisiertes) Importunternehmen ein Arzneimittel in einem anderen [EU](#)-/[EWR](#)-Mitgliedstaat ein, importiert es nach Deutschland und bringt es dann "parallel" zu dem ursprünglichen pharmazeutischen Unternehmer ebenfalls in den Verkehr. Der Parallelimporteure macht sich dabei die in Europa bestehenden Preisunterschiede auf dem Arzneimittelmarkt zunutze.

Das importierte Arzneimittel muss im Wesentlichen identisch sein mit dem Arzneimittel, für das in Deutschland bereits eine gültige nationale Zulassung für den ursprünglichen Pharmazeutischen Unternehmer besteht (Bezugs-Arzneimittel). Von dieser (Bezugs-) Zulassung darf, ebenso wie von jeder anderen Zulassung, jedoch nur der in ihr genannte Pharmazeutische Unternehmer Gebrauch machen. Daher braucht der Parallelimporteure eine eigene für Deutschland gültige nationale Zulassung.

Der Parallelimporteure hat über das von ihm importierte Arzneimittel allerdings keine derart detaillierten Informationen wie der Originalhersteller des Arzneimittels. Er ist daher nicht in der Lage, ein vollständiges Zulassungsdossier zu erstellen und dieses bei der deutschen Zulassungsbehörde einzureichen. Andererseits ist das parallel importierte Arzneimittel der deutschen Zulassungsbehörde bereits aus dem Zulassungsverfahren für das Bezugs-Arzneimittel bekannt. Aus diesem Grund kann der Parallelimporteure eine Zulassung in dem so genannten vereinfachten Verfahren erhalten, in dem nur sehr reduzierte Angaben zu dem Arzneimittel von ihm gefordert werden.

Weitere Informationen

➤ [Bekanntmachung über die Zustimmungspflicht bei der Anzeige eines Importarzneimittels aus einem neuen Importland im Parallelimport gemäß § 29 des Arzneimittelgesetzes \(\[AMG\]\(#\)\) vom 13. Juli 2018](#)

Parallelvertrieb

Nationaler Zulassungsantrag

Folgeverfahren – Änderungen und Verlängerungen

Chargenfreigabe für parallel gehandelte Arzneimittel

Aktualisiert: 21.11.2019

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[Pharmakovigilanz](#)[Hämovigilanz](#)[Gewebevigilanz](#)[IVD-Vigilanz](#)[Veterinärmedizin Pharmakovigilanz](#)[Sicherheitsinformationen \(Human\)](#)[Schulungsmaterial](#)

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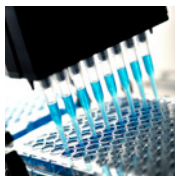
Das Paul-Ehrlich-Institut ist ein Bundesinstitut im Geschäftsbereich
des Bundesministeriums für Gesundheit.

Es fördert durch Forschung und Prüfung Qualität, Wirksamkeit und
Sicherheit biomedizinischer Arzneimittel.



The Pharmaceutical Industry in Figures

Key Data * 2020



THE PHARMACEUTICAL INDUSTRY: A KEY ASSET TO SCIENTIFIC AND MEDICAL PROGRESS

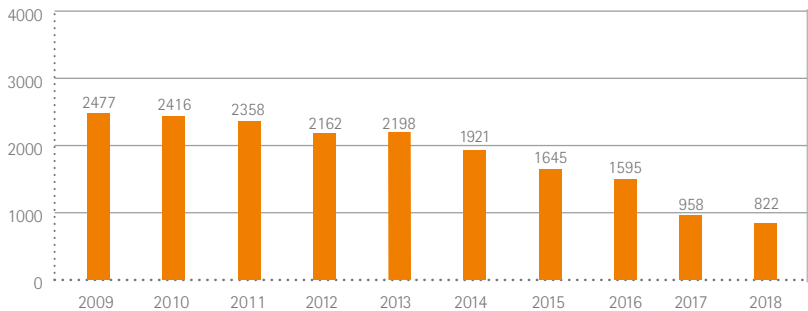
Thanks to advances in science and technology, the research-based pharmaceutical industry is entering an exciting new era in medicines development. Research methods are evolving and we have many promising prospects on the horizon – from the possibilities offered by personalised medicines, to the potential offered by harnessing the power of big data. The innovative pharmaceutical industry is driven by, and drives, medical progress. It aims to turn fundamental research into innovative treatments that are widely available and accessible to patients.

Already, the industry has contributed to significant improvements in patient well-being. Today's European citizens can expect to live up to 30 years longer than they did a century ago. Some major steps in biopharmaceutical research, complimented by many smaller steps, have allowed for reductions in mortality, for instance from HIV/AIDS-related causes and a number of cancers. High blood pressure and cardiovascular diseases can be controlled with antihypertensive and cholesterol-lowering medicines; knee or hip replacements prevent patients from immobility; and some cancers

can be controlled – or even cured – with the help of new targeted treatments. European citizens can expect not only to live longer, but to live better quality lives. Yet major hurdles remain, including Alzheimer's, Multiple Sclerosis, many cancers, and orphan diseases.



TOTAL NUMBER OF DEATHS AMONG AIDS CASES IN EUROPE (TOTAL EU/EEA)



Source: HIV/AIDS surveillance in Europe 2019, WHO Regional Office for Europe & European Centre for Disease Prevention and Control (ECDC), November 2019

THE PHARMACEUTICAL INDUSTRY: A KEY ASSET TO THE EUROPEAN ECONOMY

As well as driving medical progress by researching, developing and bringing new medicines that improve health and quality of life for patients around the

world, the research-based pharmaceutical industry is a key asset of the European economy. It is one of Europe's top performing high-technology sectors.



INDUSTRY (EFPIA total)

2000

2010

2018

2019

	Production	127,504	199,730	259,857	275,000 (e)
	Exports (1) (2)	90,935	276,357	435,300	475,000 (e)
	Imports	68,841	204,824	313,269	335,000 (e)
	Trade balance	22,094	71,533	122,031	140,000 (e)
	R&D expenditure	17,849	27,920	36,312	37,500 (e)
	Employment (units)	554,186	670,088	793,111	795,000 (e)
	R&D employment (units)	88,397	116,253	115,792	118,000 (e)
	Total pharmaceutical market value at ex-factory prices	89,449	153,684	213,358	228,200 (e)
	Payment for pharmaceuticals by statutory health insurance systems (ambulatory care only)	76,909	129,464	135,485	140,900 (e)

Values in € million unless otherwise stated

(1) Data relate to EU-27, Norway and Switzerland since 2005 (EU-15 before 2005); Croatia and Serbia included since 2010; Turkey included since 2011; Russia included since 2013

(2) Data relating to total exports and total imports include EU-28 intra-trade (double counting in some cases)

Source: EFPIA member associations (official figures) - (e): EFPIA estimate; Eurostat (EU-28 trade data 2000-2019)

MAIN TRENDS

The research-based pharmaceutical industry can play a critical role in restoring Europe to growth and ensuring future competitiveness in an advancing global economy. In 2019 it invested an estimated € 37,500 million in R&D in Europe. It directly employs some 795,000 people and generates about three times more employment indirectly – upstream and downstream – than it does directly (PwC, Economic and societal footprint of the pharmaceutical industry in Europe, June 2019). However, the sector faces real challenges. Besides the additional regulatory hurdles and escalating R&D costs, the sector has been severely hit by the impact of fiscal austerity measures introduced by governments across much of Europe since 2010.

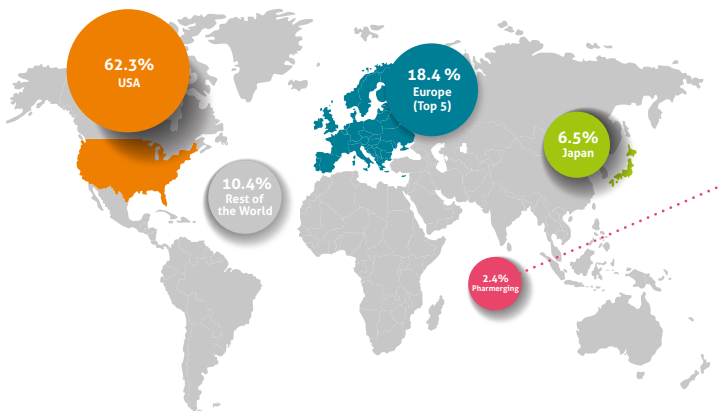
✱ There is rapid growth in the market and research environment in emerging economies such as Brazil, China and India, leading to a gradual migration of economic and research activities from Europe to these fast-growing markets. During

the period 2014-2019 the Brazilian, Chinese and Indian markets grew by 11.2%, 6.9% and 11.1% respectively compared to an average market growth of 5.4% for the top 5 European Union markets and 6.1% for the US market (source: IQVIA MIDAS, May 2020).

✱ In 2019 North America accounted for 48.7% of world pharmaceutical sales compared with 22.9% for Europe. According to IQVIA (MIDAS May 2020), 62.3% of sales of new medicines launched during the period 2014-2019 were on the US market, compared with 18.4% on the European market (top 5 markets).

✱ The fragmentation of the EU pharmaceutical market has resulted in a lucrative parallel trade. This benefits neither social security nor patients and deprives the industry of additional resources to fund R&D. Parallel trade was estimated to amount to € 5,471 million (value at ex-factory prices) in 2018.

GEOGRAPHICAL BREAKDOWN (BY MAIN MARKETS) OF SALES OF NEW MEDICINES LAUNCHED DURING THE PERIOD 2014–2019



Note:

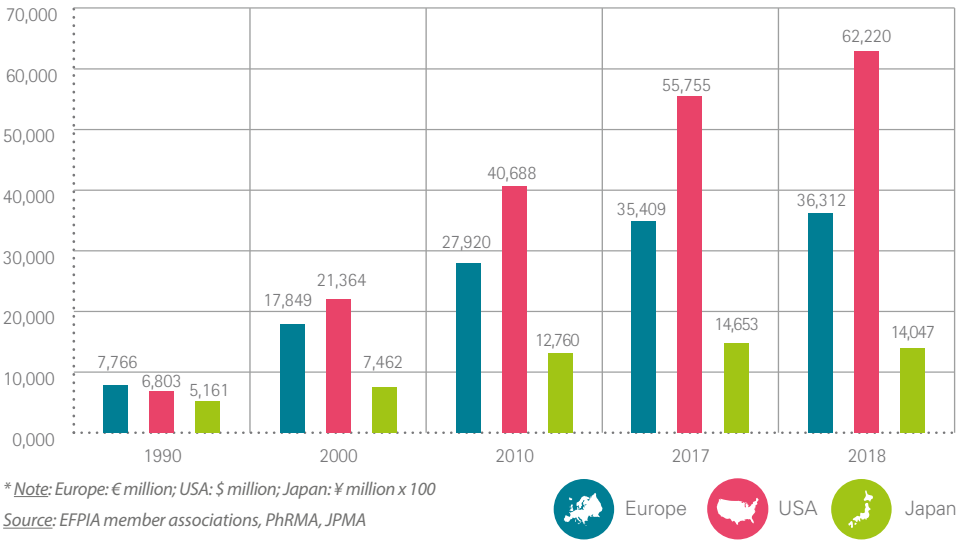
New medicines cover all new active ingredients marketed for the first time on the world market during the period 2014-2019

Europe (Top 5) comprises Germany, France, Italy, Spain and United Kingdom

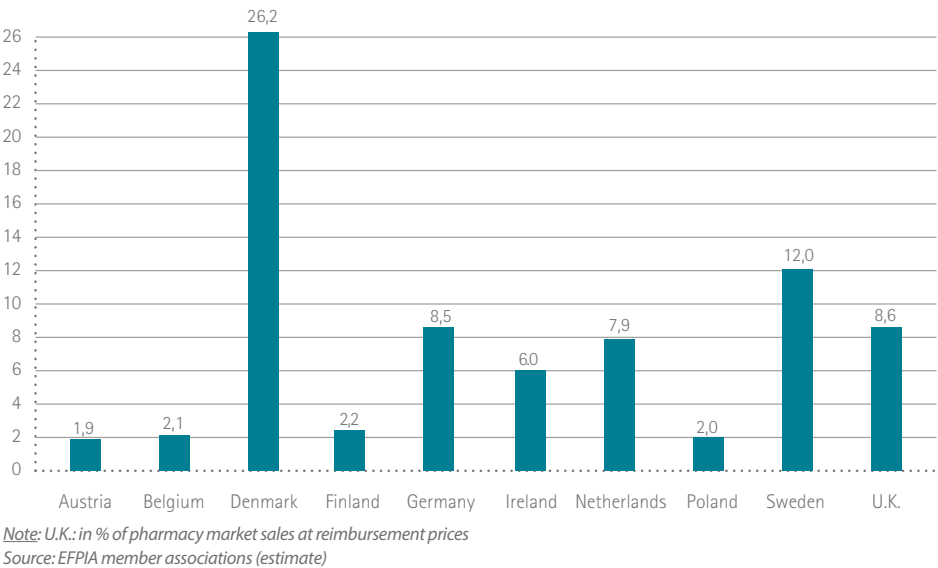
Pharmerging comprises 21 countries ranked by IQVIA as high-growth pharmaceutical markets (Algeria, Argentina, Bangladesh, Brazil, Colombia, Chile, China, Egypt, India, Indonesia, Kazakhstan, Mexico, Nigeria, Pakistan, Philippines, Poland, Russia, Saudi Arabia, South Africa, Turkey and Vietnam)

Source: IQVIA
(MIDAS May 2020)

PHARMACEUTICAL R&D EXPENDITURE IN EUROPE, USA AND JAPAN
(MILLION OF NATIONAL CURRENCY UNITS*), 1990-2018



SHARE OF PARALLEL IMPORTS IN PHARMACY MARKET SALES (%) – 2018



PHARMACEUTICAL INDUSTRY RESEARCH AND DEVELOPMENT IN EUROPE

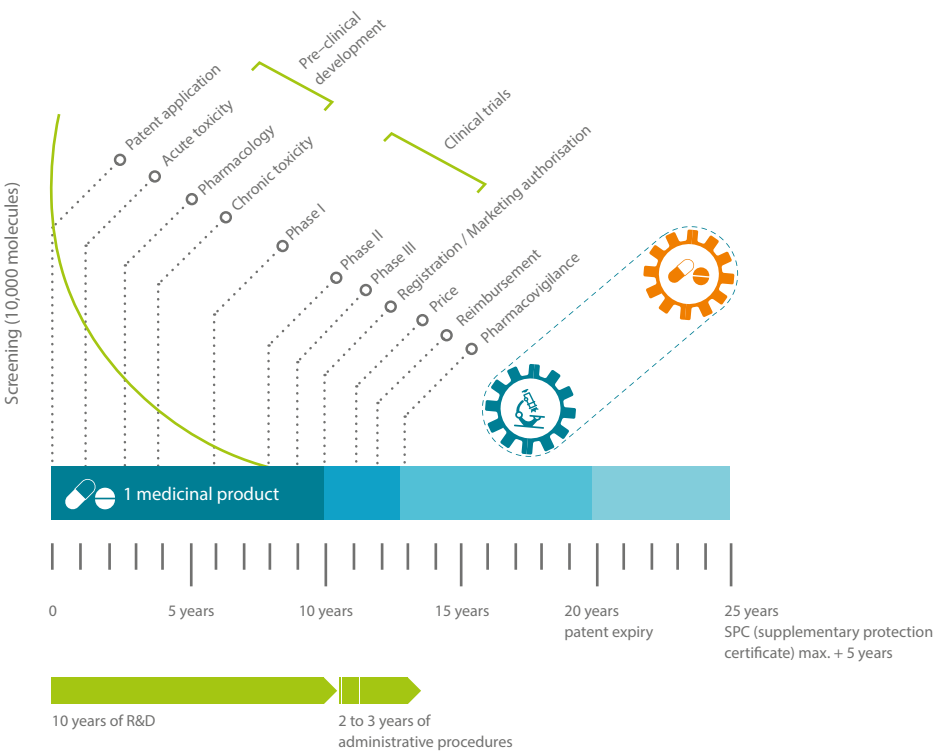
All new medicines introduced into the market are the result of lengthy, costly and risky research and development (R&D) conducted by pharmaceutical companies:

* By the time a medicinal product reaches the market, an average of 12-13 years will have elapsed since the first synthesis of the new active substance;

* The cost of researching and developing a new chemical or biological entity was estimated at € 1,926 million (\$ 2,558 million in year 2013 dollars) in 2014 (DiMasi et al, Journal of Health Economics, January 2016);

* On average, only one to two of every 10,000 substances synthesised in laboratories will successfully pass all stages of development required to become a marketable medicine.

PHASES OF THE RESEARCH AND DEVELOPMENT PROCESS



PHARMACEUTICAL INDUSTRY RESEARCH AND DEVELOPMENT IN EUROPE

EFPIA 2018	€ million		€ million
Austria	278	Latvia	n.a
Belgium	3,570	Lithuania	n.a
Bulgaria	91	Malta	n.a
Croatia	40	Netherlands	642
Cyprus	85	Norway	126
Czech Rep.	36	Poland	356
Denmark	1,629	Portugal	116
Estonia	n.a	Romania	80
Finland	216	Russia	944
France	4,451	Slovakia	n.a
Germany	7,815	Slovenia	180
Greece	51	Spain	1,147
Hungary	242	Sweden	1,104
Iceland	n.a	Switzerland	6,010
Ireland	305	Turkey	103
Italy	1,650	U.K.	5,045
TOTAL		36,312	

Note:

The figures relate to the R&D carried out in each country.

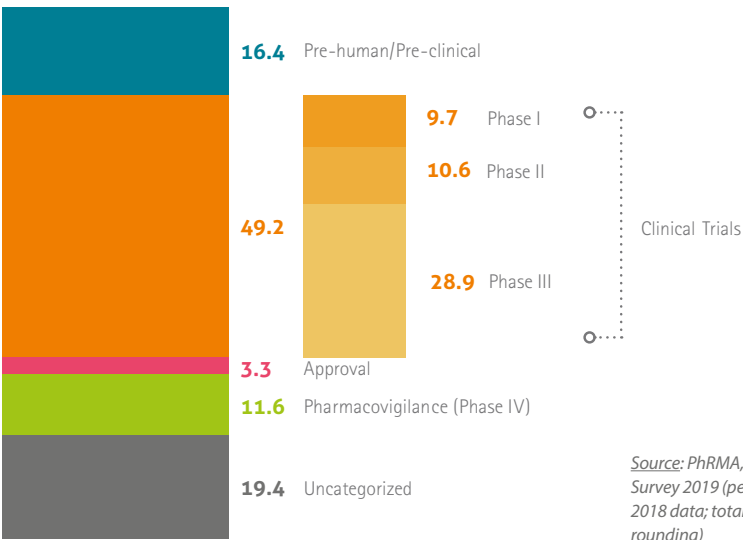
Bulgaria, France, Germany, Spain: 2017 data; Slovenia: 2016 data; Norway, Sweden: 2015 data; Cyprus, Ireland: 2013 data; Croatia, Netherlands: 2011 data

Belgium, Croatia, Denmark, France, Germany, Greece, Ireland, Italy, Netherlands, Norway (LMI members), Poland, Romania, Slovenia, Sweden (LIF members), Switzerland (Interpharma members), Turkey: estimate

Source: EFPIA member associations (official figures)

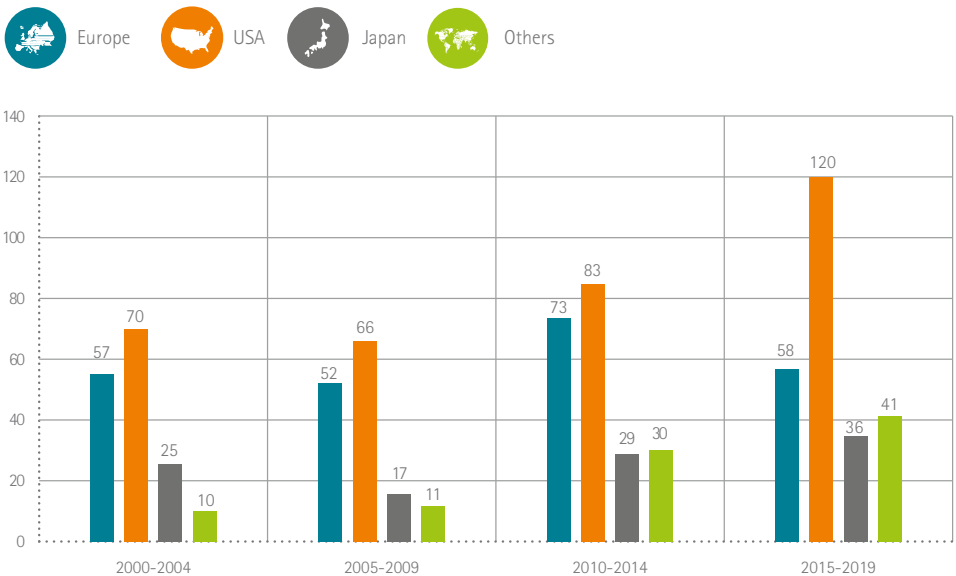


ALLOCATION OF R&D INVESTMENTS BY FUNCTION (%)



Source: PhRMA, Annual Membership Survey 2019 (percentages calculated from 2018 data; total values may be affected by rounding)

NUMBER OF NEW CHEMICAL AND BIOLOGICAL ENTITIES (2000-2019)



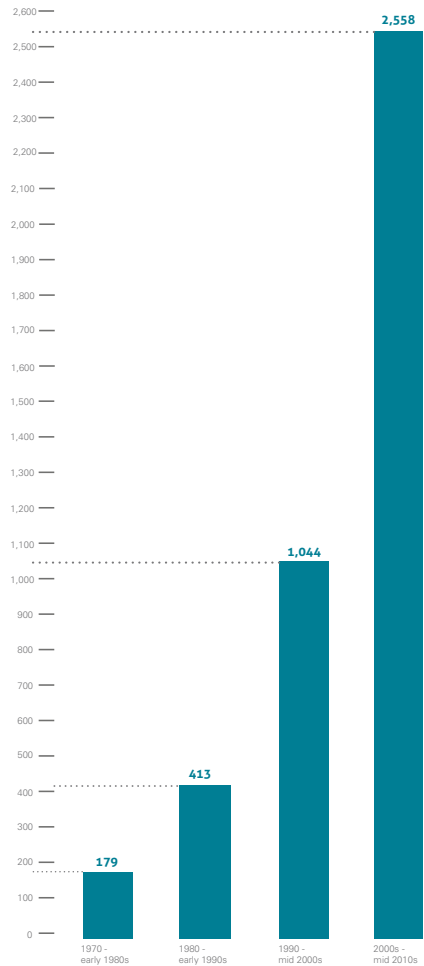
Source: SCRIIP – EFPIA calculations (according to nationality of mother company)

IMPORTANCE OF PHARMACEUTICAL R&D

In 2018 the pharmaceutical industry invested more than € 36,300 million in R&D in Europe. A decade of strong US market dominance led to a significant shift of economic and research activity towards the US during the period 1995-2005. Additionally, Europe is now facing increasing competition from emerging economies: rapid growth in the market and research environments in countries such as Brazil and China are contributing to the move of economic and research activities to non-European markets. The geographical balance of the pharmaceutical market – and ultimately the R&D base – is likely to shift gradually towards emerging economies.

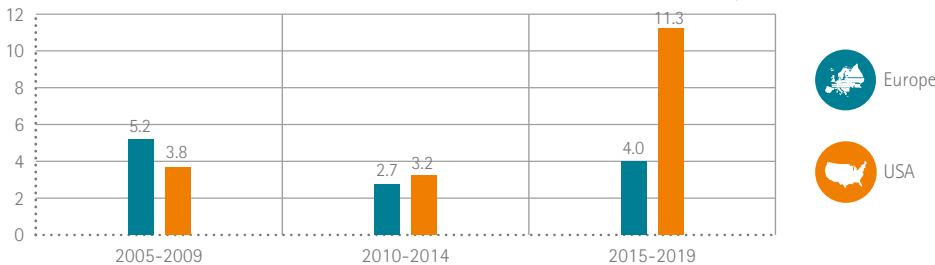
ESTIMATED FULL COST OF BRINGING A NEW CHEMICAL OR BIOLOGICAL ENTITY TO MARKET (\$ MILLION – YEAR 2013 \$)

Source: Joseph. A. DiMasi, Henry G. Grabowski, Ronald W.Hansen, *Innovation in the pharmaceutical industry: New estimates of R&D costs*, Journal of Health Economics, 47 (2016), 20-33

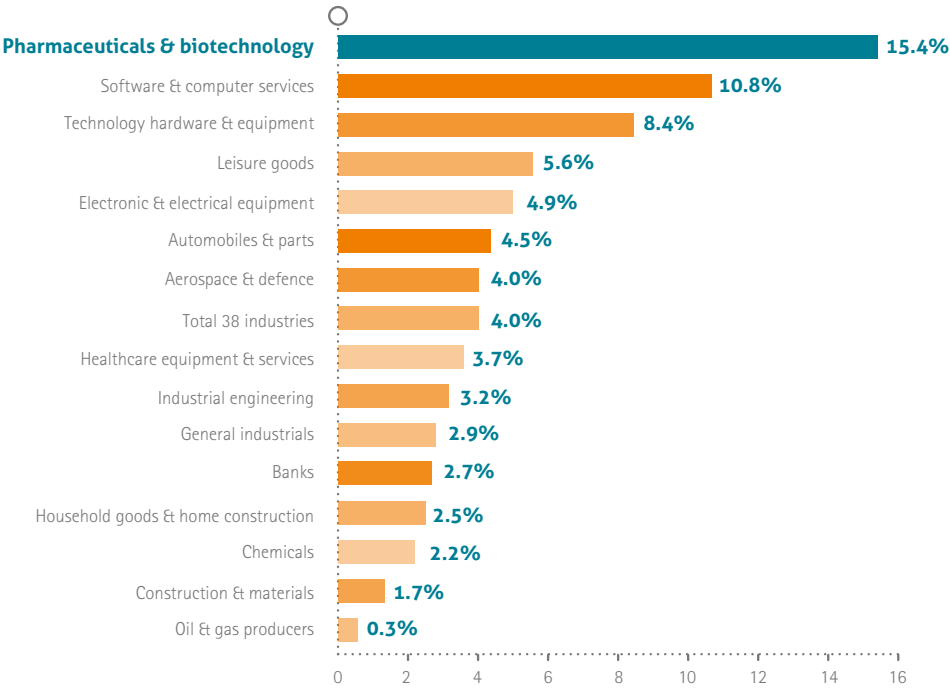


PHARMACEUTICAL R&D EXPENDITURE – ANNUAL GROWTH RATE (%)

Note: USA: data relating to period 2014-2018
Source: EFPIA, PhRMA



RANKING OF INDUSTRIAL SECTORS BY OVERALL SECTOR R&D INTENSITY
(R&D AS PERCENTAGE OF NET SALES – 2019)



Note:
Data relate to the top 2,500 companies with registered offices in the EU (551), Japan (318), the US (769), China (507) and the Rest of the World (355), ranked by total worldwide R&D investment (with investment in R&D above € 30 million).
Source: The 2019 EU Industrial R&D Investment Scoreboard, European Commission, JRC/DG RTD

According to EUROSTAT data, the pharmaceutical industry is the high technology sector with the highest added-value per person employed, significantly higher than the average value for high-tech and manufacturing industries. The pharmaceutical industry is also the sector with the highest ratio of R&D investment to net sales.

According to the 2019 EU Industrial R&D Investment Scoreboard the pharmaceutical and biotechnology sector amounts to 18.7% of total business R&D expenditure worldwide.

PHARMACEUTICAL PRODUCTION

EFPIA 2018	€ million		€ million
Austria	2,775	Latvia	157
Belgium	13,312	Lithuania	n.a
Bulgaria	121	Malta	n.a
Croatia	588	Netherlands	6,180
Cyprus	180	Norway	1,072
Czech Rep.	858	Poland	2,465
Denmark	14,391	Portugal	1,514
Estonia	n.a	Romania	655
Finland	1,773	Russia	4,537
France	23,213	Slovakia	356
Germany	32,905	Slovenia	2,010
Greece	996	Spain	14,970
Hungary	3,284	Sweden	8,153
Iceland	89	Switzerland	45,885
Ireland	19,305	Turkey	2,874
Italy	32,200	U.K.	23,039
TOTAL			259,857

Note:

All data based on SITC 54

Denmark, Latvia, Slovakia, Spain: 2017 data; Iceland: 2016 data; Bulgaria: 2015 data; Ireland: 2014 data; Romania: 2013 data; Cyprus, Netherlands: 2010 data

Croatia, Denmark, France, Ireland, Italy, Netherlands, Norway, Portugal, Slovakia, Slovenia, Spain, Sweden, Switzerland: estimate
Bulgaria, Croatia, Cyprus, France, Hungary, Ireland, Latvia, Norway, Poland, Portugal, Romania, Slovenia, Sweden: veterinary products excluded

Source: EFPIA member associations (official figures)



EMPLOYMENT IN THE PHARMACEUTICAL INDUSTRY

EFPIA 2018	Units		Units
Austria	15,411	Latvia	2,154
Belgium	37,073	Lithuania	1,220
Bulgaria	12,000	Malta	1,057
Croatia	5,220	Netherlands	15,000
Cyprus	1,140	Norway	4,000
Czech Rep.	18,000	Poland	29,873
Denmark	24,875	Portugal	7,900
Estonia	380	Romania	32,000
Finland	4,715	Russia	n.a
France	98,528	Slovakia	2,287
Germany	119,535	Slovenia	10,573
Greece	21,739	Spain	42,653
Hungary	30,700	Sweden	11,012
Iceland	500	Switzerland	46,800
Ireland	29,766	Turkey	38,000
Italy	66,500	U.K.	62,500
TOTAL			793,111

Note:

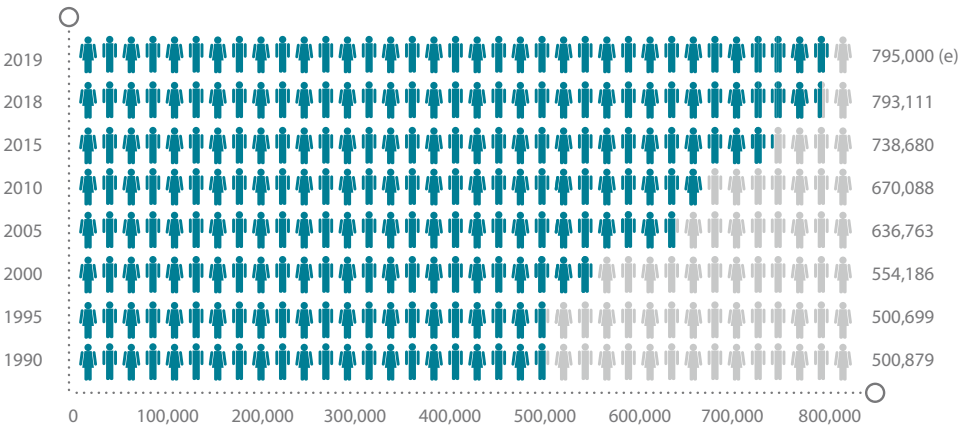
Latvia, Malta, Spain: 2017 data; Estonia: 2016 data; Sweden: 2014 data; Lithuania: 2013 data; Cyprus: 2007 data
Belgium, Bulgaria, Croatia, Estonia, France, Ireland, Italy, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovenia,
Sweden, Switzerland, Turkey, United Kingdom: estimate

Source: EFPIA member associations (official figures)

The research-based pharmaceutical industry is one of Europe's major high-technology industrial employers. Recent studies in some countries showed that the research-based pharmaceutical industry generates about three times more employment indirectly – upstream and downstream – than it does directly (PwC, Economic and societal

footprint of the pharmaceutical industry in Europe, June 2019). Furthermore, a significant proportion of these are valuable skilled jobs, for instance in the fields of academia or clinical science, which can help maintain a high-level knowledge base and prevent a European “brain drain”.

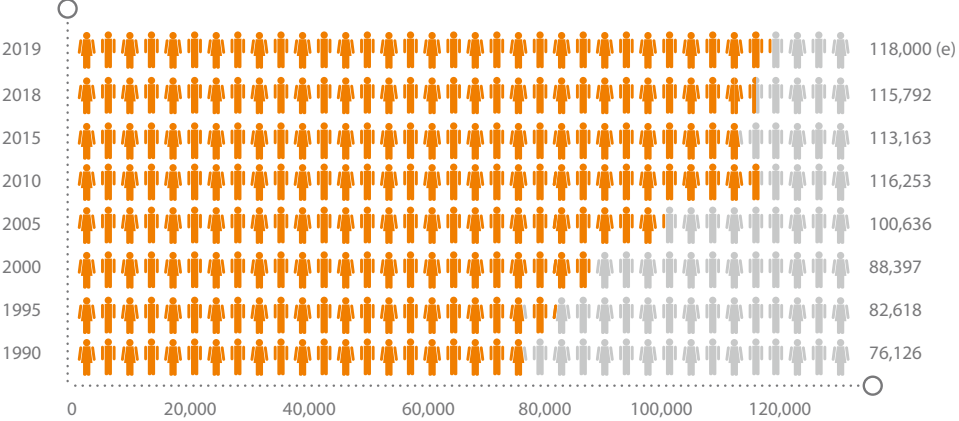
EMPLOYMENT IN THE PHARMACEUTICAL INDUSTRY (1990–2019)



Note:
Data includes Iceland (since 2017), Turkey (since 2011), Croatia and Lithuania (since 2010), Bulgaria, Estonia and Hungary (since 2009), Czech Republic (since 2008), Cyprus (since 2007), Latvia, Romania & Slovakia (since 2005), Malta, Poland and Slovenia (since 2004)

Source: EFPIA member associations (official figures) - (e): EFPIA estimate

EMPLOYMENT IN PHARMACEUTICAL R&D (1990–2019)



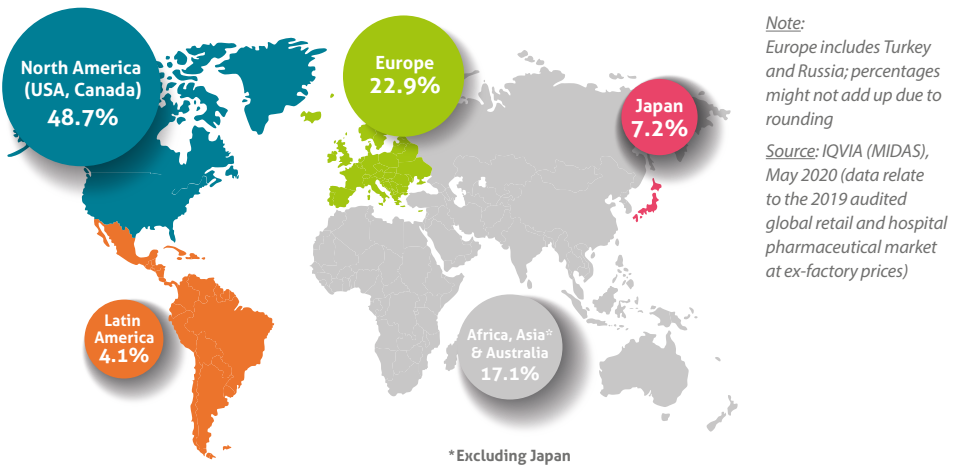
Note:
Data includes Iceland (since 2017), Greece & Lithuania (since 2013), Bulgaria and Turkey (since 2012), Poland (since 2010), Czech Republic, Estonia and Hungary (since 2009), Romania (since 2005) and Slovenia (since 2004)
Croatia, Cyprus, Latvia, Malta, Serbia, Slovakia: data not available

Source: EFPIA member associations – (e): EFPIA estimate

PHARMACEUTICAL SALES

The world pharmaceutical market was worth an estimated € 949,462 million (\$ 1,062,923 million) at ex-factory prices in 2019. The North American market (USA & Canada) remained the world's largest market with a 48.7% share, well ahead of Europe and Japan.

BREAKDOWN OF THE WORLD PHARMACEUTICAL MARKET – 2019 SALES



PRICE STRUCTURE

Distribution margins, which are generally fixed by governments, and VAT rates differ significantly from country to country in Europe. On average, approximately one third of the retail price of a medicine reverts to distributors (pharmacists and wholesalers) and the State.

BREAKDOWN OF THE RETAIL PRICE OF A MEDICINE, 2018 (%)



PHARMACEUTICAL MARKET VALUE (at ex-factory prices)

EFPIA 2018	€ million		€ million
Austria	4,393	Lithuania	694
Belgium	5,407	Malta	77
Bulgaria	1,188	Netherlands	5,358
Croatia	835	Norway	2,416
Cyprus	177	Poland	6,840
Czech Rep.	2,763	Portugal	3,230
Denmark	2,807	Romania	2,826
Estonia	325	Russia	15,106
Finland	2,570	Serbia	652
France	28,897	Slovakia	1,336
Germany	38,531	Slovenia	651
Greece	4,806	Spain	16,375
Hungary	2,437	Sweden	4,137
Iceland	147	Switzerland	5,170
Ireland	2,137	Turkey	5,881
Italy	23,769	U.K.	21,151
Latvia	269		
TOTAL			213,358

Note:

Medicinal products as defined by Directive 2001/83/EEC

Cyprus, Denmark, Finland, Iceland, Latvia, Lithuania, Norway, Russia, Slovenia, Sweden: pharmaceutical market value at pharmacy purchasing prices

Serbia: 2017 data; Malta: 2007 data

Belgium, France, Germany, Ireland, Italy, Malta, Norway, Spain, United Kingdom: estimate

Source:

EFPIA member associations (official figures) – Latvia: IQVIA

The figures above are for pharmaceutical sales, at ex-factory prices, through all distribution channels (pharmacies, hospitals, dispensing doctors, supermarkets, etc.), whether dispensed on prescription or at the patient's request. Sales of veterinary medicines are excluded.



VAT RATES APPLICABLE TO MEDICINES

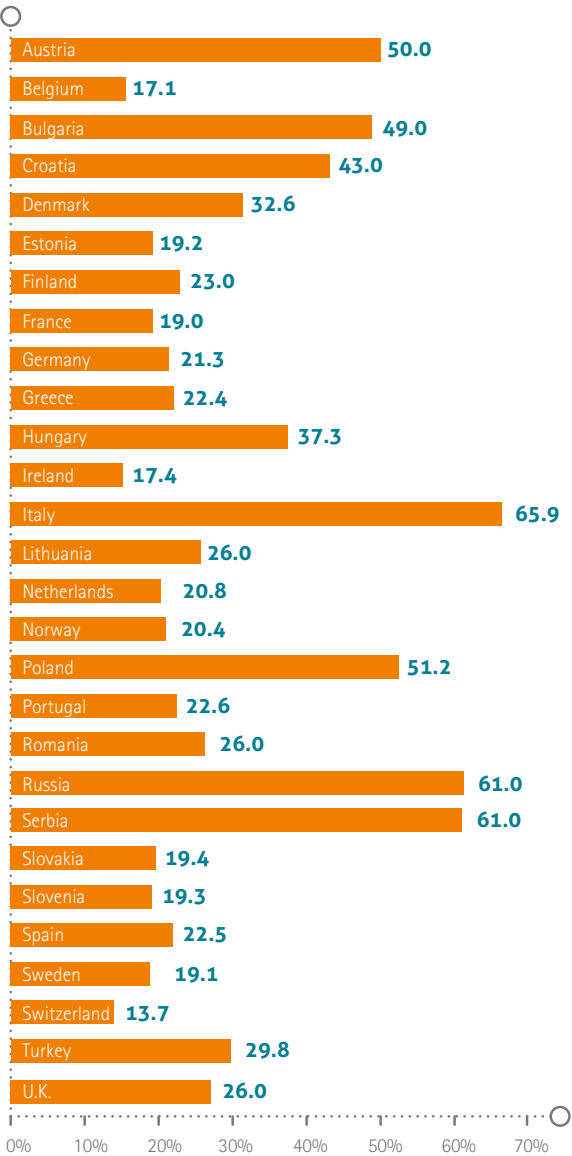
The table below shows the VAT rates applied to medicines in European countries as of 1 January 2020.

Country	Standard VAT rate (%)	VAT rates applied to medicines	
		Prescription (%)	OTC (%)
Austria	20,0	10,0	10,0
Belgium	21,0	6,0	6,0
Bulgaria	20,0	20,0	20,0
Croatia	25,0	5,0	5,0
Cyprus	19,0	5,0	5,0
Czech Rep.	21,0	10,0	10,0
Denmark	25,0	25,0	25,0
Estonia	20,0	9,0	9,0
Finland	24,0	10,0	10,0
France (1)	20,0	2,1	10,0
Germany	19,0	19,0	19,0
Greece	24,0	6,0	6,0-13,0
Hungary	27,0	5,0	5,0
Iceland	24,0	24,0	24,0
Ireland (2)	23,0	0-23,0	0-23,0
Italy	22,0	10,0	10,0
Latvia	21,0	12,0	12,0
Lithuania (3)	21,0	5,0	21,0
Luxembourg	17,0	3,0	3,0
Malta	18,0	0,0	0,0
Netherlands	21,0	9,0	9,0
Norway	25,0	25,0	25,0
Poland	23,0	8,0	8,0
Portugal	23,0	6,0	6,0
Romania	19,0	9,0	19,0
Russia	20,0	10,0	10,0
Serbia	20,0	10,0	10,0
Slovakia	20,0	10,0	20,0
Slovenia	22,0	9,5	9,5
Spain	21,0	4,0	4,0
Sweden	25,0	0,0	25,0
Switzerland	7,7	2,5	2,5
Turkey	18,0	8,0	8,0
U.K.	20,0	0,0	20,0

(1) France: reimbursable medicines 2.1%; non-reimbursable medicines 10.0% (2) Ireland: oral medication 0%; other medication 23%
(3) Lithuania: reimbursable medicines 5.0%; non-reimbursable medicines 21.0%

GENERICIS

The term ‘generic’ is widely used but its definition is not always consistent between countries. Generics are usually produced by a manufacturer who is not the inventor of the original product, and are marketed when intellectual property protection rights are exhausted.



SHARE (ESTIMATE – IN %) ACCOUNTED FOR BY GENERICS IN PHARMACEUTICAL MARKET SALES VALUE (AT EX-FACTORY PRICES), 2018

Note:
Bulgaria, Croatia, Denmark, Estonia, Finland, Greece, Ireland, Hungary, U.K.: share of generics in pharmacy market sales
Austria, Belgium, France, Germany, Italy, Netherlands, Portugal, Slovenia, Spain: share of generics in reimbursable pharmacy market sales
Lithuania, Norway, Poland, Romania, Russia, Serbia, Slovakia, Sweden, Switzerland, Turkey: share of generics in total market sales
Cyprus, Czech Republic, Iceland, Latvia, Malta: 2018 data not available
France: data relate only to those active substances listed on the official list of medicines
Definition: ‘generic’ means a medicine based on an active substance that is out of patent and which is marketed under a different name from that of the original branded medicine.
Source: EFPIA member associations

PHARMACEUTICAL EXPORTS

EFPIA 2018	€ million		€ million
Austria	9,363	Lithuania	723
Belgium	42,801	Luxembourg	268
Bulgaria	935	Malta	299
Croatia	926	Netherlands	38,633
Cyprus	317	Norway	790
Czech Republic	2,538	Poland	3,302
Denmark	13,489	Portugal	979
Estonia	92	Romania	770
Finland	740	Russia	440
France	29,450	Slovakia	408
Germany	82,609	Slovenia	3,092
Greece	1,475	Spain	10,478
Hungary	5,533	Sweden	7,987
Ireland	46,199	Switzerland	77,688
Italy	24,906	Turkey	1,014
Latvia	458	United Kingdom	26,598
TOTAL			435,300

Note:

All data based on SITC 54

Source: Eurostat (COMEXT database – May 2020)

Norway: OECD, Harmonised System Chapter 30, 2019/5; Russia: Clifar Import/Export, 2018; Switzerland: Swiss Federal Customs Administration; Turkey: Turkish Statistical Institute



PHARMACEUTICAL IMPORTS

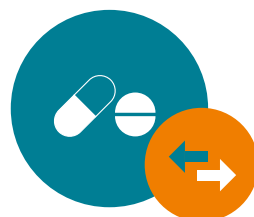
EFPIA 2018	€ million		€ million
Austria	9,036	Lithuania	1,011
Belgium	36,169	Luxembourg	475
Bulgaria	1,386	Malta	256
Croatia	1,168	Netherlands	25,259
Cyprus	269	Norway	2,022
Czech Republic	4,443	Poland	6,597
Denmark	4,020	Portugal	2,635
Estonia	494	Romania	3,067
Finland	1,973	Russia	10,294
France	24,831	Slovakia	1,733
Germany	49,398	Slovenia	1,733
Greece	3,209	Spain	14,088
Hungary	4,686	Sweden	3,970
Ireland	11,963	Switzerland	30,661
Italy	25,563	Turkey	4,021
Latvia	609	United Kingdom	26,230
TOTAL			313,269

Note:

All data based on SITC 54

Source: Eurostat (COMEXT database – May 2020)

Norway: OECD, Harmonised System Chapter 30, 2019/5; Russia: Clifar Import/Export, 2018; Switzerland: Swiss Federal Customs Administration; Turkey: Turkish Statistical Institute



PHARMACEUTICAL TRADE BALANCE

EFPIA 2018	€ million		€ million
Austria	327	Lithuania	-288
Belgium	6,632	Luxembourg	-207
Bulgaria	-451	Malta	43
Croatia	-242	Netherlands	13,374
Cyprus	48	Norway	-1,232
Czech Republic	-1,905	Poland	-3,295
Denmark	9,469	Portugal	-1,656
Estonia	-402	Romania	-2,297
Finland	-1,233	Russia	-9,854
France	4,619	Slovakia	-1,325
Germany	33,211	Slovenia	1,359
Greece	-1,734	Spain	-3,610
Hungary	847	Sweden	4,017
Ireland	34,236	Switzerland	47,027
Italy	-657	Turkey	-3,007
Latvia	-151	United Kingdom	368
TOTAL			122,031

Note:

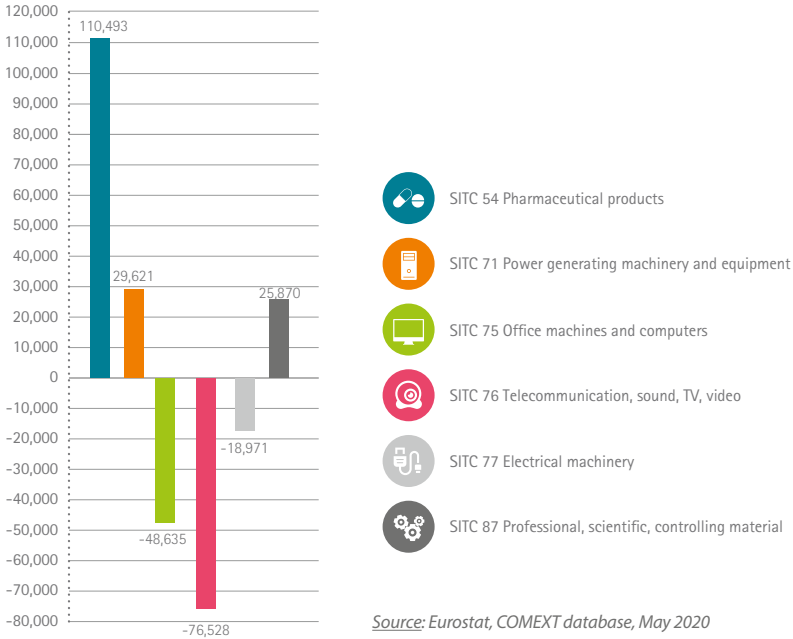
All data based on SITC 54

Source: Eurostat (COMEXT database – May 2020)

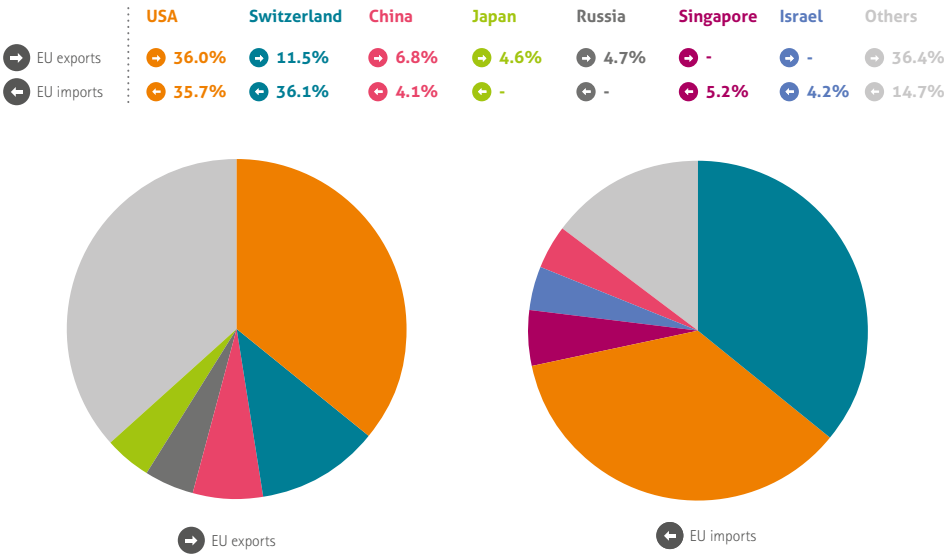
Norway, OECD, Harmonised System Chapter 30, 2019/5; Russia: Clifar Import/Export, 2018; Switzerland: Swiss Federal Customs Administration; Turkey: Turkish Statistical Institute



EU-28 TRADE BALANCE – HIGH TECHNOLOGY SECTORS (€ MILLION) – 2019



THE EUROPEAN UNION'S TOP 5 PHARMACEUTICAL TRADING PARTNERS – 2019



TOTAL SPENDING (PUBLIC AND PRIVATE) ON HEALTHCARE AS A PERCENTAGE OF GDP AT MARKET PRICES

Country	1980	1990	2000	2010	2015	2018
Austria	7.0	7.7	9.2	10.2	10.4	10.3
Belgium	6.1	7.1	7.9	10.0	10.3	10.4
Czech Republic	–	3.7	5.7	6.9	7.2	7.5
Denmark	8.4	8.0	8.1	10.3	10.2	10.5
Estonia	–	–	5.2	6.3	6.4	6.4
Finland	5.9	7.2	6.8	8.9	9.7	9.1
France	6.8	8.0	9.6	11.2	11.5	11.2
Germany	8.1	8.0	9.8	11.0	11.1	11.2
Greece	–	6.1	7.2	9.6	8.1	7.8
Hungary	–	–	6.8	7.5	7.0	6.6
Iceland	5.9	7.4	9.0	8.5	8.1	8.3
Ireland	7.5	5.6	5.9	10.5	7.3	7.1
Italy	–	7.0	7.6	9.0	9.0	8.8
Latvia	–	–	5.4	6.1	5.7	5.9
Luxembourg	4.6	5.1	5.9	7.0	5.5	5.4
Netherlands	6.5	7.0	7.7	10.2	10.3	9.9
Norway	5.4	7.1	7.7	8.9	10.1	10.2
Poland	–	4.3	5.3	6.4	6.3	6.3
Portugal	4.8	5.5	8.4	9.8	9.0	9.1
Slovakia	–	–	5.3	7.8	6.8	6.7
Slovenia	–	–	7.8	8.6	8.5	7.9
Spain	5.0	6.1	6.8	9.0	9.1	8.9
Sweden	7.8	7.2	7.4	8.5	11.0	11.0
Switzerland	6.6	7.9	9.8	10.7	11.9	12.2
Turkey	2.4	2.5	4.6	5.1	4.1	4.2
United Kingdom	5.1	5.1	6.0	8.4	9.7	9.8
Europe	6.1	6.4	7.2	8.6	8.5	8.5
USA	8.2	11.3	12.5	16.4	16.7	16.9
Japan	6.2	5.8	7.2	9.2	10.9	10.9

Note: Europe: non-weighted average (27 countries) – EFPIA calculations

Source: OECD Health Statistics 2019, May 2020

PAYMENT FOR PHARMACEUTICALS BY COMPULSORY HEALTH INSURANCE SYSTEMS AND NATIONAL HEALTH SERVICES (ambulatory care only)

EFPIA 2018	€ million		€ million
Austria	2,895	Lithuania	271
Belgium	4,481	Malta	n.a.
Bulgaria	420	Netherlands	3,104
Croatia	382	Norway	1,216
Cyprus	108	Poland	2,057
Czech Rep.	1,290	Portugal	1,255
Denmark	758	Romania	1,439
Estonia	149	Russia	1,440
Finland	1,460	Serbia	273
France	24,020	Slovakia	1,198
Germany	38,669	Slovenia	327
Greece	1,945	Spain	10,482
Hungary	1,129	Sweden	2,286
Iceland	66	Switzerland	6,084
Ireland	1,700	Turkey	5,456
Italy	7,691	U.K.	11,287
Latvia	147		
TOTAL			135,485

Note:

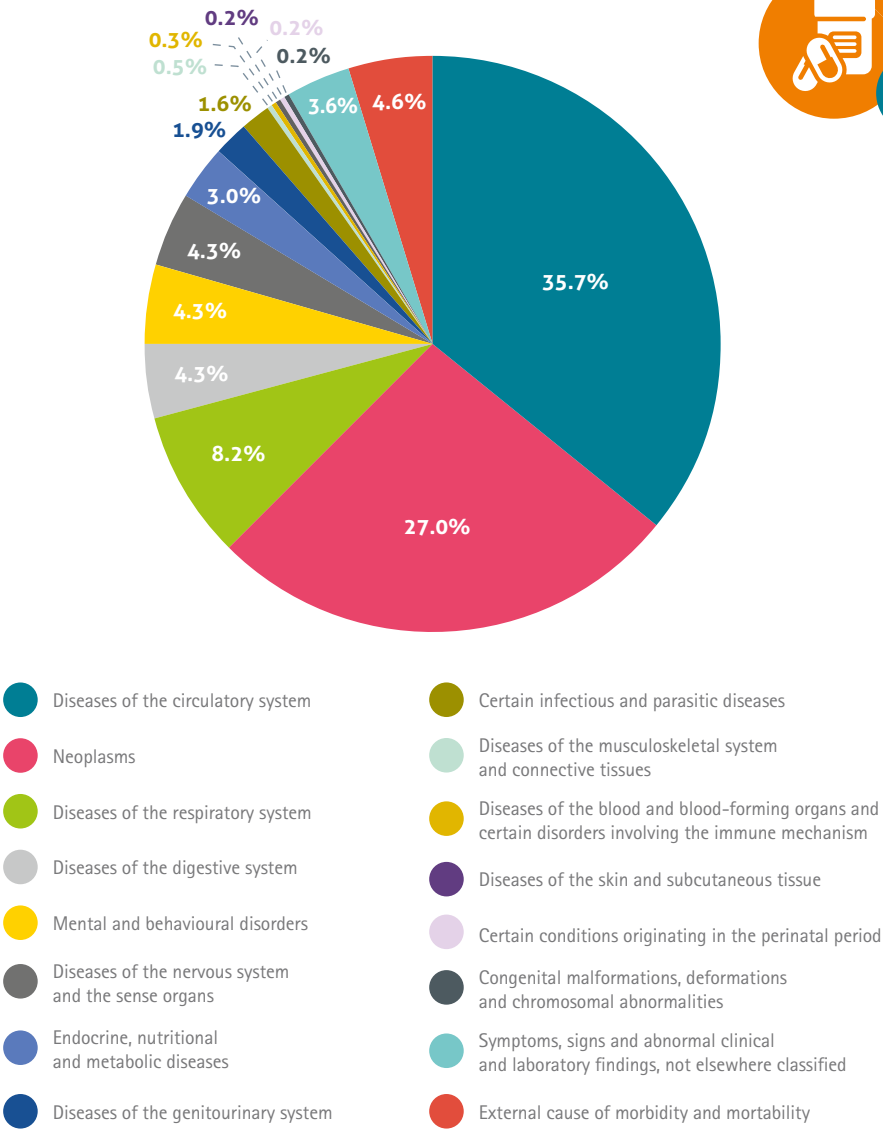
Latvia: 2017 data; Croatia: 2016 data

France, Ireland, Netherlands, Norway, Sweden, U.K.: estimate

Source: EFPIA member associations (official figures)

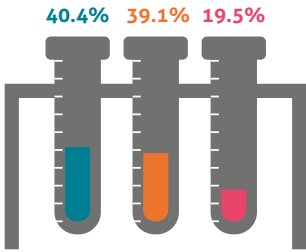


CAUSES OF DEATH BY MAJOR DISEASE AREAS IN EUROPE (EU-28)



Data Source: Eurostat, data relate to year 2016 (non-disease directly related causes of deaths: EFPIA calculations), May 2020

BREAKDOWN OF TOTAL HEALTH EXPENDITURE IN EUROPE – 2017



In-patient care (hospital)



Outpatient care & others



Medical goods (including pharmaceuticals)

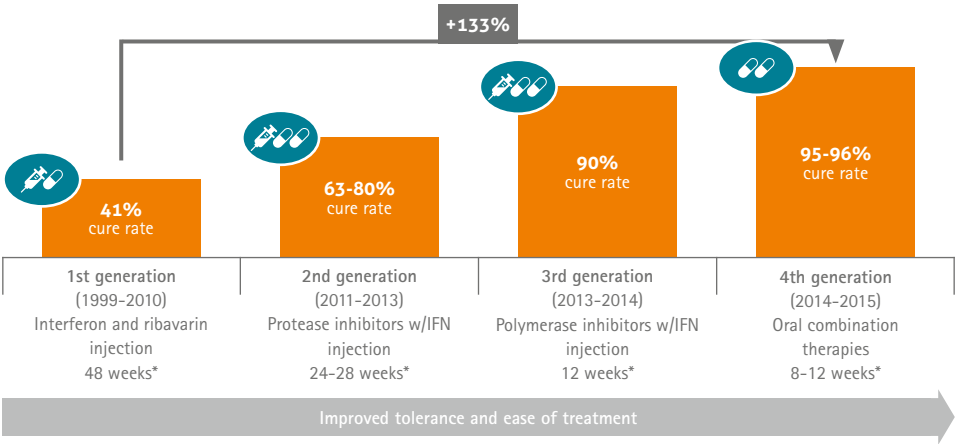
THE ADDED VALUE OF MEDICINES IN HEALTHCARE

Medicines constitute the smallest part of healthcare costs with, on average, 19.5% of total health expenditure in Europe being spent on pharmaceuticals and other medical goods. In costly diseases such as cancer and rheumatoid arthritis, medicines account for even less than 10% of the total disease costs. Medicines can also generate additional savings, for example by substantially reducing costs in other areas of healthcare, including hospital stays and long-term care costs.

Source: OECD Health Statistics 2019, May 2020 – EFPIA calculations (non-weighted average for 26 EU & EFTA countries and Turkey)

CHRONOLOGY OF HEPATITIS C TREATMENT (1999–2015)

* Hepatitis C is the leading cause of liver transplants and the reason liver cancer is on the rise



* Treatment duration, INF=interferon;

Source: PhRMA, ‘Prescription Medicines: International Costs in Context’ (2017)

EFPIA MEMBER ASSOCIATIONS

Austria

Fachverband der Chemischen Industrie Österreichs (FCIO)

Belgium

Association Générale de l'Industrie du Médicament (pharma.be)

Denmark

Laegemiddelindustriforeningen

The Danish Association of the Pharmaceutical Industry (Lif)

Finland

Lääketeollisuus ry

Pharma Industry Finland (PIF)

France

Les Entreprises du Médicament (LEEM)

Germany

Verband Forschender Arzneimittelhersteller (VfA)

Greece

Hellenic Association of Pharmaceutical Companies (SFEE)

Ireland

Irish Pharmaceutical Healthcare Association (IPHA)

Italy

Associazione delle Imprese del Farmaco (Farmindustria)

Netherlands

Vereniging Innovatieve Geneesmiddelen

Norway

Legemiddelindustrien

Norwegian Association of Pharmaceutical Manufacturers (LMI)

Poland

Employers Union of Innovative Pharmaceutical Companies (Infarma)

Portugal

Associação Portuguesa da Indústria Farmacêutica (Apifarma)

Russia

Association of International Pharmaceutical Manufacturers (AIPM)

Spain

Asociación Nacional Empresarial de la Industria Farmacéutica (Farmaindustria)

Sweden

Läkemedelsindustriföreningen

The Swedish Association of the Pharmaceutical Industry (LIF)

Switzerland

Verband der forschender pharmazeutischen Firmen der Schweiz (Interpharma)

Turkey

Arastirmaci Ilac Firmalari Dernegi (AIFD)

United Kingdom

The Association of the British Pharmaceutical Industry (ABPI)

ASSOCIATIONS WITH LIAISON STATUS

Bosnia-Herzegovina: Association of Research-based Medicine Producers (UIPL)

Bulgaria: Association of Research-based Pharmaceutical Manufacturers in Bulgaria (ARPharM)

Croatia: Innovative Pharmaceutical Initiative (iFI)

Cyprus: Cyprus Association of Pharmaceutical Companies (KEFEA)

Czech Republic: Association of Innovative Pharmaceutical Industry (AIFP)

Estonia: Association of Pharmaceutical Manufacturers in Estonia (APME)

Hungary: Association of Innovative Pharmaceutical Manufacturers (AIPM)

Iceland: Icelandic Association of the Pharmaceutical Industry (FRUMTÖK)

Latvia: Association of International Research-based Pharmaceutical Manufacturers (SIFFA)

Lithuania: The Innovative Pharmaceutical Industry Association (IFPA)

Malta: Maltese Pharmaceutical Association (PRIMA)

North Macedonia: Association of Foreign Innovative Pharmaceutical Manufacturers (HOBA)

Romania: Association of International Medicines Manufacturers (ARPIM)

Serbia: Innovative Drug Manufacturers' Association (INOVA)

Slovakia: Slovak Association of Innovative Pharmaceutical Industry (AIFP)

Slovenia: Forum of International Research and Development Pharmaceutical Industries (EIG)

Ukraine: Association of Pharmaceutical Research and Development (APRaD)

MEMBER COMPANIES

✳ Full Members

AbbVie	LEO Pharma
Almirall	Lilly
Amgen	Menarini
Astellas	Merck
AstraZeneca	Merck Sharp & Dohme (MSD)
Bayer	Novartis
Biogen	Novo Nordisk
Boehringer Ingelheim	Pfizer
Bristol-Myers Squibb	Pierre Fabre
Chiesi	Roche
Daiichi-Sankyo	Sanofi
Gilead	Servier
GlaxoSmithKline	Takeda
Grünenthal	Teva
Ipsen	UCB
Johnson & Johnson	

✳ Affiliate Members

Bial
Eisai
Esteve
Lundbeck
Otsuka
Rovi
Stallergenes
Vifor Pharma





European Federation of Pharmaceutical
Industries and Associations

**EFPIA (The European Federation of Pharmaceutical Industries and Associations)
represents the research-based pharmaceutical industry operating in Europe.**

Founded in 1978, its members comprise **36** national pharmaceutical industry associations and **39** leading pharmaceutical companies undertaking research, development and manufacturing of medicinal products in Europe for human use.

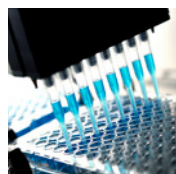
EFPIA aims to create an environment that enables its members to innovate, discover, develop and deliver new therapies and vaccines for people across Europe, as well as contribute to the European economy. EFPIA's vision is for a healthier future for Europe. A future based on prevention, innovation, access to new treatments and better outcomes for patients.

Through its membership, EFPIA represents the common views of about 1,900 large, medium and small companies including the entire European research-based pharmaceutical sector whose interests also include a significant part of the generics and biosimilars segments. Vaccines Europe (VE) is the specialised vaccine industry group within EFPIA. It represents major innovative research-based global vaccine companies as well as small and medium sized enterprises operating in Europe.

Further details about the Federation and its activities can be obtained from:



EFPIA
Leopold Plaza Building * Rue du Trône 108
B-1050 Brussels * Belgium
Tel.: +32 (0)2 626 25 55
www.efpia.eu * info@efpia.eu



01 July 2019
EMA/674304/2018

Guidance on detection and notification of shortages of medicinal products for Marketing Authorisation Holders (MAHs) in the Union (EEA)

1. Introduction

This document provides guidance to marketing authorisation holders (MAHs) for reporting of shortages of medicinal products in the Union (EEA), based on a common EU definition of shortage. It does not cover any other availability issue such as withdrawals of marketing authorisations.

An essential element to a harmonised approach for reporting and managing shortages is the use of a harmonised definition of a shortage. The lack of a common definition has meant that the detection and coordination of the management of shortages in the Union (EEA) has been inconsistent. The differences in the reporting requirements of shortages also meant that comparisons across countries were not possible. This guidance which is based on a common definition agreed by all stakeholders, gives recommendations to facilitate the detection and reporting from marketing authorisation holders to competent authorities about impending shortages. Early notification to competent authorities is a key aspect in the prevention or mitigation of a shortage by allowing sufficient time to make contingency arrangements where necessary.

The guidance will address the following areas:

- *What is a shortage?*
- *What issues should be reported by MAHs?*
- *Who is responsible for monitoring supply and reporting shortages?*
- *When should a notification be made?*
- *Who should be notified?*
- *What information should be included in notifications?*

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2. What is a shortage?

For the purpose of notification and detection of shortages by MAHs, the following definition, agreed by EMA, HMA and stakeholders, should be used:

'A shortage of a medicinal product for human or veterinary use occurs when supply does not meet demand at a national level'.

where:

- a **'shortage'** as defined, allows for identification of current, impeding or anticipated disruption of supply of a medicinal product.
- **'medicinal product'** as described in Article 1(2) of Directive 2001/83/EC and Article 1(2) of Directive 2001/82/EC. Medicinal products which contain the same active substance presented in different pharmaceutical forms and/or strengths and, when required by the national competent authority, pack sizes, are seen as individual unique medicinal products. The above definition applies to marketed human and veterinary medicines (not inclusive of medicines supplied on named patient basis or medicines supplied for compassionate use).
- **'supply'** refers to the total volume of stock of the individual medicinal product that is placed on the market by the Marketing Authorisation Holder.
- **'demand'** relates to the request for a medicinal product by a healthcare professional, veterinarian or patient in response to a clinical need. For demand to be satisfactorily met, the medicinal product will need to be acquired in time and sufficient quantity to allow continuity of best care of patients/animals. Wholesalers are usually a key supply link between MAHs and the users of medicines, and in those cases, in order to estimate demand, the quantity requested in wholesale orders should be considered.
- **'national level'** refers to the situation in a specific country, i.e. if there is insufficient supply of a medicine to meet the demands of the country overall. Logistic -related issues leading to regional supply disruption of a medicinal product e.g. delivery difficulties, national redistribution of stock, are a short term and localised problem and should not be taken into account.

3. What issues should be reported by MAHs?

Based on the above definition and irrespective of the clinical importance of a medicine, the following issues should be reported:

- All shortages which are currently affecting one or more EU member states;
- All impending/anticipated shortages which are expected to affect one or more EU member states.

The above includes all current and impending shortages which have or will occur due to regulatory issues, quality defects and/or any other causes; these include, but are not limited to GMP/GDP issues, batch failures and medicine product recalls.

4. Who is responsible for monitoring supply and reporting shortages?

Article 81 of Directive 2001/83/EC states that MAHs, and their distributors, within the limits of their responsibilities, should ensure appropriate and continued supplies to pharmacies and persons authorised or entitled to supply medicinal products so that the needs of patients in the Member State in question are met.

Furthermore, article 23a, 2nd paragraph of Directive 2001/83/EC and article 27a, 2nd paragraph of Directive 2001/82/EC state that if the product ceases to be placed on the market of a Member State, either temporarily or permanently, the marketing authorisation holder shall notify the competent authority of that Member State. Such notification shall, other than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product.

The *"Paper on the obligation of continuous supply to tackle the problem of shortages of medicines"*, which was agreed by the Ad-hoc technical meeting under the Pharmaceutical Committee on shortages of medicines on 25 May 2018, provides clarification on the responsibilities of the MAHs and wholesale distributors. The limits of the responsibilities of marketing authorisation holders and wholesale distributors should be evaluated on a case-by-case basis by the Member States. Further explanation can be found in the relevant paper.

In order to be able to notify any interruption of supply to competent authorities, MAHs must continuously monitor the supply and demand situation of their medicinal products and have an open and continuous communication with all their operators in the supply chain, such as manufacturers and wholesalers. Early communication of relevant information is essential in handling shortages.

The MAH should also be particularly vigilant where it markets medicines for which no or only limited alternatives are available, and where interruption of supply will result in a potential risk to public health (e.g. clinically important medicines) and / or animal health and welfare. For those products, competent authorities may require marketing authorisation holders to develop a shortage prevention plan, as part of their obligation to ensure continuous supply.

The reasons for shortages are multifaceted and therefore, solutions require the co-ordinated involvement of all stakeholders across the supply chain. In some cases, more general issues (e.g. temperature excursions) at some operators (e.g. wholesalers and manufacturers) could result in a shortage impacting more than one product. Consequently, operators are expected to monitor the supply situation and report any relevant information to the MAH(s). These issues can, depending on national provisions, also be reported to the competent authority independently of the MAH.

MAHs have oversight of the supply of their medicines nationally and globally. They can therefore continually align demand with supply as well as understand the impact of a given shortage on patients and prepare an appropriate response. MAH oversight is also supported by other actors in the supply chain, who themselves may be able to monitor and detect 'signals' of shortages. An example of this is where a single manufacturer is contracted to produce medicinal products or active substances for a number of MAHs. The impact of a manufacturing issue in this case could extend beyond one specific product and it is important to monitor these signals. All operators are expected to monitor for signals. Signals may also come from community pharmacies, hospital pharmacies, retailers, healthcare professionals/veterinarians, patient groups and animal owners.

MAHs are in the best position to assess relevant information, as they have visibility of their stock, both national and global, taking into account foreseen shipments from their manufacturers. Following assessment of a signal and establishment that national supply cannot meet demand, a shortage – impending or anticipated – is confirmed. MAHs should report all current or impending/anticipated medicine shortages, regardless of the perceived medicinal product's clinical importance and availability of alternative medicines.

MAHs and operators of the supply chain are expected to develop and maintain resilience in the supply chain by:

- regularly assessing supply information provided by their manufacturers and suppliers;
- regularly assessing market needs based on information provided by wholesale distributors, community pharmacies, hospital pharmacies, retailers, healthcare professionals/veterinarians or patient groups;
- developing shortage prevention and response plans.

For this purpose, MAHs are advised to utilise relevant guidance developed by professional organisations (e.g. ISPE Drug Shortages Prevention Plan, PDA Risk-Based Approach for Prevention and Management of Drug Shortages, PDA Technical Report 68).

5. When should a notification be made?

MAHs should notify the relevant EU competent authorities of any supply situation that meets the criteria outlined in section 3.

Although EU legislation requires the notification to be made no less than 2 months before the interruption in the placing on the market of the product, MAHs should notify the authorities as early as possible, as soon the shortage or the impending/anticipated shortage is confirmed. In addition there may be national reporting timeframes that should be taken into account.

Timely notification allows for early triaging, assessment and co-ordination of the medicine shortage. Early shortage notification allows for better management of the shortage by the competent authority and stakeholders and allows the competent authority to have time to validate the mitigation plan proposed by the MAHs and/or to collaborate with the MAHs and all the stakeholders (manufacturers, wholesale distributors, community pharmacies, hospital pharmacies, retailers, healthcare professionals/veterinarians or patient groups) in order to resolve the shortage or minimise the shortage impact.

The notification should be sent to the relevant authorities as early as possible even if information is limited. This can be supplemented at a later stage as further details become available as explained in section 7.

6. Who should be notified?

For all authorised medicinal products, shortage notifications should be sent to the impacted national competent authorities.

For centrally approved products, shortage notifications should be sent to EMA as well as the impacted national competent authorities.

MAHs should be aware of the appropriate authority that needs to receive shortage notifications (e.g. national regulatory body, national department of health). Details of the contact point are published on the website of the relevant competent authority. MAHs should be aware of the preferred process and format for reporting (e.g. email, pdf form, online data collection system).

7. What information should be included in notifications?

The information provided in the notification is used by the competent authority for triaging and assessing the situation. The information should therefore be as accurate and up-to-date as possible, while being comprehensive and concise at the same time.

HMA/EMA has developed a proposed template to be included within notifications (Annex 1) in cases where a reporting template is not available at national level. The MAH should endeavour to provide this information; however it is acknowledged that all of the below information may not be available at the time of notification or may change over time; outstanding or new information should be provided as soon as it becomes available or at a later point. Impact assessment details should be included when appropriate and as per national reporting practices/tools.

Individual Member States will determine the preferred method of notification (e.g. email, pdf form, online data collection system).

Annex 1: Proposed template for shortage notification

This form is not intended to notify competent authorities of the withdrawal of a marketing authorisation or a change in the marketing status of any particular product.

Template for shortage notification		
Product details	Product name*	
	Procedure Type (NAP, MRP/DCP, CP)	
	National Authorisation code/EMA Authorisation number*	
	Human medicine*	<input type="checkbox"/>
	Veterinary medicine*	<input type="checkbox"/>
	If veterinary, species authorised in MA	
	ATC code	
	Active substance(s)	
	Pharmaceutical form*	
	Strength*	
	Route(s) of administration	
	Pack size(s)	
	Details on shortage	Date of the beginning of shortage(may be anticipated date)*
Expected end date of the shortage, if applicable*		
Reason for shortage*		
Impacted countries (if known)		
Reference number of any Rapid Alert (quality/safety) related to the issue		
Other authorities notified (e.g. other NCAs, EMA), including reference to Quality Defect report if relevant		
Reference to related pending regulatory action, if relevant		
Risk assessment of impact of shortage*		
Proposed mitigation plan to deal with the shortage		
Are any actions from NCA required? If yes, what actions?		
Details of notifying person	Company name and address (MAH, duly authorised representative or wholesale distributor, if applicable)	

	Name of the person completing the form and date	
	E-mail of contact person*	
	Telephone number contact person	
Impact assessment	<u>Potential</u> alternative medicinal products: <ul style="list-style-type: none"> ➤ Same medicine in different packaging size/strength/pharmaceutical form ➤ Other medicinal product with the same active substance: <ul style="list-style-type: none"> ○ the same strength ○ the same pharmaceutical form ○ the same route of administration ➤ Authorised and marketed products in the same class (therapeutic/pharmacological subgroup) with the same indications ➤ Authorised and marketed products in other class with the same approved indications 	
	Estimated size of population affected by the shortage of this product: <ul style="list-style-type: none"> ➤ Market share of the product* (hospital and ambulatory markets) ➤ Market sales volume (monthly/six monthly) and volume of prescriptions ➤ Proportion market sales affected by shortage ➤ Estimated stock in the current supply chain ➤ Stock that will be made available at the expected end date of the shortage and at the following supplies 	
	Considering: <ul style="list-style-type: none"> - Patient/animal safety - Will patients/animals have no access to a treatment? 	

* Minimum information to be provided to competent authority to proceed with the assessment of the case.

Annex 2: Extracts of relevant Union legislation

Regulation (EC) No 726/2004¹ (Human and Veterinary)

Article 13: "1. Without prejudice to Article 4(4) and (5) of Directive 2001/83/EC, a marketing authorisation which has been granted in accordance with this Regulation shall be valid throughout the Community. It shall confer the same rights and obligations in each of the Member States as a marketing authorisation granted by that Member State in accordance with Article 6 of Directive 2001/83/EC.

Authorised medicinal products for human use shall be entered in the Community Register of Medicinal Products and shall be given a number, which shall appear on the packaging.

2. Notification of marketing authorisation shall be published in the Official Journal of the European Union, quoting in particular the date of authorisation and the registration number in the Community Register, any International Non-proprietary Name (INN) of the active substance of the medicinal product, its pharmaceutical form, and any Anatomical Therapeutic Chemical Code (ATC).

3. The Agency shall immediately publish the assessment report on the medicinal product for human use drawn up by the Committee for Medicinal Products for Human Use and the reasons for its opinion in favour of granting authorisation, after deletion of any information of a commercially confidential nature.

The European Public Assessment Report (EPAR) shall include a summary written in a manner that is understandable to the public. The summary shall contain in particular a section relating to the conditions of use of the medicinal product.

4. After a marketing authorisation has been granted, the holder of the authorisation shall inform the Agency of the dates of actual marketing of the medicinal product for human use in the Member States, taking into account the various presentations authorised.

The marketing authorisation holder shall notify the Agency if the product ceases to be placed on the market of a Member State, either temporarily or permanently. Such notification shall, other than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product. The marketing authorisation holder shall inform the Agency of the reasons for such action in accordance with Article 14b.

Upon request by the Agency, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the Agency with all data relating to the volume of sales of the medicinal product at Community level, broken down by Member State, and any data in the holder's possession relating to the volume of prescriptions".

Article 38: "1. Without prejudice to Article 71 of Directive 2001/82/EC, a marketing authorisation which has been granted in accordance with this Regulation shall be valid throughout the Union . It shall confer the same rights and obligations in each of the Member States as a marketing authorisation granted by that Member State in accordance with Article 5 of Directive 2001/82/EC.

¹ Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency:
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2004_726/reg_2004_726_en.pdf

Authorised veterinary medicinal products shall be entered in the Union Register of Medicinal Products and shall be given a number which shall appear on the packaging.

2. Notification of marketing authorisation shall be published in the Official Journal of the European Union, quoting in particular the date of authorisation and the number in the Union Register, any International Non-proprietary Name (INN) of the active substance of the medicinal product, its pharmaceutical form, and any Anatomical Therapeutic Chemical Veterinary Code (ATC Vet Code).

3. The Agency shall immediately publish the assessment report on the veterinary medicinal product drawn up by the Committee for Medicinal Products for Veterinary Use and the reasons for its opinion in favour of granting authorisation, after deletion of any information of a commercially confidential nature.

The European Public Assessment Report (EPAR) shall include a summary written in a manner that is understandable to the public. The summary shall contain in particular a section relating to the conditions of use of the medicinal product.

4. After a marketing authorisation has been granted, the holder of the authorisation shall inform the Agency of the dates of actual placing on the market of the veterinary medicinal product in Member States, taking into account the various presentations authorised.

The holder shall also notify the Agency if the product ceases to be placed on the market, either temporarily or permanently. Such notification shall, other than in exceptional circumstances, be made no less than 2 months before the interruption in the placing of the product on the market.

Upon request by the Agency, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the Agency with all data relating to the volume of sales of the medicinal product at Union level, broken down by Member State, and any data in the holder's possession relating to the volume of prescriptions.

Cessation of placing of products on market (Human)

Directive 2001/83/EC²

Article 23a: "After a marketing authorisation has been granted, the holder of the authorisation shall inform the competent authority of the authorising Member State of the date of actual marketing of the medicinal product for human use in that Member State, taking into account the various presentations authorised.

If the product ceases to be placed on the market of a Member State, either temporarily or permanently, the marketing authorisation holder shall notify the competent authority of that Member State. Such notification shall, other than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product. The marketing authorisation holder shall inform the competent authority of the reasons for such action in accordance with Article 123(2).

Upon request by the competent authority, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the competent authority with all data relating to the

² Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use:
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf

volume of sales of the medicinal product, and any data in his possession relating to the volume of prescriptions”.

Cessation of placing of products on market (Veterinary)

Directive 2001/82/EC³

Article 27a: “After a marketing authorisation has been granted, the holder of the authorisation shall inform the competent authority of the authorising Member State of the date of the actual placing on the market of the veterinary medicinal product in that Member State, taking into account the various presentations authorised.

The holder shall also notify the competent authority if the product ceases to be placed on the market of the Member State, either temporarily or permanently. Such notification shall, otherwise than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product.

Upon request by the competent authority, particularly in the context of pharmacovigilance, the marketing authorisation holder shall provide the competent authority with all data relating to the volume of sales of the veterinary medicinal product, and any data in his possession relating to the volume of prescriptions”.

Regulation (EU) 2019/6⁴

Article 58.13: “The marketing authorisation holder shall without delay inform the competent authority which has granted the marketing authorisation or the Commission, as applicable, of any action which the holder intends to take in order to cease the marketing of a veterinary medicinal product prior to taking such action, together with the reasons for such action.”

Quality Defect (Human)

Commission Directive 2003/94/EC⁵

Article 13.1: “In the case of medicinal products, the manufacturer shall implement a system for recording and reviewing complaints together with an effective system for recalling, promptly and at any time, medicinal products in the distribution network. Any complaint concerning a defect shall be recorded and investigated by the manufacturer. The manufacturer shall inform the competent authority of any defect that could result in a recall or abnormal restriction on supply and, in so far as is possible, indicate the countries of destination.

Any recall shall be made in accordance with the requirements referred to in Article 123 of Directive 2001/83/EC”.

³ Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products:
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-5/dir_2001_82_cons2009/dir_2001_82_cons2009_en.pdf

⁴ Regulation (EU) 2019/6 of the European Parliament and of the council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC
<https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R0006&from=EN>

⁵ Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use:
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2003_94/dir_2003_94_en.pdf

Quality Defect (Veterinary)

Commission Directive 91/412/EEC⁶

Article 13: "The manufacturer shall implement a system for recording and reviewing complaints together with an effective system for recalling promptly and at any time the veterinary medicinal products in the distribution network. Any complaint concerning a quality defect shall be recorded and investigation by the manufacturer. The competent authority shall be informed by the manufacturer of any quality defect that could result in a recall or abnormal restriction on the supply. In so far as possible, the countries of destination shall also be indicated. Any recall shall be made in accordance with the requirements referred to in Article 42 of Directive 811851 /EEC".

Continuity of Supply (Human)

Directive 2001/83/EC

Article 81: "With regard to the supply of medicinal products to pharmacists and persons authorised or entitled to supply medicinal products to the public, Member States shall not impose upon the holder of a distribution authorisation which has been granted by another Member State any obligation, in particular public service obligations, more stringent than those they impose on persons whom they have themselves authorised to engage in equivalent activities.

The holder of a marketing authorisation for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medicinal product to pharmacies and persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered.

The arrangements for implementing this Article should, moreover, be justified on grounds of public health protection and be proportionate in relation to the objective of such protection, in compliance with the Treaty rules, particularly those concerning the free movement of goods and competition".

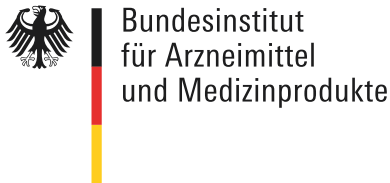
Continuity of Supply (Veterinary)

Regulation (EU) 2019/6

Article 58.2: "The marketing authorisation holder shall, within the limits of its responsibilities, ensure appropriate and continued supplies of its veterinary medicinal products."

Article 101.4: "Wholesale distributors shall, within the limits of their responsibility, ensure appropriate and continued supply of veterinary medicinal product to persons authorised to supply it in accordance with Article 103(1), so that the needs for animal health in the relevant Member State are covered."

⁶ Commission Directive of 23 July 1991 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products (91/412/EEC):
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-5/dir_1991_412/dir_1991_412_en.pdf



Lieferengpässe

Lieferengpässe für Humanarzneimittel



[<https://www2.bfarm.de/lieferengpass/lieferengpassRSS.xml>

]

RSS-Feed: Lieferengpässe für Humanarzneimittel in Deutschland (ohne Impfstoffe)

[Lieferengpässe für Humanarzneimittel in Deutschland \(ohne Impfstoffe\)](#)

[<http://lieferengpass.bfarm.de/ords/f?p=30274:2:609130577714::NO::>]

Dieser Link führt Sie direkt zur Datenbank

Das Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) bietet eine Übersicht zu aktuellen Lieferengpässen für Humanarzneimittel (ohne Impfstoffe) in Deutschland an. Die Meldungen erfolgen durch die Pharmazeutischen Unternehmer und basieren auf der im Pharmadialog erklärten Selbstverpflichtung zur Meldung von Lieferengpässen für versorgungsrelevante Arzneimittel. Die Liste der als versorgungsrelevant angesehenen Wirkstoffe wurde im [Jour Fixe zu Liefer- und Versorgungsempässen](#) regelmäßig aktualisiert. Mit der konstituierenden Sitzung des Beirates nach §52b Absatz 3b AMG am 22.07.2020 wurde der bisherige Jour Fixe zu Liefer- und Versorgungsempässen in den [Beirat](#) überführt. Damit übernimmt der Beirat in Zukunft die Aktualisierung der oben genannten Liste. Eine Meldung wird insbesondere dann für erforderlich angesehen, wenn die Anzahl an Zulassungsinhabern, der endfreigebenden Hersteller oder der Wirkstoffhersteller für einen bestimmten Wirkstoff eine kritische Grenze unterschreitet. Darüber hinaus gilt die Selbstverpflichtung zur Meldung von Lieferengpässen für alle Wirkstoffe, für die bereits in der Vergangenheit ein Versorgungsmangel eingetreten war.

Ein Lieferengpass ist eine über voraussichtlich 2 Wochen hinausgehende Unterbrechung einer Auslieferung im üblichen Umfang oder eine deutlich vermehrte Nachfrage, der nicht angemessen nachgekommen werden kann.

Das BfArM publiziert die Daten kurzfristig nach Einsendung einer entsprechenden Meldung durch den Pharmazeutischen Unternehmer. Diese werden gebeten, einen vorhersehbaren Lieferengpass spätestens 6 Monate im Voraus, unvorhergesehene Engpässe unverzüglich unter Verwendung des vorgegebenen [Formulars](#) mitzuteilen. Mit diesem Formular sind auch Folgemeldungen und die Aufhebung des Lieferengpasses mitzuteilen.

Die Meldung zu Lieferengpässen an das BfArM erfolgt unabhängig von der künftigen Regelung nach § 52b Abs. 3a AMG.

[Alles öffnen](#)

Maßnahmen des BfArM auf Basis des § 10 Absatz 1a AMG

Allgemeine Anordnung an die pharmazeutischen Unternehmer und die pharmazeutischen Großhändler zur Lagerhaltung und bedarfsgerechten Belieferung von Humanarzneimitteln (Kontingentierung)

Welche Rolle nimmt das BfArM im Zusammenhang mit Lieferengpässen ein?

Was kann das BfArM im Zusammenhang mit Lieferengpässen nicht leisten?

Informationen zu bestimmten Wirkstoffen oder Wirkstoffkombinationen

Zusatzinformationen zu gemeldeten Lieferengpässen von Arzneimitteln und Wirkstoffen oder Wirkstoffkombinationen



RSS-Feed: Zusatzinformationen zu gemeldeten Lieferengpässen von Arzneimitteln und Wirkstoffen oder Wirkstoffkombinationen

Suchbegriff	Alle Wirkstoffe	Alle Jahre
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- 24.09.2020
Informationsbrief zu NULOJIX® (Belatacept): Aktualisierte Information zu der vorübergehenden Einschränkung der Lieferfähigkeit
Wirkstoff Belatacept
[PDF139KB](#)
- 12.08.2020
Lieferengpass zu Erwinase® 10.000 I.E./Durchstechflasche
Wirkstoff Crisantaspase
[zum Artikel](#)
- 21.07.2020
Lieferengpass für TEMGESIC® Ampullen, 0,3 mg, Injektionslösung
Wirkstoff Buprenorphin
[PDF305KB](#)
- 21.07.2020
Lieferengpass für TEMGESIC® forte sublingual
Wirkstoff Buprenorphin
[PDF361KB](#)

4 July 2019
EMA/632473/2018

Good practice guidance for communication to the public on medicines' availability issues

Recommendations for EU national competent authorities and EMA to ensure
adequate public information

1. Introduction

Medicine shortages or problems relating to the availability of medicines are a multifactorial problem involving a wide range of stakeholders, from patients and animal owners to the pharmaceutical industry. In addition to measures to improve reporting and management of availability problems, measures aimed at improving communication of such issues to the public play an important role in minimising their potential impact. There is also a need for more systematic involvement and interaction with stakeholders, especially on issues with potential impact on patients. Timely and comprehensive information is necessary to ensure planning, rationing of existing stocks and prevention of stockpiling. Advice to healthcare professionals and patients on potential alternative medicinal products is often needed. This approach to communicating shortages would also help to maintain and improve trust in the regulatory system.

Most shortages and availability problems are managed at national level; some are managed at EU level. Processes for communication to the public are already in place at EU and national level, however communication practices vary amongst member states and there is a need to review and consolidate existing practices into a single document providing clear and harmonised guidance to EU national competent authorities and EMA, promoting good practices and improving EU coordination.

1.1. Purpose of the document

This document provides EU national competent authorities and EMA with key principles and examples of good practices for communication to the public on shortages for human and veterinary medicines as well as availability issues due to revocations or cessations of marketing authorisations. The document is intended for guidance only. Implementation should be a matter for EMA and EU national competent authorities taking into account available resources and the communication needs within their territory.

It aims to promote good practice by:

- Enhancing current communication to the public and ensuring a multidisciplinary approach within regulatory authorities;
- Aligning criteria for publication across the EU network;
- Increasing visibility and accessibility of information on the availability of medicines;
- Fostering interaction with stakeholders.

This document is based on the results of a survey of all EU member states carried out by the [HMA-EMA task force](#) to collect information on how issues related to shortages and availability of medicines are measured and communicated to the public.

The guidance addresses the following areas:

- *Who* should communicate
- *Who* is the target audience
- *Which* format or tools
- *What* information to be published
- *When* to publish
- *How* to involve stakeholders in the preparation and dissemination of information
- *Internal* collaboration
- *Examples* of communication to the public and interaction with stakeholders

Shortages referred to in this guidance are to be understood in the context of the harmonised definition agreed by EMA-HMA in the "Guidance on detection and notification of shortages of medicinal products for Marketing Authorisation Holders (MAHs) in the Union (EEA)":

'A shortage of a medicinal product for human or veterinary use occurs when supply does not meet demand at a national level'.

The definition applies to all shortages that are already affecting or that are expected to affect one or more EU member states in the future.

It applies to prescription and non-prescription medicines alike.

1.2. Key recommendations for good practice on publication of information on availability issues

The below recommendations have been drawn up based on the results of the survey on existing practices in member states and take into account the outcome of the [workshop](#) held at EMA in November 2018 where stakeholders raised transparency and visibility of availability issues as crucial elements for good shortage management. The recommendations also draw on EMA's experience in publishing information, which has been well established for medicine shortages affecting more than one member state where an assessment and recommendations are made at EU-wide level.¹

¹ <https://www.ema.europa.eu/en/human-regulatory/post-authorisation/medicine-shortages/shortages-catalogue>

Potential negative effects that could follow communication such as stockpiling need to be considered when communicating and choosing the optimal timing and level of visibility are important to minimise this risk.

It is recommended that information on shortages should be kept separate from information on revocations and cessations of marketing authorisations. This will allow distinguishing between the permanent disruption in the case of cessations and revocations of marketing authorisations and temporary supply disruptions in the case of shortages. However it is recommended that this information should be easily accessible and interlinked.

Key recommendations for shortages		
Criteria for national competent authorities to make information publicly available	<ul style="list-style-type: none"> shortages of medicines within their territory (nationwide issues rather than local issues). Ideally competent authorities should not apply selection criteria for publication and should communicate on all shortages occurring nationwide. In some instances, this communication may complement information issued centrally by EMA. 	
Criteria for EMA to make information publicly available	<ul style="list-style-type: none"> shortages of medicines (that are centrally or nationally authorised) where the shortage affects more than one member state and EMA's scientific committees have given recommendations to healthcare professionals (a DHPC). 	
Format and tools	<ul style="list-style-type: none"> EU national competent authorities and EMA should use a systematic listing (usually in the form of a catalogue, one for human medicines and one for veterinary medicines) to communicate on shortages. For shortages with a high impact on patients or animals, consideration should be given to using high-profile communication tools (i.e. press release) in addition to systematic listing in the catalogue. Regardless of the tools used, all shortages issues should be easily accessible on a webpage of the regulatory authority. The content of the catalogue should be easily searchable. Non-machine readable data formats (such as PDFs) are not recommended and should be avoided as far as possible. Providing colour-coded or symbol-differentiated information for shortages could help to distinguish between different shortage situations (indicating impact and status of supply situation). The use of electronic Product Information (ePI), once this is implemented across the EU, will offer opportunities to better communicate information on shortages in a timely and targeted manner. 	
Information to be published in the catalogue	Details of medicine	<ul style="list-style-type: none"> Trade name Active ingredient (INN) Pharmaceutical form and strength MAH

Key recommendations for shortages		
		<ul style="list-style-type: none"> For veterinary medicines the species
	Details on shortage	<ul style="list-style-type: none"> Date of the beginning of the shortage (may be anticipated date) or availability issue Expected end date of the shortage, if applicable Reason for shortage and actions taken to mitigate shortage
	If applicable, advice for healthcare professionals patients, veterinarians or animal keepers	<ul style="list-style-type: none"> Potential alternative medicinal products, if applicable, which may include imported medicines Recommendations for change in clinical practice/ change in use of medicine/ use of a suitable alternative
	Updates to current status of shortage	<ul style="list-style-type: none"> Updates should be issued to reflect resolution or any change in recommendations, if applicable
Timing of publication	<ul style="list-style-type: none"> Publication should occur once the shortage has been confirmed by the marketing authorisation holder for the affected medicine and, if applicable, recommendations have been agreed. The exact timing may be determined at national level taking into account national requirements. However, early communication to the public is encouraged and important to allow for adequate planning and to ensure continuity of care. Updates should be issued to reflect any relevant change in the situation including recommendations. For supply situations that have been resolved, this should be reflected as soon as the notification from the marketing authorisation holder has been received that the shortage is resolved. Once a shortage is declared as resolved, there may be a delay before supplies are fully re-established and it is recommended that a disclaimer is included to explain this in shortages communications. A record of supply problems that have been resolved should be kept for a set period of time, i.e. at least 6 months. 	
Audience	<ul style="list-style-type: none"> Primarily healthcare professionals and patients, or veterinarians and animal owners. Other regulators and industry (including wholesale distributors). <p>To address this wide audience, the language used in any communication should be public friendly, concise and should use lay terms.</p>	

Key recommendations for shortages	
Collaboration with stakeholders	<ul style="list-style-type: none"> • EU national competent authorities and EMA should consider involving relevant stakeholder groups (in particular patients', consumer and healthcare professional organisations) on availability issues, especially in those with higher potential impact on patient care. Wholesale distributors may also be involved for questions on sourcing of medicines. Involvement should aim at obtaining advice and feed-back on potential suitable alternatives and recommendations, if applicable, as well as feedback on whether key messages are well communicated and how to ensure adequate dissemination. • EU national competent authorities and EMA should consider sharing the final communication with marketing authorisation holders for information. • EU national competent authorities and EMA should explore ways to multiply their communication through relevant organisations' channels (patients, healthcare professionals, consumer organisations, animal owners, veterinarians), learned societies, professional/medical journals, media (press, TV), newsletters, and potentially electronic prescribing systems (enabling the electronic generation, transmission, and filling of a medical prescription). To increase visibility and knowledge about shortage catalogues, communication campaigns may be considered at national level.
Internal collaboration within the network	<ul style="list-style-type: none"> • For the assessment and communication of shortages, advice and consultation may be sought where needed from the Single Point of Contact (SPOC) network.² • Ideally, communication staff within EU national competent authorities or EMA should be involved in the drafting of relevant communication.

Key recommendations for other availability issues	
Criteria for national competent authorities to make information publicly available	<ul style="list-style-type: none"> • revocations or suspensions of marketing authorisations within their territory. • relevant cessations of marketing authorisations in their territory. For medicines, where the cessation of marketing authorisation is due to commercial reasons and other generic options remain on the market, the inclusion into the catalogue is optional.
Criteria for EMA to make information publicly available	<ul style="list-style-type: none"> • revocation or suspension of centrally and nationally authorised medicines.

² Single Point of Contacts (SPOC) are contact points at each human and veterinary medicines regulatory agency in the EU/EEA responsible for sharing information with other SPOCs and coordinating subsequent actions in relation to shortages and availability of authorised medicines. They have been nominated by the Task Force on Medicines Availability with the aim to facilitate better prevention, identification, management and communication of shortages and availability issues.

Key recommendations for other availability issues		
	<ul style="list-style-type: none"> cessations of marketing authorisations for centrally authorised medicines. 	
Format and tools	<ul style="list-style-type: none"> EU national competent authorities and EMA should use a systematic listing (usually in the form of a catalogue, one for human medicines and one for veterinary medicines) to communicate on other availability issues. For other availability issues with a high impact on patients or animals, consideration should be given to using high-profile communication tools (i.e. press release) in addition to systematic listing in the catalogue. 	
Information to be published in the catalogue	Details of medicine	<ul style="list-style-type: none"> Trade name Active ingredient (INN) Pharmaceutical form and strength MAH For veterinary medicines the species
	Details on availability issue	<ul style="list-style-type: none"> Date of the beginning of the cessation or revocation Reason for availability issue
	If applicable, advice for healthcare professionals patients, veterinarians or animal keepers	<ul style="list-style-type: none"> Potential suitable alternatives, if applicable Recommendations for change in clinical practice/ change in use of medicine/ use of suitable alternatives
Timing of publication	<ul style="list-style-type: none"> For suspensions and revocations of marketing authorisations: <ul style="list-style-type: none"> Publication as soon as the suspension or revocation has been recommended, and recommendations (if applicable) have been agreed. Updates to reflect any change in recommendations, if applicable. For relevant cessations of marketing authorisations: publication at time of cessation. It is good practice to keep a public record for at least 6 months. 	
Audience	See recommendations for shortages	
Collaboration with stakeholders	See recommendations for shortages	
Internal collaboration within the network	See recommendations for shortages	

2. Annex I. Full analysis

In May 2018, EMA and HMA carried out a survey to map public communication on shortages and availability of human medicines³ by EU regulators. The purpose was to assess, qualitatively and quantitatively, how EU regulators communicate to the public on shortages and supply issues.

The results of the survey build on existing knowledge on communication practices gained from previous work which led to the development of [EMA's public catalogue on shortages](#).

The survey comprised a questionnaire with 7 questions on the public communication practices in individual EU member States.

The questionnaire focused on public communication activities to the general public, mainly in relation to shortages.

The survey was sent to the Single Point of Contact (SPOC) nominated for human and veterinary medicines at the relevant regulatory authority for each Member state.

For human medicines, the survey was sent to 33 SPOCs (28 EU Member states, including 2 SPOCs for Germany to cover the two regulatory agencies (BfArM and PEI), including EMA and 3 for EEA). Of these, 30 responded. The response rate was 90%.

For veterinary medicines, the survey was sent to 30 SPOCs and 27 responded. The response rate was 90%.

The survey found the following results:

- For human medicines a majority (87%) of EU regulatory authorities (national competent authorities and EMA) already publish information on shortages on their website.
- Amongst the authorities that publish information, a majority (69%) do not have set criteria for publication and publish on any shortage that is reported. Only selected member states have criteria for publication based on the duration of the shortage and the criticality of the medicine.
- Most authorities also communicate on other issues such as revocation or suspension of medicines (50%) or withdrawals of medicines due to commercial reasons (70%). However this information is not necessarily reflected in the listing of shortages and various other communication tools may be used (such as press releases for individual availability issues).
- Globally, a similar picture for human medicines can be seen as in the EU. In the USA, the Association of Health System Pharmacists and the Food and Drug Administration publish a web listing of medicine shortages^{4,5} Both listings include information on current and resolved shortages as well as other information for patients and consumers. The websites contain concise information on products affected by the shortage, the reason for the shortage, suitable alternatives and the expected resolution date. The information on the FDA website covers 'medically necessary' medicines as well as those considered non-medically necessary for which the FDA has received multiple requests for information. However it does not include information on shortages of brief duration.
- For veterinary medicines, the picture is similar with fewer EU regulatory authorities publishing information with only 52% publishing information on shortages on their website.

³ This guidance applies only to human medicines at present, however a similar approach will be taken to address veterinary medicines.

⁴ <http://www.ashp.org/menu/DrugShortages/CurrentShortages.aspx>

⁵ <https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages>

Based on the analysis of the survey results the following key areas for communication on availability have been identified:

Key recommendations

Public communication should be considered for

- **any shortage** of a medicine that affects the whole country (nationwide issues rather than local issues).
- **revocations** or **suspensions** of medicines.
- **cessations** of marketing authorisations. For cessation of marketing authorisations due to commercial reasons, information may be less relevant for stakeholders as these medicines can usually be substituted.

2.1. Which format and tools?

The survey found the following results for the formats and tools used by regulatory authorities:

- For human medicines, 88% of authorities who already publish information on availability issues, usually do this in the form of a systematic listing, i.e. a catalogue format. The majority of authorities (69%) do not have set criteria for publication and publish all reported shortages. Only selected member states have criteria for publication related to the duration of the shortage and the criticality of the medicine.
- In addition to the shortage catalogue EU regulatory authorities (national competent authorities and EMA) use a variety of communication tools to inform on availability issues: Press releases (57%), newsletters (30%) and social media (23%).
- For veterinary medicines, the proportion of authorities that use a catalogue listing is 64%. Most of those (64%) do not use any selection criteria when publishing information. Communication tools used by veterinary regulatory authorities are press releases professional organisations and professional journals.

A catalogue listing is ideal for providing information on shortages as it allows quick one-stop referencing and is ideal for stakeholders looking for specific information. Presentation of information can be summarised in bullet-point format and colour coded to highlight new and more relevant shortages.

It is envisaged that in the future a single portal will give access to all information on availability issues from EU regulatory authorities. While the single portal is being built, as an interim solution, both the HMA webpage (<https://www.hma.eu/598.html>) and the EMA Webpage (<https://www.ema.europa.eu/en/human-regulatory/post-authorisation/medicine-shortages/shortages-catalogue>) provide a listing of links to national shortage catalogues.

Key recommendations

EU national competent authorities should use a **systematic listing** in a catalogue to communicate on the following issues:

- **shortages** of medicines affecting the country. In some instances this communication complements information issued centrally by EMA. Ideally regulatory authorities should not apply selection criteria for publication and should communicate on any nationwide shortage (as per the agreed EMA-HMA definition).
- **revocations** or **suspensions** of medicines within their territory.
- **cessations** of marketing authorisations in their territory. For cessation of marketing authorisations due to commercial reasons, this should be decided at national level depending on the relevance to stakeholders (especially for generics where there may be many other generic alternatives).

EMA should use a **systematic listing** in a catalogue to communicate on the following issues:

- **shortages** of medicines (centrally or nationally authorised) where the shortage affects more than one member state and EMA's scientific committee has given recommendations (a DHPC).
 - **revocations** or **suspensions** of centrally and nationally authorised medicines.
 - **cessations** of marketing authorisations for centrally authorised medicines.
- For availability issues with a high impact on patients or animals, EU national competent authorities and EMA should consider using additional communication tools (press releases, newsletter or social media) and reflect the information on the homepage. High-patient impact is usually associated with safety-related issues or unavailability of a critical medicine.
- Regardless of the tools used, all availability issues should be accessible on a single webpage.

2.2. What information to publish

When the decision to publish a shortage in a catalogue has been made, the information to publish should be brief, concise but sufficient for healthcare professionals and patients or veterinarians and animal owners to identify the medicine involved and take the required actions. The information is based on information published by those member states who already publish (see annex I) and is summarised in the table below:

Table 1: Recommendations for publishing information on medicine's availability issues

Information to publish in the catalogue	
Details of medicine	<ul style="list-style-type: none">• Trade name• Active ingredient (INN)• Pharmaceutical form and strength• MAH• For veterinary medicines the species should be specified
Details on availability issue/shortage	<ul style="list-style-type: none">• Date of the beginning of the shortage (may be anticipated date) or availability issue

Information to publish in the catalogue	
	<ul style="list-style-type: none"> For shortages, expected end date of the shortage Reason for availability issue or shortage
Advice for healthcare professionals/ patients, if applicable	<ul style="list-style-type: none"> Potential alternative medicinal products, if applicable Recommendations for change in clinical practice/ change in use of medicine, if applicable
Updates to current status of availability issue/shortage	<ul style="list-style-type: none"> Updates to reflect resolution or any change in recommendations, if applicable

2.3. When to publish

Communication to the public needs to be timely and up-to-date to ensure effective planning. The survey found that:

- EU national competent authorities and EMA always update their published information on shortages, as new information becomes available and when the shortage is resolved.
- In addition, some member states (35%) review their information at set time intervals (ranging from daily to monthly).
- Once a shortage is resolved, most authorities remove the information (62%) and only 38% keep this information on their website.
- For veterinary medicines, 71% of EU regulatory authorities also update their information as new information becomes available. 27% review the information at set time intervals. Once a shortage is resolved 57% of authorities remove the information from the website.

Key recommendations

- For **shortages**: publication should occur once the shortage has been confirmed by the MAH and recommendations have been agreed (if applicable). The exact timing may be determined at national level taking into account national requirements. Updates should be issued to reflect any potential change in the recommendations. For supply situations that have been resolved this needs to be reflected as soon as notification is received that the shortage is resolved. This could be by updating the catalogue listing to mark the medicine as available again. It is good practice to keep a record of supply problems that have been resolved for a set period of time, i.e. at least 6 months.
- For **suspensions** and **revocations** of marketing authorisations: publication should be as soon as a recommendation for suspension or revocation has been given. Updates should be issued to reflect any potential change in the recommendations.
- For relevant **cessations** of marketing authorisations: publication should be at time of cessation.

2.4. Who is the target audience

- For human medicines most EU national competent authorities and EMA mainly target healthcare professionals (100%) and patients (92%) in communication. Industry and other regulators are also targeted in 60% of the cases.

- For veterinary medicines 93% target veterinarians and 64% are targeting animal owners. Wholesalers are also targeted in 57% of the cases, industry and regulators less frequently (in 36% and 43% of the cases).
- Healthcare professionals and patients, veterinarians and animal owners are the key audience who require timely accurate and up-to-date information from public health authorities on availability issues. This is particularly important as information from other sources on availability issues is sparse and early knowledge is important to allow for early planning and adjustment of clinical practice. Other regulators and industry (including wholesale distributors) are less often targeted but would also benefit from early information.

Key recommendations

- Public communication by EU national competent authorities and EMA should primarily target patients and healthcare professionals for human medicines and veterinarians and animal owners for veterinary medicines.
- Other regulators and industry (including wholesale distributors) should also be targeted.
- To address this wide audience the language of any communication should be public friendly, concise and using lay terms.

2.5. Other communication tools used and how to involve stakeholders in the preparation and dissemination of information

It is important to involve stakeholders in the preparation of public communication documents to address their concerns and information needs.

The survey found that:

- For human medicines 54% of authorities who communicate on availability issues overall also engage with their target audience in their communication. For veterinary medicines it is only 26% who engage with their target audience. In both cases, it is not clear whether this is seeking active advice or rather for dissemination only.
- EU national competent authorities and EMA use a variety of communication tools to disseminate information on availability issues: Communication through relevant organisations' channels (patients, consumers, healthcare professionals or learned societies) (63% for human medicines and 48 % for veterinary medicines), press releases (57% and 48% for veterinary medicines), professional/medical journals (57% for human medicines and 48% for veterinary medicines), media (press, TV) (33% for human medicines and 30% for veterinary medicines), newsletters (30% for human medicines and 20% for veterinary medicines), social media (23% for human medicines and 26% for veterinary medicines).

Some EU authorities feed information about shortages into the national electronic patient health systems (EMR) and electronic prescribing systems (7% for human medicines and 11% for veterinary medicines). Thus, healthcare professionals and veterinarians will get instant alerts about shortages when prescribing or dispensing the medicine in question.

Key recommendations

- EU national competent authorities and EMA should consider involving relevant stakeholder groups (patients, consumers and healthcare professional organisations) on availability issues especially in those with higher potential impact on patient care.
- Wholesale distributors may also be involved for questions on sourcing of medicines. Involvement should aim at obtaining advice and feed-back on potential suitable alternatives and recommendations when applicable as well as for ensuring that the key messages are well communicated and ensuring adequate dissemination.
- EU national competent authorities and EMA should consider sharing the final public communication for information with marketing authorisation holders for information.
- EU national competent authorities and EMA should explore ways to multiply their communication through relevant organisations' channels (patients, consumers, animal owners, veterinarians, healthcare professionals or learned societies), professional/medical journals, media (press, TV), newsletters, and potentially electronic prescribing systems. Other means to explore to interlink shortage information could be electronic product information.

2.6. Internal collaboration

The survey found that most communication materials are prepared by the departments involved in the assessment of the availability issue (i.e. inspection) but often also involve communication colleagues (57% for human medicines, 30% for veterinary medicines).

As an outcome of this review it is recommended to systematically consider involvement of communication staff in the drafting of relevant communication to ensure that it fulfils the needs of the target audience.

In addition during the assessment and communication of a shortage member states should seek advice and consultation where needed using the the Single Point of Contact (SPOC) network.

2.7. Examples of public communication and interaction with stakeholders

Based on the survey feedback, the following initiatives were identified in selected EU member states as examples of public communication and collaboration which could potentially be implemented in other member states:

- A monthly newsletter highlighting new and relevant availability issues
- Involving stakeholders i.e. in disseminating information on shortages
- Alerts (pop-ups) on shortages in electronic patient records and electronic prescription systems to alert doctors and pharmacists at the point of prescribing or dispensing the medicine in question.
- Collaboration with the most commonly used sources of medicinal product information among healthcare professionals (i.e. electronic pharmaceutical compendiums). In some countries compendiums publish real-time alerts on important safety issues, shortage situations etc., providing instant information for the patient or physician.

2.8. Review

It is proposed that public communication practices in EU member states on availability issues will be reviewed regularly and this guidance will be updated accordingly and as needed.

3. Annex II. Information currently provided in shortage catalogues

Table 1: Information provided in shortage catalogues for human medicines by individual EU authorities

EU authority	Trade name	Active ingredient (INN)	Pharmaceutical form	Strength	MAH	Cause of shortage	Start date of shortage	Estimated end date of shortage	Alternatives available, without details	Alternatives available, with details	Other
Austria	X	X	X	X	X	X	X	X			X
Belgium	X	X	X	X	X	X	X	X			
Bulgaria	X	X	X	X	X		X				X
Croatia	X	X	X	X	X	X	X	X			X
Czech Republic	X		X	X			X			X	
Denmark	X	X	X	X			X			X	X
Estonia	X	X	X	X	X			X			
Finland	X	X	X	X	X		X	X			
Germany (PEI)	X	X	X	X	X		X	X		X	X
Germany (BfArM)	X	X	X	X	X	X	X	X	X	X	X
Greece	X	X	X	X	X		X	X	X		
Hungary	X	X	X	X	X	X	X	X	X		
Iceland	X	X	X	X					X	X	
Italy	X	X	X	X	X	X	X	X	X		X
Latvia	X	X	X	X			X	X	X		
Lithuania	X	X	X	X	X	X	X	X	X	X	
Netherlands											X
Norway	X	X	X	X	X	X	X	X	X	X	
Romania	X	X	X	X	X	X	X	X			
Slovak Republic	X		X	X	X		X	X			X
Slovenia	X		X	X			X	X			
Spain	X	X	X	X			X	X	X		X
Sweden	X	X	X	X	X		X	X		X	X
EMA	X	X	X	X		X	X	X			X

Table 2: Information provided in shortage catalogues for veterinary medicines by individual EU authorities

EU authority	Trade name	Active ingredient (INN)	Pharmaceutical form	Strength	Species	MAH	Cause of shortage	Start date of shortage	Estimated end date of shortage	Alternatives available, without details	Alternatives available, with details	Other
Austria	X	X	X	X			X		X			X
Belgium	X	X	X	X	X		X	X	X		X	
Denmark	X	X	X	X				X			X	X
Estonia	X	X	X	X				X	X			
Finland	X	X	X	X				X	X			
Germany (PEI)	X	X						X			X	
Greece	X	X	X	X	X	X	X					
Liechtenstein		X						X				X
Norway	X	X	X	X		X	X	X	X	X	X	
Slovenia	X		X	X				X	X			
Spain		X			X							
Sweden	X	X	X	X	X				X		X	
UK	X	X	X	X					X	X		



EUROPÄISCHE KOMMISSION GENERALDIREKTION GESUNDHEIT UND LEBENSMITTELSICHERHEIT

Gesundheitssysteme, Arzneimittel und Innovation
Arzneimittel: Qualität, Sicherheit, Innovation

Die Bewältigung des Problems der Arzneimittelknappheit mittels Verpflichtung zur kontinuierlichen Versorgung — Diskussionspapier Vereinbart auf der Ad-hoc-Fachsitzung des pharmazeutischen Ausschusses zum Thema Arzneimittelknappheit am 25. Mai 2018

*Antwort auf die Aufforderungen des Rates¹ und des Europäischen Parlaments² zur Überwachung der Durchführung von Artikel 81
[und 23a] der Richtlinie 2001/83/EG³*

Dieses Dokument soll die Durchführung der Artikel 81 und 23a der Richtlinie 2001/83/EG zur Schaffung eines Gemeinschaftskodexes für Humanarzneimittel erleichtern.

Hier werden häufig gestellte Fragen (und die diesbezüglichen Antworten) zur Umsetzung der Vorschriften dargelegt, die für Inhaber von Genehmigungen für das Inverkehrbringen von Arzneimitteln und für Arzneimittelgroßhändler gelten. Nationale Rechtsvorschriften bleiben hiervon unberührt.

Das vorliegende Dokument stützt sich auf die Antworten der Mitgliedstaaten auf einen im Herbst 2017 initiierten Fragebogen zu den Maßnahmen, die im Zusammenhang mit Artikel 81 der Richtlinie 2001/83/EG in den Hoheitsgebieten der Mitgliedstaaten durchgeführt wurden. Gegebenenfalls wird auch die einschlägige Rechtsprechung berücksichtigt. Weitere Informationen über besondere, zur Bewältigung der Arzneimittelknappheit eingeführte nationale Maßnahmen finden sich in der von der Kommission erstellten Zusammenfassung der in dem Fragebogen für Mitgliedstaaten erteilten Antworten.

Die im vorliegenden Diskussionspapier geäußerten Ansichten stellen weder eine formale Auslegung des Unionsrechts dar, noch sind sie rechtsverbindlich. Letztendlich kann nur der Europäische Gerichtshof eine verbindliche Auslegung des Unionsrechts vornehmen.

Bestimmungen der EU-Rechtsvorschriften

Artikel 81 lautet: *Der Inhaber der Genehmigung für das Inverkehrbringen eines Arzneimittels und die Großhändler, die dieses in einem Mitgliedstaat tatsächlich in Verkehr gebrachte Arzneimittel vertreiben, stellen im Rahmen ihrer Verantwortlichkeit eine angemessene und kontinuierliche Bereitstellung des Arzneimittels für Apotheken und zur Abgabe von Arzneimitteln zugelassene Personen sicher, damit der Bedarf der Patienten in dem betreffenden Mitgliedstaat gedeckt ist. Die Regelungen zur Durchführung dieses Artikels sollten darüber hinaus im Einklang mit den Bestimmungen des Vertrags, insbesondere mit den Bestimmungen über den freien Warenverkehr und den freien Wettbewerb, durch Gründe des Schutzes der öffentlichen Gesundheit gerechtfertigt sein und in einem angemessenen Verhältnis zu diesem Ziel stehen.*

Artikel 23a lautet: *Wenn das Inverkehrbringen des Arzneimittels in einem Mitgliedstaat vorübergehend oder endgültig eingestellt wird, meldet der Inhaber der Genehmigung für das Inverkehrbringen dies der zuständigen Behörde dieses Mitgliedstaates. Diese Meldung erfolgt spätestens zwei Monate vor der Einstellung des Inverkehrbringens des Arzneimittels, es sei denn, dass außergewöhnliche Umstände vorliegen. Der Inhaber der Genehmigung für das Inverkehrbringen informiert die zuständige Behörde über die Gründe für solche Maßnahmen gemäß Artikel 123 Absatz 2. Auf Aufforderung der zuständigen Behörde, insbesondere zu Zwecken der Pharmakovigilanz, stellt der Inhaber der Genehmigung für das Inverkehrbringen der zuständigen Behörde alle Daten im Zusammenhang mit dem Umsatzvolumen des Arzneimittels sowie alle ihm vorliegenden Daten im Zusammenhang mit dem Verschreibungsvolumen zur Verfügung.*

Welche Verantwortlichkeiten haben die Inhaber der Genehmigung für das Inverkehrbringen bezüglich der Verpflichtung zur kontinuierlichen Versorgung?

Der Inhaber der Genehmigung für das Inverkehrbringen hat die Versorgung mit ausreichendem zeitlichem Vorlauf und in angemessenen Mengen sicherzustellen, damit die Nachfrage der Patienten in einem Mitgliedstaat gedeckt werden kann. Zu diesem

¹ Informelle Tagung der Gesundheitsminister, informelle Tagesordnung des Rates (Beschäftigung, Sozialpolitik, Gesundheit und Verbraucher) — Gesundheit, 3.-4. Oktober 2016.

² <http://www.europarl.europa.eu/sides/getDoc.do?type=REPORT&reference=A8-2017-0040&format=XML&language=DE>

³ Richtlinie 2001/83/EG des Europäischen Parlaments und des Rates vom 6. November 2001 zur Schaffung eines Gemeinschaftskodexes für Humanarzneimittel (ABl. L 311 vom 28.11.2001, S. 67).

Zweck stellt der Inhaber der Genehmigung für das Inverkehrbringen eine kontinuierliche Versorgung zur Deckung des Bedarfs der Arzneimittelgroßhändler (einschließlich Vollsortimenter) und Personen, die zur Abgabe von Arzneimitteln an die Öffentlichkeit befugt sind, sicher. Besondere Aufmerksamkeit sollten Inhaber der Genehmigung für das Inverkehrbringen bei Produkten walten lassen, bei denen der Herstellungsprozess (oder ein Teil desselben) von einer einzigen Einrichtung abhängig ist (z. B. einer Quelle für Ausgangsstoffe, einem Wirkstoffhersteller, einem Endprodukthersteller oder einem Chargenfreigabebetrieb). Besonders aufmerksam muss der Inhaber der Genehmigung für das Inverkehrbringen auch dann vorgehen, wenn er Arzneimittel in den Verkehr bringt, für die keine oder nur begrenzte Alternativen zur Verfügung stehen und bei denen eine Einstellung der Versorgung zu einem potenziellen Risiko für die öffentliche Gesundheit führen kann, wie es beispielsweise bei Arzneimitteln gegen lebensbedrohliche Erkrankungen und bei kritischen⁴ oder unentbehrlichen Arzneimitteln⁵ (z. B. Impfstoffen) der Fall ist. Hinsichtlich solcher Produkte können die zuständigen Behörden den Inhabern der Genehmigung für das Inverkehrbringen vorschreiben, im Rahmen ihrer Verpflichtung zur Sicherstellung einer kontinuierlichen Versorgung einen Plan zur Vermeidung von Arzneimittelknappheiten auszuarbeiten.

Aus Artikel 23a in Verbindung mit Artikel 81 ergibt sich, dass die Inhaber einer Genehmigung für das Inverkehrbringen jede Unterbrechung der Arzneimittelversorgung rechtzeitig (mindestens zwei Monate vorher) melden müssen. Eine solche Meldung sollte insbesondere Daten über das Umsatz- und Verschreibungsvolumen und nach Möglichkeit auch Angaben zu potenziellen alternativen Arzneimitteln enthalten. Des Weiteren sollten Informationen über die geschätzte Dauer der Versorgungsunterbrechung und die zu ihrer Behebung getroffenen Abhilfemaßnahmen in die Meldung aufgenommen werden. Um der zuständigen Behörde eine Bewertung der Lage zu ermöglichen, sollten in der Meldung auch die Gründe für die Unterbrechung hinreichend ausführlich beschrieben werden. Zur Überwachung von Knappheiten auf ihrem jeweiligen Markt können auch die Mitgliedstaaten bei den Inhabern der Genehmigung für das Inverkehrbringen Daten über Umsatz- und Verschreibungsvolumen anfordern.

Welche Verantwortlichkeiten haben Großhändler bezüglich der Verpflichtung zur kontinuierlichen Versorgung?

Großhändler müssen die kontinuierliche Versorgung von Apothekern und zur Abgabe von Arzneimitteln an die Öffentlichkeit befugten Personen sicherstellen, damit der Bedarf der Patienten in dem Gebiet, in dem der Großhändler seinen Sitz hat, gedeckt werden kann. Je nach den in dem oder den betroffenen Mitgliedstaat(en) bestehenden gemeinwirtschaftlichen Verpflichtungen⁶ kann der Großhändler verpflichtet sein, sämtliche Arzneimittel (wenn es sich bei dem betreffenden Großhändler um einen Vollsortimenter handelt) oder aber einen Satz vorab festgelegter Arzneimittel in regelmäßigen (beispielsweise täglichen) Abständen für ein bestimmtes geografisches Gebiet bereitzustellen. Großhändler dürfen andere Großhändler unter der Voraussetzung beliefern, dass sie in dem geografischen Gebiet, für das sie verantwortlich sind, ihren gemeinwirtschaftlichen Verpflichtungen sowie der Nachfrage der Apotheken und der zur Abgabe von Arzneimitteln an die Öffentlichkeit befugten Personen nachkommen können.

Wie weit erstrecken sich ihre Verantwortlichkeiten?

Die Grenzen für die Verantwortlichkeiten der Inhaber von Genehmigungen für das Inverkehrbringen und der Großhändler sind von den Mitgliedstaaten im jeweiligen Einzelfall zu bewerten. Es folgen Beispiele für Fälle, in denen Inhaber von Genehmigungen für das Inverkehrbringen unter Umständen keine Verantwortung tragen:

- wenn ein Arzneimittelvertreiber durch die Ausfuhr bzw. Lieferung an einen anderen Kunden in einem anderen Mitgliedstaat unbewusst eine Knappheit auslöst (solange er die im Verhältnis zur Größe des Markts in dem betreffenden Mitgliedsstaat üblichen Bestellungen erfüllt hat);
- wenn eine Knappheit dadurch ausgelöst wird, dass in dem betreffenden Mitgliedstaat alternative, von einem anderen Unternehmen hergestellte Arzneimittel knapp sind und somit die Nachfrage steigt.

Großhändler sind unter Umständen dann nicht verantwortlich, wenn die Inhaber von Genehmigungen für das Inverkehrbringen nicht in der Lage sind, in einem Mitgliedstaat die Bereitstellung ausreichender Arzneimittelbestände zur Deckung des Bedarfs von Apotheken oder von zur Abgabe von Arzneimitteln an die Öffentlichkeit befugten Personen zu ermöglichen.

Kann ein Mitgliedstaat die Lieferung von Arzneimitteln an Wirtschaftsbeteiligte in anderen EU-Mitgliedstaaten beschränken, um das Risiko von Arzneimittelknappheiten zu mindern?⁷

Mitgliedstaaten können Maßnahmen zur Vermeidung oder Überwindung von Arzneimittelknappheiten treffen, indem sie den freien Warenverkehr innerhalb der EU beschränken.⁸ Die Behörden der Mitgliedstaaten können durch Großhändler erfolgende

⁴Soweit diese Arzneimittel auf nationaler Ebene definiert worden sind oder in dem von der Europäischen Arzneimittel-Agentur erstellten Dokument erwähnt werden. http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/01/WC500159381.pdf

⁵http://www.who.int/medicines/news/2017/20th_essential_med-list/en/

⁶ Die Verpflichtung der Großhändler, ständig ein Sortiment von Arzneimitteln bereitzuhalten, das den Anforderungen eines bestimmten geografischen Gebiets genügt, und die rasche Verfügbarkeit dieser Arzneimittel innerhalb des genannten Gebiets zu gewährleisten.

⁷ Allgemein als „Ausfuhrbeschränkungen“ bekannt.

Arzneimittellieferungen an Wirtschaftsbeteiligte in anderen EU-Mitgliedstaaten beschränken und eine vorherige Meldung oder Genehmigung solcher Tätigkeiten vorschreiben, solange derartige Beschränkungen als für den Schutz von Leben und Gesundheit der Menschen angemessen, erforderlich und verhältnismäßig gerechtfertigt werden können, indem sie das Auftreten von Arzneimittelknappheiten verhindern.⁹ Der Anwendungsbereich der Meldungen oder Genehmigungen ist auf Arzneimittel zu beschränken, die bereits knapp sind oder bei denen das Risiko einer Knappheit besteht; dabei ist die Verfügbarkeit alternativer Behandlungen zu berücksichtigen.

Beschränkungen für Lieferungen außerhalb des betreffenden Mitgliedstaats müssen auf der Grundlage transparenter, öffentlich zugänglicher, nichtdiskriminierender und den Wirtschaftsbeteiligten vorab bekannter Kriterien in einer solchen Weise erlassen werden, dass Willkür bei der Verhängung solcher Beschränkungen ausgeschlossen ist. Entscheidungen von Behörden der Mitgliedstaaten sollten durch Beschwerden bei den maßgeblichen nationalen Verwaltungs- oder Justizbehörden angefochten werden können. Entscheidungen, in denen Ausfuhren abgelehnt werden, müssen vor Gericht angefochten werden können.¹⁰

Darüber hinaus müssen die Melde- oder Genehmigungsverfahren hinsichtlich ihrer Dauer und Kosten angemessen sein, damit Wirtschaftsbeteiligte nicht abgeschreckt werden. Die bei Großhändlern angeforderten Informationen müssen auf das für eine sachkundige Entscheidung erforderliche Minimum beschränkt werden (beispielsweise die Menge der auszuführenden oder zu liefernden Produkte, die Bezeichnung der Arzneimittel).

Lieferbeschränkungen für besondere, gelistete Arzneimittel können als geeignet betrachtet werden, wenn:

- die Liste nur für Arzneimittel gilt, bei denen eine Knappheit wahrscheinlich oder sicher ist, beispielsweise Arzneimittel, bei denen das verfügbare Volumen den derzeitigen Bedarf der Patienten in dem betreffenden Mitgliedstaat nicht decken kann;
- die Liste anhand von im Voraus bekannten Kriterien erstellt wird;
- in der Liste die Verfügbarkeit alternativer Behandlungen in dem betreffenden Mitgliedstaat berücksichtigt wird;
- die Liste regelmäßig unter Berücksichtigung der zuletzt aufgetretenen Arzneimittelknappheiten oder der von Arzneimittelknappheiten ausgehenden Risiken für die öffentliche Gesundheit überarbeitet wird;
- innerhalb eines angemessenen Zeitraums über die Anwendung der Liste entschieden wird;
- die Entscheidungen bei den maßgeblichen Verwaltungsbehörden oder Gerichten angefochten werden können.

⁸ Urteile in den verbundenen Rechtssachen C-468/06 bis C-478/06, Randnr. 75.

⁹ Siehe Artikel 36 des Vertrags über die Arbeitsweise der Europäischen Union.

¹⁰ Urteil in der Rechtssache C-390/99, Canal Satélite Digital.



EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

Health systems, medical products and innovation
Medical products: quality, safety, innovation

Summary of Responses to the Questionnaire on the Measures implemented in the Member States territories in the context of Article 81 of Directive 2001/83/EC

The questionnaire is linked to the call of the Council and the European Parliament to examine and monitor Article 81 of Directive 2001/83/EC of the pharmaceutical legislation, which introduces an obligation for continuous supply of medicinal products¹.

Article 81 of Directive 2001/83/EC:

With regard to the supply of medicinal products to pharmacists and persons authorised or entitled to supply medicinal products to the public, Member States shall not impose upon the holder of a distribution authorisation which has been granted by another Member State any obligation, in particular public service obligations, more stringent than those they impose on persons whom they have themselves authorised to engage in equivalent activities.

The holder of a marketing authorisation for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medicinal product to pharmacies and persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered.

The arrangements for implementing this Article should, moreover, be justified on grounds of public health protection and be proportionate in relation to the objective of such protection, in compliance with the Treaty rules, particularly those concerning the free movement of goods and competition.

Responses have been received from 27 MS (AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LV, MT, NL, PL, PT, RO, SE, SI, SK, UK) and NO.

1. How is the obligation of continued supply transposed in your country as far as marketing authorisation holders (MAH) are concerned?

From the feedback received it appears that the obligation to ensure appropriate and continued supply has been transposed in a literally sense by the majority of the respondents (e.g. AT, BE, BG, CZ, DE, DK, EE, EL, ES, FI, FR, HR, IE, IT, LT, NL, PL, RO, UK).

Additional provisions, however, have been included in some countries:

- FI requires that the MAH ensures a constant availability of the product to wholesalers and pharmacies.
- In FR, appropriate measures to prevent and overcome supply difficulties are required to be in place and in case of shortages information must be provided to the authorities, hospital pharmacies, pharmacies, wholesalers and healthcare professionals, if needed.
- IT requires the MAHs to supply the pharmacies with the medicinal product unavailable in the national distribution network within 48 hours.
- DK, NL and PL require the MAH to provide, upon request, information about the amount of product that can be delivered to the market.

¹ https://ec.europa.eu/health/sites/health/files/files/committee/78meeting/pharm730_6ii_shortages_of_medicines.pdf
<http://www.europarl.europa.eu/sides/getDoc.do?type=REPORT&reference=A8-2017-0040&format=XML&language=EN>

- RO requires that the MAH ensures supplies equal to at least the average monthly turnover of the product over the past three months.
- In SE, there is a specific obligation on the MAHs to supply certain medicinal products subject to reimbursement. A MAH who also distributes medicinal products has an obligation to supply medicinal products to pharmacies as soon as possible.
- SK also places a specific obligation on the MAHs to supply medicinal products subject to reimbursement.

Some MS responses did not indicate that national legislation directly requires the MAH to ensure continued supply (e.g. CY, LV, MT, NO, SI) although this might be implied in some instances by the requirement to notify temporary or permanent supply interruptions to the authorities.

In NL, specific provisions have been included in the purchasing contracts between health insurers and MAH:

- If a contract has been entered, delivery is mandatory;
- Periodic (weekly or bi-weekly) reports of supply status for the health insurer;
- Penalty clause in the event of unavailability;
- Suppliers must have a contingency plan;
- Selection of another supplier for as long as supply problems persist.

2. What are the responsibilities of wholesale distributors in your country stemming from the transposition of the obligation of continued supply (i.e. public service obligation)? Do you distinguish between full-line distributors and other distributors?

(According to Directive 2001/83/EC, the public service obligation is “the obligation placed on wholesalers to guarantee permanently an adequate range of medicinal products to meet the requirements of a specific geographical area and to deliver the supplies requested within a very short time over the whole of the area in question.”)

Responsibilities of wholesale distributors/ public service obligation

The majority of respondents indicate that wholesale distributors are obliged to ensure continued and adequate supply (e.g. AT, BE, BG, CZ, DK, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LV, NL, MT, PL, PT, SE, SI, UK). The transposition of the distributors' responsibilities is linked to the transposition of the MAH obligations and hence in several instances the national legislation specifies "within the scope of their relevant/respective responsibilities" (e.g. AT, BE, ES, HR, IE, MT) or combines the responsibilities through the wording "in cooperation" or "in collaboration" with wholesale distributors (e.g. LT, PT).

In some instances the obligation specifies supply in quantities/time intervals adequate for the needs of patients (e.g. CZ, ES, PL) and refers to the needs of a specific geographic area (e.g. HR, PT, CY) and permanent assortment of products (e.g. IT).

Additional specifications have been implemented in some cases:

- Some respondents indicated also the maximum delivery time permitted e.g.: 48 hours for CZ, 12 working hours in IT, 24h in SE, 24 working hours in ES, 24-48h in NO. NO also may require delivery outside the opening hours of the pharmacies. SK requires a 24h delivery only for medicines subject to reimbursement.
- In CZ, the distributor has the right to request from the MAH a supply corresponding to the distributor's market share and the MAH is obliged to fulfil the request. The distributors are legally obliged to proceed in compliance with measures issued by the authorities for the purposes of safeguarding the availability of medicines.
- FR requires that the wholesalers should respect their distribution territory and public service obligation by holding stock to cover the usual needs of clients for minimum 2 weeks, delivering within 24 hours the orders received before Saturday 14:00, and participating in the weekend on-call duty to deliver orders within 8 hours.

- IE indicated an expectation by the authorities that the wholesaler has detailed procedures in place on the ways how appropriate and continued supplies are ensured and that these procedures have been demonstrated to be effective (this may include allocation quotas).
- Some respondents indicated that the wholesalers are obliged to notify the authorities of supply failure (e.g. in DK on every weekday before 12pm) and about the expected duration of the discontinuation (e.g. HU). Sometimes the wholesale distributors are also obliged to submit supply data and information so that the authorities can monitor the supply situation on the national market (e.g. LT).
- FI has separate legislation for importers of life-saving or essential medicines requiring the distributors to hold an obligatory surplus stock (mandatory reserve supply of 3-10 months sales calculated from previous year's sales); the reason for this law is the lack of manufacturers of essential medicines in Finland. There is compensation to the stockists defined in the Finnish legislation.
- RO requires that wholesalers ensure the public service obligation permanently by setting up insurance stocks equal to the average monthly sales for each drug in the list they distribute and honour any justified order received from the beneficiaries with whom they have contractual relationship.

Distinction between full-line distributors and other distributors

Most of the responses indicate that the national legislation does not distinguish between full-line and other distributors (e.g. AT, BG, CY, CZ, DK, EE, ES, FI, HR, IE, IT, LT, LV, NL, MT, NO, PL, PT, RO, SE, UK).

BE, DE, FR and SI make a distinction between full-line distributors (linked to the public service obligation) and other distributors, whereas SI distinguishes between full-line, contact-line and short-line distributors.

- BE legislation requires that the full-line distributors are at least obliged to permanently possess a stock allowing meeting the normal daily supply demand in their region of operation. The full-line distributors are obliged to make a commitment to deliver medicines to the entities authorised for distribution to the public and to take all necessary measures to ensure emergency deliveries within 24 hours of the order.
- In DE full-range wholesalers are obliged, within the framework of their responsibility, to guarantee a demand-oriented and continuous supply to the pharmacies with which they do business. The same obligation applies analogously to other types of wholesalers and their stock.
- FR requires that wholesalers should respect their distribution territory and public service obligation by holding stock to cover the usual needs of clients for minimum 2 weeks, delivering within 24 hours the orders received before Saturday 14:00, and participating in the weekend on-call duty to deliver orders within 8 hours. A distinction is made between full-line distributors and other distributors, because wholesalers are the owners of their stocks and consequently are subject to public service obligations as foreseen by the French Public Health Code. On the contrary, storage depositories are not the owner of the medicines; thus, they are not subject to the public service obligation.
- In SI, the public service obligation is very explicit for wholesalers. Wholesale distributors must guarantee a permanent and adequate range of medicinal products that may be marketed in accordance with the public service obligation of supply within a relatively short period of time, i.e. within 24 hours on weekdays or within a maximum of 72 hours at weekends and holidays after receipt of an order.

3. **What are the limits of their responsibilities in your country?**

The responses indicate that the limits of the responsibilities of MAHs and wholesale distributors are determined by the following:

- practical limits of availability from manufacturers or other wholesalers, e.g. if there is no API available, no medicinal product can be produced or supplied or in case of disruptions due to manufacturing problems and product suspension/withdrawal (e.g. AT, EE, FI, LV, RO, SE, PL);
- the responsibility of the wholesaler is limited by products they stock (e.g. NO);
- delivery time depends on the distance to the place of delivery (e.g. LV);
- MAHs are not subject to public service obligation which applies only to full-line wholesalers (e.g. FR);
- wholesale distributors do not have to be proactive and investigate other ways of supply (e.g. DK);
- the wholesale distributors' obligation to ensure continuous supply only applies to medicinal products subject to reimbursement or with a price agreement (e.g. LV, SK);
- wholesalers and manufacturers may apply for exemption from obligatory storages in some situations (e.g. FI).

4. **What are the responsibilities of manufacturing authorisation holders and how are they connected to the responsibilities of the marketing authorisation holder and the wholesale distributors? Is consultation with the authorities and notification of shortages obligatory?**

The responses to Question 4 varied considerably and are summarised and grouped by relevance below:

Responsibilities of manufacturing authorisation holders

In general, there are no specific responsibilities for manufacturers. However, in FI manufacturers are also required to hold obligatory stocks, if the medicinal products which they import or manufacture, are defined in the legislation of obligatory stocks.

Connection of the manufacturing authorisation holder's responsibilities to marketing authorisation holder's (MAH) responsibilities

DK, FR, LT, PL either require or expect a contract between the MAH and manufacturer (when these are different companies).

In EL, manufacturers should notify immediately the marketing authorisation holder (MAH) of any quality problem that may lead to product recall or abnormal availability of a product.

In ES, MAHs are required to have a prevention plan for supply problems if they report many disruptions of supply or shortages that affect to critical medicines.

In IE, both manufacturers and MAHs have obligations to ensure continued supply to patients, independently of each other, as the two actors are handled under separate national legislation. A single company may have obligations as a wholesaler, a manufacturer and a marketing authorisation holder under actor specific legislation.

Connection of the manufacturing authorisation holder's responsibilities to wholesale distributors' responsibilities

EE requires that manufacturers and wholesale distributors of medicinal products must ensure a continuous and sufficient choice of medicinal products and expedient delivery within the territory of Estonia.

In FI, HR, LT, UK manufacturers that supply their own or imported products are also considered as wholesalers and the same requirements apply as for wholesalers (including public service obligation).

FR requires that there is a contract between the MAH or the manufacturer and the storage depository.

In PL, manufacturing authorisation holders/marketing authorisation holders have legal obligation to deliver to wholesalers.

RO obliges the MAH to ensure that each product is distributed by at least 3 distributors.

Is consultation with the authorities and notification of shortages obligatory?

In some MS, the manufacturers are also required to notify in case of shortages (LV, NL, NO, PT). NO requires that national manufacturers report to the authorities while other manufacturers inform the MAH. PT requires manufacturing authorisation holders to immediately notify the authorities of any quality issue that might lead to a recall or might restrict the normal supply of medicinal products/IMPs.

HU moderates meetings between different members of the distribution chain in case of shortages.

5. Is there a specific definition of product supply disruption or shortage in your national legal order or other regulatory guidance? If yes, please describe it including a reference. Is it linked to a specific medicinal product² and to a specific territory³? Is it linked to the public service obligations referred to under questions 1 and 2?

The responses to Question 5 are summarised and grouped by relevance below:

Definition of product supply disruption or shortage in the national legal order or other regulatory guidance

Most of the respondents reported that there is no specific definition of supply disruption or shortage in their respective national legislation (e.g. AT, BG, BE, CY, CZ, DE, DK, EE, EL, ES, FI, HR, IE, IT, MT, NO, PL, SE, UK).

DE, DK, ES and SE reported to have definitions/classifications in their internal procedures.

In some MS, national legislation does not directly define shortages, but this is implied from the obligation to notify (HU, LV, NL, PT) or from the methodology for determining a sufficient stock of medicinal products (SK).

NL defines supply disruptions in the instructions for notifications to marketing authorisation holders and a shortage from a patient perspective in their regulatory guidance.

FR defines a product supply disruption as the incapacity for a pharmacy or a hospital pharmacy to dispense a medicinal product to a patient within 72 hours⁴. The origin of the product supply disruption could be a drug shortage or a disruption within the supply chain. Thus, the drug shortage is defined as the inability to manufacture a medicinal product while the disruption within the supply chain is defined as the lack of supply to pharmacies in the absence of drug shortage.

RO considers a decrease for seven consecutive days of stock at national level (for the category of drugs with the same substance), pharmaceutical form and concentration, under the average monthly turnover as a shortage alert situation.

SI defines a disruption in the supply of a medicinal product as a state of the market where business entities responsible for market supply in Slovenia fail to provide the required amounts of medicinal products at the appropriate time⁵. This definition applies to all entities of the distribution chain (manufacturers, MAHs, wholesalers and pharmacies).

² Do you assess the shortage in the light of a specific authorised medicinal product or a class of products

³ Do you assess the shortage in the light of the situation in a specific region affected or at national level

⁴ French Health Code (Article R. 5124-49-1)

⁵ Article 6 ZZdr-2, item No. 36

Definition linked to a specific medicinal product and to a specific territory

DE, FR reported that its definition is not linked to a specific medicinal product and a specific territory.

LV links its definition to a specific product and to the national territory.

In SI, a disruption in supply (a shortage) is technically treated on the product-level, however it can refer also to a group of products, and be treated as such in a rather general way. In terms of regional/geographic treatment, shortages are always treated on a national level in Slovenia, regardless if they occur only in a particular part of the country.

SK links the determination of a sufficient stock to products included in a reference group. A distinction of seasonal use is also made.

Definition linked to the public service obligations referred to under questions 1 and 2

DE, FR reported that its definition is not linked to the service public obligations referred to under question 1 and 2.

6. Are there specific legal and/or other regulatory measures for critical or essential medicines (e.g. buffer stock)? If yes, do you have a definition of critical or essential medicines, do you use the WHO list of essential medicines or apply another solution? Please provide the definition and describe how you maintain and update the list of critical or essential medicines and describe any practical implementation issues.

Specific legal and/or other regulatory measures for critical or essential medicines (e.g. buffer stock)

Several responses indicated that there is no specific legal or regulatory measures for critical or essential medicines (e.g. AT, BE, CY, CZ, DK, EE, EL, ES, LV, NL, MT, PL, SK). In EE, discussions with different stakeholders and governmental bodies are ongoing to clarify, if an initiative to introduce new legal measures for critical or essential medicines is necessary.

In BE, a decision tree is currently in a testing phase (till mid 2018). The aim of this decision tree is to detect critical supply problems quickly. By following the different steps of the decision tree one is able to decide if alternative medicines are available. If not, other solutions are sought. When the outcome shows that there is no alternative medicinal product available additional information about the supply problem is published. Flagging of shortages affecting critical or essential medicines is being considered.

DE has introduced as a basic requirement for the supply relevance of an essential active substance or combination of active substances. Medicinal products classified as critical in Germany contain essential active substances which are subject to special regulatory supervision due to an increased supply risk. Special monitoring by the authorities is required, in particular, where only one marketing authorisation holder (MAH), or only one manufacturer responsible for batch-release, or only one manufacturer of active substances is available.

FI has specific legislation in place in relation to e.g. life-saving or essential medicines (see also point 2).

FR has specific legal measures in its healthcare law for essential/critical medicines.

NO has a buffer stock arrangement in place. Similarly, SE has emergency preparedness stocks with certain antidotes and antivirals that are managed by the authorities in accordance with government decisions. Sweden does not have a national list of essential medicines; the lists are managed at a county level.

SI has legal measures in place for essential and indispensable medicines⁶.

⁶Article 17 Zzdr-2

Definition of critical or essential medicines

BE defines a medicine as critical or essential when there is no alternative treatment available. However, at this time there is no precise definition/description.

DE introduced a distinction between essential and critical medicines/active substances (see 6.1.)

ES has the following definitions in place:⁷

- Essential medicinal product: A medicinal product whose absence in the market may cause a problem of great care impact due to any of the following reasons:
 - o A medicinal product that has no therapeutic alternatives available in the market (therapeutic gap).
 - o A medicinal product that, despite having therapeutic alternatives available, accounts for a large share of the market and the alternatives are not able to cover the lack generated.
 - o A medicinal product whose absence, regardless of whether there are therapeutic alternatives available or not available in the market, has a high economic impact on the health system. (Therapeutic gap from the point of view of pharmaceutical provision).
- Critical medicinal product: A medicinal product identified with a potential risk of causing supply or shortage problems due to any of the following reasons:
 - o It is a medicinal product that has no available therapeutic alternatives
 - o It has a complex manufacturing process and/or only one supplier

FR definition: Critical medicines or therapeutic class of critical medicines are defined as medicines for which disruption of treatment is life-threatening or irreversibly progressive, or without which the patient could be severely harmed (short or mid-term) considering the potential evolution of the disease.⁸

IT, LV, NL, UK refer to the definition of critical medicinal product and the related criteria that were adopted by an EMA working group on shortages on 3 September 2013 and distinguish them from the list of essential medicines prepared by WHO.⁹

SI defines essential and indispensable medicinal products; Essential medicinal products are those that are, based on the latest knowledge in biomedical sciences as well as on the systemic definitions within the framework of national health priorities and taking account of the sustainability of public finances, considered indispensable for the provision of health care to people or animals and are placed on the list of essential medicinal products. Indispensable medicinal products are those that are not included in the list of essential medicinal products and for which a tertiary health care provider or an expanded expert panel for the relevant area establishes new scientific grounds based on which the authorities shall enter the products on the list of indispensable medicinal products.

Use of the WHO list of essential medicines or another solution

DE compiled a list of essential active substances based on proposals of medical specialists and the WHO list of essential medicines.

EE has made publicly available an overview of how many of the marketed medicinal products do not currently have any alternative treatment in Estonia (either they were the only medicine containing this active substance, because of the content of the active substance, or a special dosage form).

ES has compiled a list of essential medicines, based on previous shortages problems, which is not public. The list is based on the WHO list of essential medicines but additional criteria based on the definitions and past experience are also used.

⁷ AEMPS Strategy against shortages "Reflection paper on availability of medicines"

⁸ Article L. 5111-4 of the French public health code)

⁹ EMA/24304/2016, Criteria for classification of critical medicinal products for human and veterinary use Shortages due to GMP non-compliance/quality defects

In FI there is no specific definition for an essential medicine per se. The list of essential medicines to be stored is based on consultation of clinical experts. The list is updated and published once a year on the agency's homepage. The agency is committed to assess the need for updating the list of pharmaceutical substances every second year.

FR has developed a list of ATC classes and vaccines which are deemed as critical medicines. On this basis, the MAH should use the following criteria to identify the critical medicines for which a shortage prevention plan is needed:

- The absence of available alternatives in sufficient quantity on the French territory;
- The market share of the medicinal product in France and the market shares of the identified alternatives;
- The weaknesses in the manufacturing process of the product, e.g. the absence of alternate sites of manufacturing and/or packaging for raw materials, finished products, packaging articles; the complexity of these processes or those relative to the storage or to the transport of the product.

IT prepares a weekly report on medicines under shortage highlighting all situations where an alternative is not available on the Italian market

In MT, the Government Hospital has an online formulary list which includes essential medicinal products, vitamins, food supplements and borderline substances. Apart from the Government Hospital Formulary List, a specified Out Patient's Formulary list covering chronic conditions is also available. This list is intended for use by the Pharmacy Of Your Choice (POYC) scheme, and government pharmacies.

NO established its own list. There are two arrangements in Norway: one for general practice and another one for hospitals. For primary care the requirement of two months extra stock for use in general practice applies (wholesalers legislation). There is also an agreement between hospitals and wholesalers for supply of certain critical products. It is the responsibility of the hospitals to select the products on this list.¹⁰

PT published a notice containing a list of APIs in relation to which the pharmacies must inform the authorities, within 48 hours, of any lack of access to medicines experienced¹¹. This communication can be done by telephone or using a dedicated email address. This list of APIs was based on the WHO list of essential medicines and has not been updated since 2012 due to Portugal's stable profile of diseases' prevalence and incidence.

SI has a list of essential and indispensable medicinal products. In this list, essential medicinal products are identified by the common name, pharmaceutical form, strength and the method of prescribing and dispensing. On the proposal of the agency, the list of essential medicinal products is determined by the minister. Essential medicines and indispensable medicines may correspond to an officinal product which also may be marketed. The list of essential medicinal products and the list of indispensable medicinal products are published on the agency's website.¹²

7. Which other actions (not mentioned under questions 1 and 2 and not related to Article 23a) are the MAH, distributors, or pharmacies required to take when anticipating or experiencing product supply disruption? Which legal or regulatory measures are in place (e.g. supply continuity plan for the production, information obligations in the supply chain)?

No other actions than those referred to in points 1 and 2 or related to Article 23a of the Directive 2001/83/EC are required in AT, BE, CZ, DK, EE, HR, IE, IT, MT and NO.

Other responses indicate a wide range of legal and/or regulatory measures for the prevention or management of shortages:

¹⁰ https://lovdata.no/dokument/SF/forskrift/1993-12-21-1219/KAPITTEL_10#KAPITTEL_10

¹¹ Informative Notice number. 235/CD/8.1.6, of 21th November of 2012

¹² <http://www.jazmp.si/humana-zdravila/podatki-o-zdravilih/zdravila-na-trgu/>

BG requires that with termination of the sales of a medicinal product from the Positive Medicines List and where within the frame of the relevant INN there is no other authorised medicinal product, the MAH notifies in writing the Ministry of Health and the National Council of Medicinal Products Prices and Reimbursement not later than 18 months prior to the date of discontinuation of the sales. Prior to the discontinuation of the sales, the MAH is obliged to secure sufficient quantities of the respective medicinal product for satisfying the health needs. When the authorities receive a signal of termination of sales of a medicinal product (with the exception of cases under Article 23a), the BDA performs a check within 30 days. While performing the check, the BDA may request information from the MAH on termination of the sales of the concrete medicinal product, as well as from the wholesalers about the available quantities of the products. Information obligations in the supply chain and inspections on site are applied.

In CY the authorities are informed of any drug shortages and based on the current use and availability of alternatives, communicate with the MAH to ensure stock controlling and to avoid serious disruptions of the market supply. Additionally, the Procurement Department of the Ministry of Health may procure alternative products or products from other markets in order to respond to emergencies.

DE requires that MAHs inform hospitals in case of known shortages of prescription medicines for inpatient treatment. MAHs report supply disruptions on a voluntary basis to the German authorities if:

- the supply shortage relates to marketed medicinal products of essential active substances for which three or less MAH, manufacturers responsible for batch-release, or manufacturers of active substances are available;
- the market share of the medicinal product affected by the supply disruption is more than 25%;
- supply shortage has already been reported in the past for the concerned active substances.

EL requires the MAH to inform the authorities of any marketing cessation (permanent or temporary) or shortage. This information should be notified at least 3 months before cessation of the product. In addition, product supply shortages are also notified by healthcare professionals or patients. The Greek authorities evaluate the impact of the shortage on public health.

In ES other actions which are required from marketing authorisation holders/distributors in case of a supply disruption are:

- Obtaining units of medicinal products in supply shortage, labelled in other languages or with expiry date shorter than 6 months, to be authorised by the Spanish Agency of Medicinal Products and Medicine Devices, allowing their placing on the market under exceptional circumstances. These units are only to be commercialised to hospitals (to MAH).
- Importing medicinal products with the same composition as the affected medicinal product, from other countries (foreign medicinal product) (to MAH).
- Revision of supply chain of the units recently distributed and cancelation of the exports, when applicable (to MAH and distributors).
- Restriction of the supply to allocate the units for indications without another therapeutic alternative, to extend the duration of the available units (to MAH).

FI requires that wholesalers inform pharmacies directly or via their full-line distributors of any disruptions to their normal availability of medicinal products and that pharmacies hold stocks as follows: “The amount of medicinal products, the equipment and supplies for administering medicinal products, and the dressings kept by a pharmacy must correspond to its usual customer needs.”

FR adopted specific legal measures for critical medicines or therapeutic class of critical medicines for which the MAH should develop and implement prevention/management plans in order to prevent and/or mitigate impact on patients, to warn of (prevent) any drug shortage. In this context, MAH should declare to the French agency the list of their medicines for which prevention/mitigation plans are implemented. The list of the critical medicines for which prevention/mitigation plans are set up, should be mentioned in the site master file. These documents should be available to the authorities on demand. The prevention/mitigation plans are based on the risk analysis of the production and distribution cycle of the related medicinal product. These plans should anticipate measures to be implemented according to the weaknesses identified and the market shares of the related product: e.g.

security stocks of products, alternate production sites and also identification of alternatives. Moreover, the MAH should inform the French authorities of any shortage/risk of shortage of critical medicines. When a MAH anticipates, notices or is informed about a situation of drug shortage of a critical medicine, it should inform immediately the agency and specify the lead-time for shortage, the available stocks, the deadline for the end of shortage and (if necessary) the identification of alternatives. In case of critical medicines, the measures described in the shortage prevention/mitigation plan should also be provided. The MAH should implement, with the agreement of the agency, alternative solutions to deal with the situation and for critical medicines the measures described in the prevention/mitigation plan and have to inform the healthcare professionals.

IE has implemented an expectation for wholesalers that are the same legal entity and co-located with a retail pharmacy business, where the predominant business activity of the wholesale function is to parallel trade medicines out of Ireland. The expectation is that the wholesale entity will establish and use a dedicated account with its supplier for the purposes of procuring medicines for onward wholesale distribution, including parallel trading.

LT foresees the legal possibility of supplying unauthorised medicinal products: the named medicinal products (according to Article 5 of Directive 2001/83/EC), unauthorised relevant medicinal products (according to Article 126a of Directive 2001/83/EC), and unauthorised products in emergencies. Lithuanian legislation also establishes the possibility to supply authorised medicinal products in foreign language packages (according to Article 63 of Directive 2001/83/EC). Lithuania, Latvia, Estonia have signed an agreement on use of the common Baltic packages, which facilitates the authorisation of medicinal products in these countries.

LV links additional obligations (*not detailed in the response*) to the reimbursement of medicinal products.

NO expects that wholesalers avoid exports of medicinal products that would create shortages and applies a crises management regulation in extreme cases (high number of patients where lack of medication will have severe consequences), but considers this measure unsuitable for ordinary supply disruptions.

PT has created an online platform for the notification and management of the shortage (“*SIATS platform*”) and established a legal mechanism to monitor the exportation/EU distribution of medicinal products: the *ex-ante* notification list. If a given medicine is included in the *ex-ante* notification list, and its supply to the national market is compromised, the authorities may temporarily ban the export or the distribution of that medicine to other EU countries. PT uses the following methodology to assess the notified shortages:

- Assessment of the length of the shortage, market share of the product (sales declared) and evident alternative medicines (e.g. other brand with the same API available) – performed by INFARMED, I.P.;
- Preliminary classification of the shortage regarding the impact on national market, as high, medium or low – performed by INFARMED, I.P.;
- Assessment of available alternative medicines (asking clinical experts’ opinion), if the shortage is considered of high or medium impact – performed by INFARMED, I.P.;
- Upgrade of preliminary classification, if applicable (existence of alternatives) – performed by INFARMED, I.P.;
- Preparation of a mitigation plan when the impact of the shortage on the national market is considered high or medium – performed by the MAH.

RO has put in place a dedicated email address and a website platform where pharmacists or patients can notify the absence of a medicine from the market. The authorities verify the notifications and take appropriate measures.

SE requires agreements between stakeholders (MA-holder, distributors and pharmacies) that describe how each stakeholder should handle such a situation. There are for example rules for information obligations in the supply chain and the industry is committed to good accessibility of medicinal products.

In SI, pharmacies are obliged to perform the service of delivering the product to the purchasing party (individual on the outpatient basis, corporate on inpatient basis). Combined with the public service obligation from wholesalers, this provides a strong demand-side mechanism for assurance of the product when prescribed in an out-patient or in-patient setting.

In SK, wholesalers can export a classified medicinal product only with the agreement of the MAH of the classified medicinal product. The classified medicinal product must be delivered to the pharmacy within 48 hours from order.

UK has developed voluntary joint regulator-industry best practice guidelines that give advice to companies on what to do in the event of a shortage.¹³ This guidance recommends that companies communicate with the authorities as soon as possible about impending shortages that are likely to have an impact on patient care. This allows consideration of the available options for continued supply, which might include expediting regulatory procedures, commissioning clinical advice if required or identifying alternative sources of supply. The guidance also advises companies to consider whether/how best to communicate a supply problem to the National Health Service. In some cases, for example, the company will send a letter to affected clinicians and pharmacists, while in others, a note in the pharmaceutical/ trade press might be sufficient. In most cases, companies alert the wholesalers and other customers when a product is unavailable. Many pharmaceutical companies also operate their own out of stock portal on their company website that customers can subscribe too. The UK authorities recognise the need to have a central portal or webpage available about national medicine shortages and it is working with the National Health Service to develop and manage a nationally available website for medicines shortages information which should contain up to date information on shortages, their duration and recommended action where available.

8. Article 23a of Directive 2001/83/EC obliges the marketing authorisation holder to notify the authority if a product ceases to be placed on the market even temporarily. Do you make this information available to the distributors or pharmacies? Is there any other compulsory reporting of interruption of supply to the NCA, to distributors or pharmacies or to patients? Is this information publicly available? Are there penalties for non-compliance?

The responses to Question 8 are summarised and grouped by relevance below:

Do you make this information available to the distributors or pharmacies? Is there any other compulsory reporting of interruption of supply to the NCA, to distributors or pharmacies or to patients?

The responses indicate varying practices and requirements of reporting and information sharing.

The authorities in AT do not make this information available to distributors or pharmacies, however the MAH shares this information with distributors and pharmacies, hence they know if a product ceases to be placed on the market. The MAH is obliged to notify the agency of shortages linked to quality defects.

BE has reported that a notification tool has been made available to communicate changes in the commercialisation status of a medicine (start or stop of commercialisation, temporary unavailability or return on the market). All notified data are introduced in the national database of medicinal products authorised in Belgium. A new platform will be developed in 2018. This platform will facilitate the notification of the commercialisation/supply problems by the marketing authorisation holder and will automatically update the information in the national database. Furthermore an exchange of information will be possible between pharmacists/distributors and marketing authorisation holders.

DE does not publish the Article 23a notifications. In case of unforeseen shortages the MAH is required to notify the authorities without delay, while for planned supply interruption the notification is required 6 months in advance.

¹³<https://www.gov.uk/government/publications/notification-and-management-of-medicines-shortages-abpi>
<https://www.gov.uk/government/publications/notification-and-management-of-medicines-shortages-bgma>

In CY, the authorities may instruct the MAH to notify a shortage to pharmacies.

EE publishes selected information about a shortage for pharmacies, distributors and other stakeholders.

In FI, reporting of this information is compulsory.

FR requires that appropriate measures to prevent and overcome supply difficulties are in place. In case of shortage, information should be provided to pharmacies, hospital pharmacies, wholesalers and healthcare professionals if needed. Moreover, the firm that is responsible for marketing of the medicinal product in France should implement permanent emergency call centres (or an equivalent system) to allow direct contact with pharmacies and wholesalers. The emergency call numbers should be available for healthcare professionals.

NO makes this information available to distributors or pharmacies.

In PL, the public authorities do not make this information available to wholesalers or pharmacies.

SI publishes related information within 5 working days. MAHs, parallel distributors and wholesalers are obliged, at the request of the authorities, to provide data on sales volumes in Slovenia. Business entities that carry out pharmacy services or are engaged in the retail marketing of medicinal products in specialised stores shall submit to the authorities information on purchasing and dispensing of medicinal products. Health care service providers shall submit to the Slovenian authorities information on the purchase and consumption of medicinal products. Data on the volume of the sales, purchase, dispensing and consumption of medicinal products shall include the quantity of individual medicinal products and their buying and selling values for a specified period of time. The detailed requirements, manner, frequency and periods for data reporting and data models for communication and data reporting are laid down by the authorities. There is one single form that is adapted for reporting of various events and provides means for explanation and justification of the MAH's action, together with a request to assess the impact of its action (i.e. cessation of marketing) on public health. The form 281-04 (in Slovenian only) is available on JAZMP website.¹⁴

UK requires, in addition to the provisions of Art.23a, that MAHs notify their intention not to apply for a renewal of the marketing authorisation or to withdraw the product from the market in a third country (whether temporarily or permanently) and the action is based on any of the grounds set out in Article 116 or 117(1) of Directive 2001/83/EC.

Is this information publicly available?

The majority of respondents indicate that they publish information related to supply interruptions; however, the type and extent of this information varies. In general, this information is available at NCA's websites. Additional information is published in some cases:

ES also publishes information on available therapeutic alternatives, if the product will be imported or if supply is restricted to hospitals). In addition the Spanish Agency publishes informative notes on their webpage when a shortage of a medicinal product has an important impact on public health, or specific guidance for healthcare professionals or patients is needed.

Additionally, in HU, the public and the healthcare professionals are provided with information via newsletter, e-mail and phone.

In NO, specific shortage situations are published as news with advice to doctors, pharmacies and patients. Alerts to doctors are also implemented in the "Electronic Patient Journal" systems providing instant information about a specific medicine package (strength) at the point of prescribing and through the Norwegian Pharmaceutical Product Compendium.¹⁵ For patients, an app has been released where patients can register their medicines allowing them to access and receive relevant information (as alerts about shortages and deregistrations).

¹⁴ http://www.jazmp.si/fileadmin/datoteke/obrazci/SFE/Obr_281-04.docx

¹⁵ See red box on webpage <https://www.felleskatalogen.no/medisin/>

In PT information on medicine shortages notified by the MAHs on an electronic platform is accessible to prescribers through a link to prescription software allowing them to be informed in advance about the availability of a medicine.

Are there penalties for non-compliance?

Most respondents indicate that the national legislation foresees certain sanctions for non-compliance; these range from revocation of licences to financial penalties in varying amounts.

BG has no specific provision for imposing a fine on the MAH who fails to fulfill this obligation. However, the common fine for infringement of the relevant legislation is BGN 3,000 to 9,000.

CY foresees an administrative fine up to 34,000 € for failure to comply with the obligations set out in article 23a of the Directive 2001/83/EC (Section 14 of the National Legislation).

Since 2011, CZ has imposed financial penalties on MAHs in 99 cases of non-compliance (of which 94 are legally valid), in total amount of 2,651,000 CZK.

ES has penalties for non-compliance in its legislation. There are three very serious penalties and fines up to 1 million €.

In FI there are certain possibilities of prohibitions and revocations to the license holders if the conditions for granting the marketing authorisations no longer exist or requirements concerning manufacture or import are no longer met as required in the pharmaceutical legislation. However, so far no penalties have been imposed in case of not reporting as required.

FR applies penalties in case of non-compliance. These sanctions can be administrative measures or fines as mentioned in question 11.

HR foresees a fine between HRK 100,000 and HRK 150,000 for failing to act in accordance with the provisions of its pharmaceutical legislation.

In PT if an MAH does not comply with its obligations to electronically notify the authorities of shortages (if the notification isn't made at all or if the shortage is reported with delay), a warning can be issued or legal action against the MAH initiated if the noncompliance is recurrent.

LV applies penalties in this context.

RO applies penalties for not notify an interruption of supply to the MAH and the distributors and pharmacies have to inform the authorities if a justified order is not honoured.

SK foresees penalties between 500 € and 25,000 €.

In the UK a breach of Article 23a by the MAH is a criminal offence.

AT, DE, EE, NO do not impose penalties for non-compliance.

9. **Do you have any specific export restrictions in place to mitigate the shortage or the risk of shortage of medicines? If yes, what is their precise scope and what criteria are they based on? (e.g. prior notification for shipments within a certain timeline, dynamic list of products...)**

- a) **Do they apply in the same way for the exports to other EU Member States and to third countries?**
- b) **Are they based on generally applicable measures only ¹⁶or also on individual decisions of the state authorities¹⁷?**
- c) **Are substitutable medicinal products/therapies taken into account in such export restrictions?**
- d) **Are such export restrictions considered as part of transposition of the public service obligations under Article 81?**
- e) **What kind of information do you publish regarding the specific export restrictions taken?**

There are no specific export restrictions in relation to shortages in AT, BE, BG, CY, DE, DK, HR, IE, IT, LV, MT, NL, NO, SE, SI and UK.

However indirect measures with potentially equivalent effect have been introduced in some cases, such as SI, where there are explicit public service obligation provisions in place which act as a deterrent to the business policies of wholesalers that would lead to the exhaustion of the national markets.

Export restriction measures in the context of shortages exist in CZ, EE, EL, ES, FI, FR, HU, PL, PT, RO and SK.

a) Do they apply in the same way for the exports to other EU Member States and to third countries?

Yes: CZ, EE, EL, FI, FR, PL, PT, SK.

b) Are they based on generally applicable measures only or also on individual decisions of the state authorities?

The responses indicate that both general and/or individual measures may be taken.

c) Are substitutable medicinal products/therapies taken into account in such export restrictions?

Yes: CZ, EE, EL, ES, FI, FR, PT

No: SK

d) Are such export restrictions considered as part of transposition of the public service obligations under Article 81?

Yes: CZ, EE, ES, FI, FR, PT, SK

No: EL

e) What kind of information do you publish regarding the specific export restrictions taken?

The responses indicate that the most common information published is a list of specific medicinal products (e.g. with current availability problems or mandatory reserves).

10. **How are you determining and monitoring the shortage situation (e.g. by comparing supply and consumption data) for a particular medicinal product?**

a) **Is this monitoring linked to the export restrictions referred to in question 8?**

¹⁶ e.g. general ban for all exports applicable for all economic operators

¹⁷ e.g. individual decision to block the export for an individual economic operator (decision on case by case basis)

b) **Do you plan using, for the purpose of monitoring the data gathered, the secure repository system developed in the scope of Commission Delegated Regulation (EU) 2016/161 of 2 October 2015?**

The responses indicate that the most common practices involve contacts with the industry, monitoring of supply and consumption data and impact analyses (e.g. availability and stocks of alternative products). Monitoring can take place through electronic information systems/platforms crosslinking supply problems with export notifications. More than half of the respondents is considering the use of the EU secure repository system.

a) Is this monitoring linked to the export restrictions referred to in question 8?

Yes: CZ, EE, EL, ES, FI, PL

No: BE, CY, DE, FR, LT, NO, RO, SI

EE looks at the import and export history of the medicinal product, and if it has been exported recently or has the potential to be exported, an export restriction is considered.

FI makes its decisions based on monitoring of supply and consumption data.

b) **Do you plan using, for the purpose of monitoring the data gathered, the secure repository system developed in the scope of Commission Delegated Regulation (EU) 2016/161 of 2 October 2015?**

Yes: AT, CZ, EE, EL, ES, HR, IT, LV, SI

Under consideration: BE, CY, FR, LT, MT, PL, PT, RO

No: DE, FI, IE, NL, NO, SE, UK

11. **Are there specific penalties for interruption of supply/shortages? (e.g. suspension of distribution authorisation or marketing authorisation, fines for export or shipment of medicines to other Member States in case of shortages)? If yes, did you impose sanctions during the last 10 years and have the penalties for shortage resulted in reluctance from the MAH to inform you about shortages, or in deregistration of the medicinal product?**

The responses indicate that most authorities foresee sanctions (administrative or financial penalties); however, the majority of respondents have not applied them in the context of shortages in the last 10 years. No reluctance from the MAH to inform the authorities about shortages, or deregistration of the medicinal product as a consequence of specific sanctions in the context of supply interruption has been reported.

In CY, the national legislation provides for the imposition of an administrative fine up to 34,000 € for the failure to comply with the obligation to notify any disruptions/shortages in supply. No fines however have been imposed the past 10 years with regard to this obligation.

In CZ the MAHs can be fined up to the 20,000,000 CZK if they fail to fulfil their obligations; no sanctions in the context of Art. 23a of Directive 2001/83/EC were imposed in the past 10 years. CZ has imposed penalties on distributors in three cases of non-compliance with the prohibition of export in case of shortages (1.5 million CZK); one case is currently being reassessed (400,000 CZK) following an appeal filed by the company.

EE can fine wholesalers for infringing an export ban under the Code of Misdemeanour Procedure.¹⁸

EL has legal provisions for penalties for insufficient coverage of patients' needs.

ES has established penalties for MAH that stop the distribution of a medicinal product since it can only be suspended under exceptional conditions adequately justified once the authorization of the Spanish agency is issued. There are also specific penalties for exporting medicines when this activity

¹⁸ <https://www.riigiteataja.ee/en/eli/513072017004/consolide>

has been forbidden by the agency. ES imposed sanctions in the last 5 years on companies that did not notify supply disruptions. Nowadays, those companies report regularly its supply disruptions.

In FI there are certain possibilities of prohibition and revocation of licences if the conditions for granting the marketing authorisations no longer exist or requirements concerning manufacture of import are no longer met as required by the pharmaceutical legislation. However, so far no penalties have been imposed in case of not reporting as required.

FR foresees penalties for interruption of supply/shortages or risk of supply. There are many specific penalties (administrative or financial) for infringement of certain obligations, including the non-reporting of interruption of supply by the MAH to the authorities (ANSM) or the non-compliance with the public services obligations by the wholesalers. For example, when an inspection reveals that the activity of a wholesaler can lead to shortages (e.g. export of medicines that were intended to the French market, or failure to comply with the public service obligations), the ANSM can impose administrative sanctions like injunctions, or suspensions of the distribution authorisation. ANSM can impose financial penalties too. The amount of the penalty will not exceed 10 % of the firm's France turnover in the preceding business year, but limited to 1 million €. During the last 10 years, the following sanctions were taken against wholesalers following deficiencies in public service obligations/risk of shortages:

- nine injunctions (warning letters prior to 2014),
- six suspensions of the authorisation, and
- two financial penalty procedures have been initiated.

HR foresees fines for failing to act in accordance with the obligation of continued supply and failing to notify the authorities about shortage/supply disruption (see also answer to question 8). The Croatian authorities did not impose any sanctions during the last 10 years because of reluctance from the MAH to inform about a shortage. In addition to the fines, the "sunset clause" provision applies if a medicinal product has not been on the market for three consecutive years.

HU imposes penalties (fines) if it is proven that the MAH or wholesaler violated his obligation to supply.

IE only applies general penalties for the non-compliance with legislation by manufacturers, wholesalers and marketing authorisation holders. There are no specific penalties or fines for parallel trade relating to shortages. No sanctions have been imposed on marketing authorisation holders thus far and, given the relatively small size of the Irish market, IE feels that it may not address the issue of ensuring continued supply to Irish patients.

In IT, in case of violation of the Public Service Obligation or GDP, the distributor may be sanctioned and its authorization suspended or revoked; no other specific sanctions (fines, MA suspensions etc.) are foreseen with respect to the Marketing Authorization Holders.

LT authorities have the right to write the Protocol of Administrative Offences according to the Code of administrative offences in case a MAH does not perform its obligations. The protocol is submitted to the Administrative Court and the court takes a decision on the imposition of penalties. The Lithuanian agency has not issued any protocols on the basis of supply disruptions for the entire period.

NL applies penalties for violation of the MAH commitment to supply wholesale distributors and pharmacies and for untimely notification of expected shortages (currently 45,000-150,000€).

PT foresees fines between 2,000€ and 15% of the responsible person's turnover or 180,000€, depending on whichever is lower, for wholesalers or MAHs that don't comply with the obligation of supply the geographic relevant market, for MAHs that don't comply with the obligation to notify a shortage or for wholesalers that don't comply with the obligation to notify exportation in the terms explained in question 9. In the last 10 years, no fines were imposed in the context of non-compliance with shortage notification requirements, but regarding other non-compliances a total of 232 administrative offence processes were installed.

SE can revoke the wholesale license if the wholesaler fails to deliver medicinal products to pharmacies. There are no specific penalties for interruption of supply/shortages except in the cases

related to the obligation to supply reimbursable products (fines between 5,000 – 10,000,000 SEK). One case of a fine for the interruption of supply has been reported (20,000 SEK).

SI foresees penalties and has detailed legal provisions in place for their application. The legislation distinguishes between minor and major offences. The sanctions are imposed as fines for the legal entity (e.g. an economic operator), responsible person of the legal entity, and an individual. Examples of offences are: failure to communicate certain data, failure to fulfil the public service obligations and failure to fulfil the obligations of wholesalers. The fines range from 800 to 4,000 € for minor offences and from 8,000 to 120,000 € for major offences.

SK also applies financial penalties.

In the UK penalties exist in the pharmaceutical legislation for non-compliance with the legal provisions. Sanctions have not been applied to MAHs to date and MAHs continue to notify medicines shortages.

AT, BG, DE, DK, EE, IE, LV, NO have no specific sanctions for interruption of supply.

12. In the case of a MAH informing you of its plans to discontinue the marketing of a medicinal product (deregistration), where no other alternative is available, what actions are taken? Is there a dialogue with the MAH, concerning the consequences of the shortage?

Most respondents indicate that in case of deregistration/shortage a dialogue with the MAH is initiated.

PT has a dedicated working group dealing with the assessment of impact of supply discontinuation and engages in discussions with the MAH in order to minimise the impact of deregistration/shortages.

On the other hand, CZ does not engage in a dialogue with MAHs in case of deregistration.

Measures implemented in this context may include, among others:

- Shortage impact and substitution assessment (indicated by most of respondents).
- In some MS, the MAH should provide with information about therapeutic alternatives (ES, SI)
- In FR, essential medicinal products cannot be withdrawn from the market until an alternative solution has been identified.
- Stock monitoring: EL checks the potential alternatives stocks belonging to the same therapeutic category. The Greek authorities contact pharmaceutical companies, marketing authorisation holders of alternative medicinal products in order to communicate the problem and ask for potential increase of production and product stock).
- Notification of cessation at least one year in advance for essential medicines (FR).
- Special/exceptional import and manufacturing authorisations (CZ, EE, EL, ES, IT, LV, LT, NO, PT, RO).
- Fee reductions: providing some benefits e.g. fee reduction for the MAHs of certain, essentially important products with low sale data is under discussion in HU.
- Information to different actors in the supply chain and healthcare professionals (DK, EL, HR).

13. Can you describe some real life examples on how to act on shortage of essential medicinal products, in order to minimize the consequences of the shortage? What has worked, and what has not worked? Please share you experience.

[Answers removed due to their commercially sensitive nature.]

Availability of medicines

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This content applies to human and veterinary medicines.

Improving the availability of medicines authorised in the European Union (EU) is a key priority for the European medicines regulatory network. Shortages or other problems with the availability of medicines create challenges for the medicine supply chain, with a potentially serious impact on human and animal health.

Since 2016, a task force set up by the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) looks at availability issues, including medicines that are authorised but not marketed and supply chain disruptions, to improve continuity of supply of human and veterinary medicines across Europe. This builds on the network's efforts since 2012 to improve processes for handling shortages caused by good manufacturing practice (GMP) non-compliance.

Impact of COVID-19 pandemic

The European medicines regulatory network is closely monitoring the impact of the COVID-19 pandemic on the human and veterinary medicine supply chains in the EU. For more information, see [Availability of medicines during COVID-19 pandemic](#).

Medicine shortages

Medicine shortages can occur for many reasons, such as manufacturing difficulties or [problems affecting the quality of medicines](#) that can impact on patient care.

In the EU, most medicine shortages are dealt with at national level by [national competent authorities](#). However, EMA can be involved in certain situations, for example when a medicine shortage is linked to a **safety concern** or affects **several Member States**.

Regulatory authorities within and outside Europe are increasingly working together to prevent shortages and to limit their impact whenever they occur. The [European medicines regulatory network](#) aims to minimise the impact of medicine shortages on patients by:


- working with pharmaceutical companies to resolve manufacturing and distribution issues;
- sharing information with [international partners](#) about alternative sources of supply;
- seeking input from [patients](#) and [healthcare professionals](#) on the impact of medicine shortages, to support decision-making;
- taking measures to allow alternative medicines or suppliers to be used.

Public information on shortages from EMA


Since 2016, EMA publishes a public catalogue for shortages assessed by its [Committee for Medicinal Products for Human Use \(CHMP\)](#) and/or the [Pharmacovigilance Risk Assessment Committee \(PRAC\)](#), providing **clear information and recommendations**, if relevant, to patients, healthcare professionals and other stakeholders. For more information, see:

- [Shortages catalogue](#)

For a list of national medicine registers in the Member States of the EU and the EEA, see [National registers of authorised medicines](#).

EMA's communications on shortages are in line with the [HMA/EMA good practice guidance on communicating shortages to the public](#) and EMA's discussion paper on  [Communication by EMA on supply shortages of medicinal products](#)

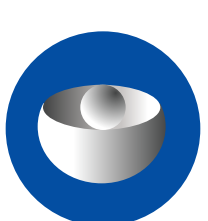
EU-level coordination on medicines availability

EMA and the [Heads of Medicines Agencies \(HMA\)](#) created an [HMA/EMA Task Force on the Availability of Authorised Medicines for Human and Veterinary Use](#)  in December 2016 to provide strategic support and advice to tackle **disruptions in supply** of human and veterinary medicines and ensure their **continued availability**.

Its key priorities include:

- looking at ways to minimise supply disruptions and avoid shortages by facilitating approval and marketing of medicines using the existing regulatory framework (for example by work sharing and reduced timetables when possible);
- developing strategies to improve prevention and management of shortages caused by disruptions in the supply chain (for example developing guidance for companies on reporting of shortages);
- encouraging best practices within the pharmaceutical industry to prevent shortages;
- improving sharing of information and best practices among EU regulatory authorities to better coordinate actions across the EU;
- fostering collaboration with stakeholders and enhancing communication of supply problems to EU citizens.

For more information on the task force's work and composition, see:



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The European Medicines Agency (EMA) and its partners in the European medicines regulatory network are putting measures in place to help prevent and mitigate possible disruptions to the supply of medicines in the European Union (EU) during the COVID-19 pandemic. Extraordinarily, EMA is acting as central coordinator in supporting Member States' activities in this area during the pandemic.

Supply disruptions or medicine shortages could occur during the pandemic as a result of:

- temporary lockdowns of manufacturing sites;
- travel restrictions impacting exports;
- export bans;
- increased demand for medicines used to treat COVID-19 patients;
- stockpiling by hospitals, by individual citizens or at Member State level.

Some Member States have indicated that they are starting to experience shortages of certain **medicines being used to treat COVID-19 patients** or are expecting shortages to occur shortly. These medicines include medicines used in intensive care such as certain anaesthetics, antibiotics and muscle relaxants, and medicines used off-label for COVID-19.

To avoid shortages due to stockpiling, some Member States are **imposing restrictions** on the quantities that can be prescribed to or purchased by citizens.

EU Executive Steering Group on Shortages of Medicines Caused by Major Events

To provide strategic leadership for **urgent and coordinated action** to prevent and mitigate supply disruptions within the EU during the pandemic, the European medicines regulatory network has established the **EU Executive Steering Group on Shortages of Medicines Caused by Major Events**.

The Group is composed of representatives of EMA, the European Commission, the Heads of Medicines Agencies (HMA), the Coordination groups for Mutual-recognition and Decentralised Procedures for human and veterinary medicines (CMDh and CMDv) and risk communication specialists.

It is chaired by the European Commission.

EMA publishes updates on the steering group's activities:

- EU actions to support availability of medicines during COVID-19 pandemic – update #7(08/06/2020)
- EU actions to support availability of medicines during COVID-19 pandemic – update #6(15/05/2020)
- EU actions to support availability of medicines during COVID-19 pandemic – update #5(08/05/2020)
- EU actions to support availability of medicines during COVID-19 pandemic – update #4(30/04/2020)
- EU actions to support availability of medicines during COVID-19 pandemic – update #3(24/04/2020)
- EU actions to support availability of medicines during COVID-19 pandemic – update #2(20/04/2020)
- Update on EU actions to support availability of medicines during COVID-19 pandemic(10/04/2020)

Enhanced monitoring system for medicines used for treating COVID-19

An enhanced **fast-track** monitoring system is in place to help prevent and mitigate supply issues with crucial medicines used for treating COVID-19 patients.

Under this system, each pharmaceutical company is appointing a **single contact point** (industry single point of contact or i-SPOC) who will report to EMA all ongoing or anticipated shortages of medicines used for treating COVID-19, irrespective of their authorisation route. This mechanism is similar to the single point of contact (SPOC) network that EMA and the national competent authorities already use to exchange information on shortages.

EMA compiles the information received from companies and shares it with the steering group for decision on **EU-level measures**.

The EU Executive Steering Group on Shortages of Medicines Caused by Major Events set up the system in collaboration with pharmaceutical companies

EMA, together with the EU Member States and pharmaceutical companies, launched the system on 17 April 2020.

Initially, the system will focus on **medicines used in intensive care** (such as anaesthetics, antibiotics, resuscitation drugs and muscle relaxants), which are in greatest demand, before extending to a broader range of medicines.

Pharmaceutical companies should continue to report shortages to the national competent authorities concerned in parallel, in line with their **existing obligations**.

Continuous monitoring of supply chains

The European medicines regulatory network is continuously monitoring the impact of the pandemic on the human and veterinary medicine supply chains in the EU closely.

Although most medicine shortages are normally dealt with at national level, during the COVID-19 pandemic, extraordinarily EMA is acting as a **central coordinator**, supporting Member States' activities in preventing and mitigating supply disruptions.

For more information on how EMA and the national competent authorities deal with and communicate on medicine shortages, see:

- Availability of medicines
- Shortages catalogue

Guidelines for EU Member States

The European Commission has published guidelines for EU Member States with **concrete actions** for preventing medicine shortages during the pandemic.

The guidelines focus on the rational supply, allocation and use of medicines to treat **COVID-19 patients** but also cover any medicine at risk of shortage due to the pandemic:

- Guidelines on the optimal and rational supply of medicines to avoid shortages during the COVID-19 outbreak
- Statement by Ursula von der Leyen, President of the European Commission, on guidelines to ensure supply and availability of medicines (English version)

Guidance for companies

Guidance is available for companies on **adaptations to the regulatory framework** to address challenges arising from the COVID-19 pandemic. For more information, see:

- Guidance for medicine developers and companies for COVID-19: Guidance on regulatory expectations and flexibility (human medicines)
- Guidance for medicine developers and companies for COVID-19: Guidance on regulatory expectations and flexibility (veterinary medicines)

Related content



- Coronavirus disease (COVID-19)
- COVID-19: latest updates
- Guidance for medicine developers and other stakeholders on COVID-19
- Public-health advice during COVID-19 pandemic
- Treatments and vaccines for COVID-19
- EMA's governance during COVID-19 pandemic
- Availability of medicines
- Shortages catalogue
- National competent authorities (human)
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Press briefing - 14 May 2020



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CONTACT

European Medicines Agency
Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands
Tel: +31 (0)88 781 6000
For delivery address, see:
How to find us

The United Kingdom (UK) withdrew from the European Union (EU) on 31 January 2020 and is no longer an EU Member State. EMA is in the process of making appropriate changes to this website. If the site still contains content that does not yet reflect the withdrawal of the UK from the EU, this is unintentional and will be addressed.



Medikamentenengpässe in der EU: Ursachen und Lösungen

Werden durch das Coronavirus die Arzneimittel knapp? Warum gibt es Lieferengpässe und was will das Parlament dagegen tun?



Arzneimittelknappheit

https://multimedia.europarl.europa.eu/en/combating-medicine-shortages-in-the-eu_N01-PUB-200716-MEDS_ev

Engpässe bei Medikamenten und medizinischer Ausrüstung stellen ein ernstzunehmendes Risiko für Patienten dar und setzen nationale Gesundheitssysteme unter Druck. Die Ausbreitung des Coronavirus hat das bereits bekannte Problem der Medikamentenknappheit in Europa noch verschärft.

Im April 2020 warnte die [European University Hospital Alliance](#), ein Zusammenschluss von neun der wichtigsten Universitätskliniken Europas, davor, dass die Vorräte an Anästhetika, Antibiotika und Medikamenten, die als mögliche Therapien gegen Corona getestet werden, aufgrund des erhöhten Bedarfs auf Intensivstationen bald nicht mehr ausreichen könnten. Produktionsausfälle, logistische Probleme, Ausfuhrverbote und Hamsterkäufe sind weitere Faktoren für potenzielle Engpässe während der Covid-19-Krise.

Das Europäische Parlament hat am 17. September 2020 [eine Entschließung angenommen](#), in der gefordert wird, Europas Unabhängigkeit im Gesundheitsbereich abzusichern. Die Versorgung soll gewährleistet, die lokale pharmazeutische Produktion gefördert und nationale Gesundheitsstrategien auf EU-Ebene besser koordiniert werden.

Warum werden Medikamente knapp?

Medikamentenlieferengpässe haben sich in der EU zwischen 2000 und 2018 verzwanzigfacht. Nach [Angaben der Kommission](#) sind insbesondere weitverbreitete, "essenzielle" Medikamente betroffen.

Über 50 %

Bei mehr als der Hälfte der nicht lieferbaren Medikamente handelt es sich um Mittel zur Krebstherapie, Antiinfektiva (Impfstoffe) und Arzneimittel zur Behandlung von Erkrankungen des Nervensystems (Epilepsie, Parkinson).

Medikamentenengpässe beruhen auf vielen Ursachen. Dazu zählen Probleme bei der Herstellung, Parallelimporte (bei denen Preisunterschiede von Medikamenten in EU-Ländern ausgenutzt werden, um Profit zu machen), Quoten, steigende Nachfrage aufgrund von Epidemien oder Naturkatastrophen und Preispolitik.

Außerdem ist die EU zunehmend von Drittländern, hauptsächlich von China und Indien, abhängig, wenn es um die Herstellung von Wirkstoffen, chemischen Substanzen und Medikamenten geht.

Die geopolitische Dimension der Arzneimittelknappheit

- 80 % der Arzneimittelwirkstoffe werden in China und Indien hergestellt.
- 40 % der in Europa verkauften Fertigarzneimittel kommen aus China und Indien.
- Aus China und Indien kommen 60 % der weltweiten Produktion von Paracetamol. Bei Penicillin sind es sogar 90 %; bei Ibuprofen 50 %.

Welche Lösungen schlägt das Parlament vor?

In ihrer EntschlieÙung begrüÙen die EU-Abgeordneten das [neue EU-Gesundheitsprogramm "EU4Health"](#), das darauf abzielt, die Verfügbarkeit von Medikamenten und medizinischem Gerät zu verbessern. Sie treten jedoch für noch mehr Maßnahmen auf EU-Ebene ein, um die Pharmaproduktion in Europa zu fördern und Mindestqualitätsstandards im Gesundheitsbereich festzulegen.

Außerdem fordern die Abgeordneten:

- Schaffung **finanzieller Anreize für Unternehmen**, pharmazeutische Wirkstoffe in Europa zu produzieren, und Prüfung ausländischer Direktinvestitionen in Produktionsbetriebe;
- Einrichtung einer europäischen strategischen Reserve an Arzneimitteln, im Stile einer "**europäischen Notfallapotheke**", um das Risiko von Engpässen zu verringern;
- Austausch **bewährter Praktiken** bei der Lagerhaltung;
- Förderung der **gemeinsamen Beschaffung** von Medikamenten auf EU-Ebene;
- **Vereinfachung des Arzneimittelverkehrs** zwischen den Mitgliedstaaten.

Bereits 2017 forderte das Parlament in einer Entschließung mehr Transparenz bei den Kosten von Forschung und Entwicklung, öffentlicher Finanzierung und Marketingausgaben.

Im April legte die EU-Kommission [Leitlinien](#) vor, um sicherzustellen, dass Menschen in Europa während des Covid-19-Ausbruchs Zugang zu unentbehrlichen Arzneimitteln haben. Sie rief die Mitgliedstaaten auf, Exportverbote aufzuheben und eine Bevorratung zu vermeiden, die Produktion zu steigern oder neu zu organisieren, die optimale Verwendung von Arzneimitteln in Krankenhäusern zu fördern und die Arzneimittelausgabe in Apotheken zu verbessern.

EU-Arzneimittelstrategie

Die Entschließung fordert die Kommission auf, die Fragen der Verfügbarkeit, Zugänglichkeit und Bezahlbarkeit von Medikamenten sowie der Importabhängigkeit im Rahmen der neuen [EU-Arzneimittelstrategie](#) zu behandeln. Die neue Strategie, die Ende des Jahres erwartet wird, soll Maßnahmen beinhalten, um den Zugang zu sicheren und bezahlbaren Medikamenten zu verbessern, Innovationen im EU-Pharmasektor zu fördern, Marktlücken zu schließen (z.B. durch Entwicklung [neuer antimikrobieller Mittel](#)) und die direkte Abhängigkeit von Wirkstoffen aus Drittländern zu verringern.

Weitere Informationen

[Verfahrensschritte](#)

[EPRS Briefing](#)

[Europäische Arzneimittel-Agentur: Medikamentenengpässe \(Katalog\)](#)

[Pressemitteilung \(Europäische Kommission\): Coronavirus: Kommission ruft Mitgliedstaaten dazu auf, die Arzneimittelversorgung und -verfügbarkeit zu optimieren \(8.4.2020\)](#)



2019 EAHP MEDICINES SHORTAGES REPORT

MEDICINES SHORTAGES IN EUROPEAN HOSPITALS

Medicines shortages in the hospital sector - prevalence, nature and impact on patient care

2019 Medicines Shortages Survey results

3 168 total responses

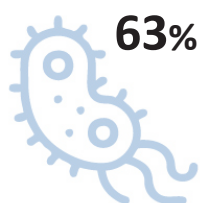
Hospital pharmacists:

2136 responses from 39 countries

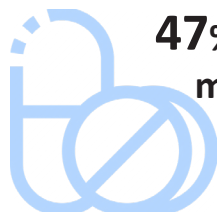
Are medicines shortages a
current problem?

95% (2019) vs 91.8% (2018)

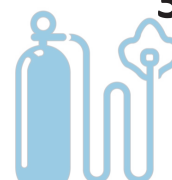
Type of medicines most frequently in shortage



63% Antimicrobial
agents



47% Oncology
medicines



38% Anaesthetic
agents

How often did you experience shortages with
products from one manufacturer?



81% More than three times

Type of impact medicines shortages had on patient care

42% Delays in care
or therapy

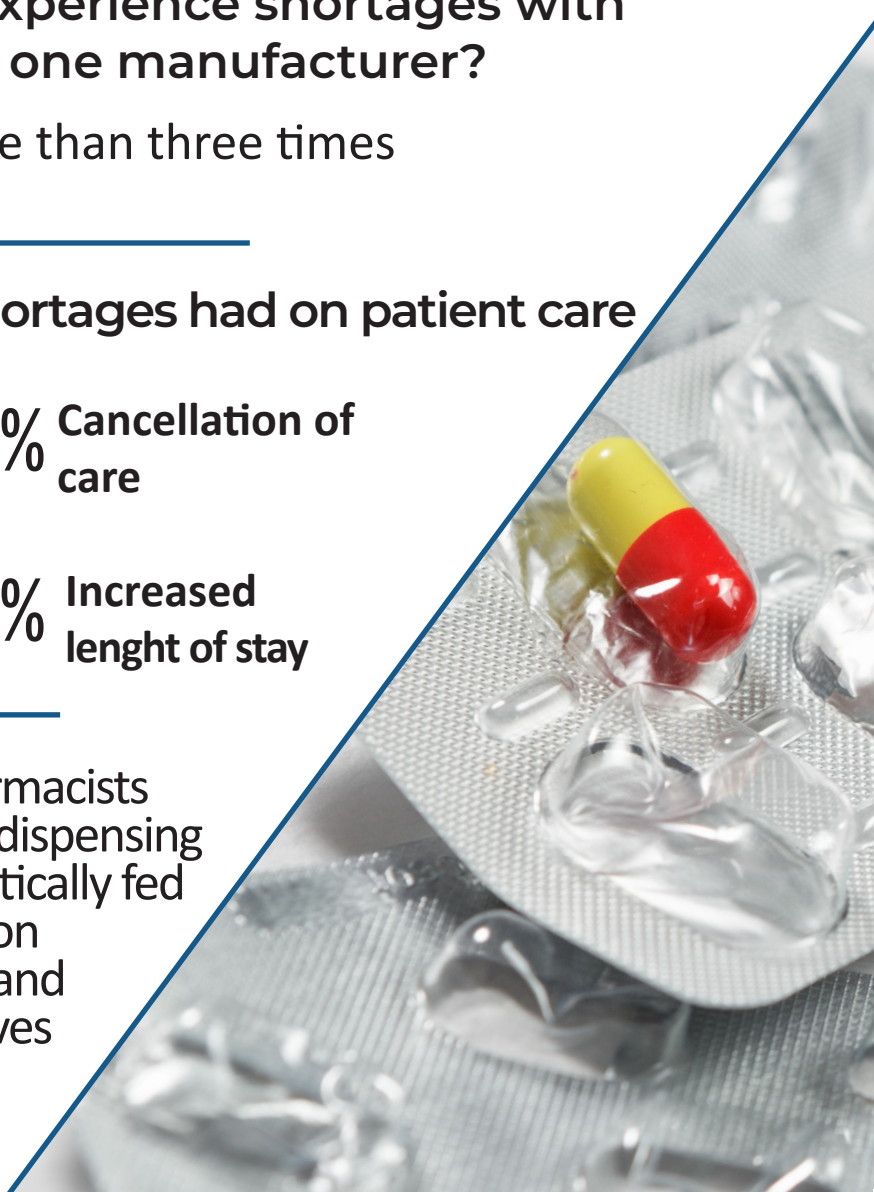
27% Cancellation of
care

28% Suboptimal
treatment

18% Increased
length of stay



70% of hospital pharmacists
reported that prescribing/dispensing
IT system are not automatically fed
with information on
ongoing shortages and
potential alternatives



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FOREWORD

BY THE PRESIDENT

The results of the 2019 Medicines Shortages Survey of the European Association of Hospital Pharmacists (EAHP) were collected between November 2019 and mid-January 2020. They showed that more and more patients are suffering deterioration in their health status, as they cannot receive their prescribed medicines promptly, creating a serious public health threat in Europe. With the COVID-19 pandemic unfolding in Europe, the situation will presumably worsen. EAHP, consequently, welcomes the efforts of the European Medicines Agency (EMA) and its partners in the European medicines regulatory network.

For hospital pharmacists, it is now time to act. The problem should not only be tackled since it will further increase during the COVID-19 pandemic but because it has already been persisting for over 10 years. The survey on the causes of medicines shortages, to be prepared by the European Commission in 2020, is the first step towards targeted pan-European action. Given that medicines shortages are impacting patient care in all Member States, a strong EU commitment is very much needed to adequately address certain causes of medicines shortages. The measures at European level should be supported by national action.

Targeting shortages through a mix of reactive and proactive measures

EAHP believes that medicines shortages cannot be tackled by a single act alone. Consequently, the Association is working towards the application of reactive and proactive measures. On the reactive side, the implementation of Section 2.5 of the European Statements of Hospital Pharmacy, encouraging the adoption of contingency plans for shortages, will be further advanced. Also, individual hospital pharmacists will continue to raise awareness within their hospitals and exchange with prescribers and managers on the best-suited solutions for patients. Other reactive measures include increasing transparency, carrying out prospective risk assessments and compounding medicines for individual patients when and where appropriate.

On the proactive side, EAHP is pushing for the adoption of prudent tendering procedures that move away from 'the winner takes it all' solutions. Procurement practices focusing solely on the price have in recent years created more and more unintended problems due to players pulling out of different national markets. Adjusting the number of winners of a tender would not only support health competition between manufacturers but also lower the risk of single supplier dependence. Also, EAHP is encouraging discussions on the sensible pricing for older yet essential medicines, to ensure that these products remain on the market.

Communication on medicines shortages

The improving communication, in particular between hospital pharmacists and other supply chain actors, remains one of EAHP's priorities. As a reliable catalogue of medicines in shortage across Europe, listing reasons, estimated duration, and other advice to pharmacies, prescribers and patients is still missing, EAHP acknowledges the work carried out by the task force on the availability of authorised medicines for human and veterinary use of the Heads of Medicines Agencies (HMA) and EMA throughout 2019. However, given the limitation of the current catalogue to medicines shortages of centrally authorised products, EAHP would like to reiterate its request towards the HMA/EMA task force. The development of a comprehensive communication strategy on shortages should be considered to guarantee that all supply chain actors, including hospital pharmacists, receive adequate and timely information on the shortage of medicines.

Awareness-raising about the problems caused for patients by medicines shortages now needs to be turned into concrete action. In particular, to lower the impact that the COVID-19 outbreak will have on the availability of active pharmaceutical ingredients and medicines in Europe. EAHP commits to working on the implementation of reactive and proactive measures and hopes that also other stakeholders affected by medicines shortages are joining this initiative.

Petr Horák
President

European Association of Hospital Pharmacists

EXECUTIVE SUMMARY

Hospital pharmacists have been working for over 10 years on the subject of medicines shortages. Due to the lack of information on this topic, EAHP has started to collect evidence on medicines supply shortages in the hospital sector, its prevalence, nature and impact on patient care. Surveys conducted in 2013, 2014 and 2018 provided detailed insights into the situation in Europe. In particular, the percentage of hospital pharmacists reporting shortages to be an issue in terms of delivering the best care to patients has seen a significant increase with 91.8% respondents in 2018, compared to 86.2% in 2014 stressing that medicines shortages are a problem faced in their hospital pharmacy.

This negative trend has continued to materialise in EAHP's 2019 Medicines Shortages Survey which gathered in total 3168 responses from hospital pharmacists, patients, physicians, nurses and other healthcare professionals coming from 39 different European countries. The number of hospital pharmacists which reported that medicines shortages are a major problem in their hospital increased from 91.8% in 2018 to 95% in 2019. In comparison only 89% of other healthcare professionals, 72% of physicians and 69% of nurses considered medicines shortages to be a current problem in the hospital they are working in, in terms of delivering the best care to patients.

More than half of the respondents from the different professional groups that participated in EAHP's survey, except nurses for which the response rate was slightly lower, indicated that they personally experienced how medicines shortages negatively impacted one or more of their patients. Delays in care or therapy, cancellation of care, suboptimal treatment and increased monitoring were frequently reported as impacts on patient care. Physicians even saw an increased length of hospital stay triggered by a medicine shortage.

For the first time, EAHP gathered information on possible reasons for shortages. The top three answers for hospital pharmacists and other healthcare professionals were the global shortage of an active pharmaceutical ingredient (API), manufacturing and supply chain problems. Physicians named the price of a medicine, supply chain problems and issues related to parallel export as the main reasons for shortages. Nurses observed that problems with shortages were caused by the price of a medicine, manufacturing problems and supply chain problems. The feedback on tendering was mixed, with hospital pharmacists and other healthcare professionals indicating that tendering is carried out at many different levels in the different European countries. Hospital pharmacists are mainly involved in tendering processes carried out at hospital level. Engagement in procedures at country or regional level is lower.



Also, the feedback for the question investigating the usefulness of the national reporting system, in case such a system exists, was mixed. Around half of the participating hospital pharmacists, nurses and other healthcare professionals deemed their national reporting system useful and regularly updated. Among the group of physicians, slightly more than 1/3 agreed with this statement. In comparison to the information collected in 2018, the groups of medicines most frequently in shortage did not change considerably. Antimicrobial agents (63%), oncology medicines (47%) and anaesthetic agents (38%) were named by hospital pharmacists as top three medicines frequently in shortage in 2019. In 2018, hospital pharmacists reported antimicrobial agents (77%), preventive medicines such as vaccines (43%) and oncology medicines (39%) as medicines most frequently in shortage.

The large majority of respondents confirmed the communication of information on medicines shortages within their workplace. Exchanges by email, by phone or via face-to-face meetings were the preferred medium through which information was shared. Question 20 (for hospital pharmacists)¹ put forward the following five proposals and asked respondents to rank them in accordance with their usefulness:

1. Better enforcing the mandatory early notification of a medicine shortage.
2. Ensuring appropriate staffing levels in order to lower the impact that medicines shortages currently have on the overall patient services.
3. Conducting a European wide analysis of the causes to provide targeted solutions.
4. Strengthening collaboration between the European countries and the European institutions.
5. Mandating improved communication among all stakeholders (manufacturers, parallel traders, wholesalers and healthcare professionals).

Proposal number 1 and number 5 were deemed the most useful solution by hospital pharmacists, other healthcare professionals, nurses and physicians. The free text responses to question 21 (for hospital pharmacists)² showed that improving communication, obliging manufacturers to share information about medicines shortages in a timely manner and applying prudent tendering/procurement mechanisms that ensure that there is more than one supplier per medicine/API in Europe could be the most useful solutions to help tackle the problem of medicines shortages.



1. Question 43 (for physicians) | question 64 (for nurses) | question 100 (for other healthcare professionals): How would you rank the usefulness of the following proposals? (0 = not useful | 5 = very useful).

2. Question 44 (physicians) | question 65 (nurses) | question 101 (other healthcare professionals): Do you have another proposal that is currently being applied in your hospital/ your country that could help alleviate the problem of medicines shortages? (free text).



BACKGROUND

For the first time EAHP expanded the scope of its Medicines Shortages Survey and reached out to patients, physicians, nurses and other healthcare professionals.

Information on medicines shortages collected by EAHP in 2014 and 2018 shed light on the impact medicines shortages have on patients and hospital pharmacists. For the 2019 edition of EAHP's Medicines Shortages Survey, the decision was taken to expand the survey to physicians, nurses and other healthcare professionals working in the hospital environment. Also, patients were encouraged to provide feedback on their experiences with medicines shortages. Data from these groups were collected between 7th November 2019 and 13th January 2020. The survey questions were made available via SurveyMonkey in Bosnian/Croatian, English, French, Greek, Italian, Portuguese, Romanian, Serbian, Slovak and Spanish.

EAHP's survey activities in the field of medicines shortages are closely linked to the European Statements of Hospital Pharmacy, in particular Statement 2.5 ('Each hospital pharmacy should have contingency plans for shortages of medicines that it procures.'). Consequently, question 19 of the 2019 Medicines Shortages Survey specifically investigated the existence of contingency plans or protocols in hospitals.

The 2019 edition of EAHP's Medicines Shortages Survey explored issues linked to communications of medicines shortages within hospitals and possible reasons for shortages and their impact on patients. In addition, current management strategies were collected by asking how survey participants would like to see medicines shortages handled and/or resolved.

An analysis aimed to detect statistically significant differences in the percentage of respondents in a country reporting shortages to be 'a problem in terms of delivering the best care to patients and/or operating the hospital pharmacy' between 2018 and 2019 surveys were performed.

Terminology

p	p-value
t	t-value
d	Effect size
df	Degrees of freedom

RESPONSE RATES

Hospital pharmacists submitted 2136 responses to the 28 questions posed by the 2019 Medicines Shortages Survey. The table below provides information on the response rate per country to EAHP's Medicines Shortages Surveys in 2014, 2018 and 2019. The response rate increased by 28% from 2018 (N=1666) to 2019. The countries which saw the biggest increase in response between 2018 and 2019 were France (+166 responses), Germany (+129 responses), the Czech Republic (+88 responses) and Slovakia (+77 responses).

Country	Responses (2019)	Responses (2018)	Responses (2014)	Country	Responses (2019)	Responses (2018)	Responses (2014)
Albania	2	1	0	Lithuania	2	1	8
Andorra	3	0	0	Luxembourg	7	3	0
Austria	44	29	21	Malta	3	6	11
Belgium	135	90	94	Montenegro	6	4	0
Bosnia & Herzegovina	26	19	9	Netherlands	29	20	11
Bulgaria	9	3	6	North Macedonia	34	14	4
Croatia	23	26	25	Norway	21	21	11
Cyprus	2	2	1	Poland	12	32	13
Czech	114	26	4	Portugal	129	85	42
Denmark	2	10	25	Romania	69	24	2
Estonia	12	17	15	Russia	1	1	0
Finland	12	33	1	Serbia	77	20	8
France	358	192	3	Slovakia	100	23	16
Germany	207	78	10	Slovenia	22	18	5
Greece	110	84	14	Spain	198	190	105
Hungary	37	33	12	Sweden	77	5	0
Iceland	2	9	4	Switzerland	83	67	7
Ireland	43	51	47	Turkey	8	61	5
Italy	34	73	41	United Kingdom	83	291	7
Latvia	0	4	2				

Table 1 Response rate of hospital pharmacists (N=2136) to EAHP's Medicines Shortages Surveys conducted in 2014, 2018 and 2019 grouped by country.

For the first time data from physicians, nurses, patients and other healthcare professionals were collected. 385 patients provided feedback to 8 patient-specific questions (questions 73 to 80 in the survey) which touched on the experiences that they had with medicines shortages during their hospital stay. The 29 questions (questions 81 to 109 in the survey) addressed to 'other healthcare professionals' were the same as those asked to hospital pharmacists. The only difference lays in an additional question that gathered information on the professional background of those choosing to answer the survey for 'other healthcare professionals'. 289 responses were received from other healthcare professionals.

The questions for physicians and nurses omitted the section investigating the influence of medicines tendering. 209 physicians provided input via the 21 questions addressed to them (questions 30 to 50 in the survey). Nurses were asked 22 questions on the reasons for and management of shortages and its impact on patients (questions 51 to 72 in the survey). 149 answers were received from nurses.

Country	Patients	Physicians	Nurses	Other Healthcare Professionals	Country	Patients	Physicians	Nurses	Other Healthcare Professionals
Albania	-	1	-	1	Latvia	-	-	-	1
Armenia	-	1	-	-	Luxembourg	-	1	-	-
Austria	-	2	-	-	Malta	-	-	-	1
Azerbaijan	1				Netherlands	4	2	2	9
Belgium	7	11	1	4	Norway	1	-	-	3
Croatia	-	1	5	1	North Macedonia	-	-	1	-
Cyprus	-	-	-	1	Poland	-	-	-	1
Czech Republic	2	4	33	4	Portugal	16	8	1	8
Denmark	2	2	1	-	Romania	73	39	6	49
Estonia	-	-	-	2	Serbia	6	3	10	13
Finland	1	-	-	-	Slovakia	57	49	61	24
France	52	5	3	34	Slovenia	-	1	-	3
Germany	6	1	-	4	Spain	5	6	1	11
Greece	72	59	13	27	Sweden	1	1	1	14
Hungary	1	-	-	-	Switzerland	1	-	1	5
Iceland	-	-	-	3	Turkey	1	-	-	-
Ireland	2	-	2	23	Ukraine	-	1	-	-
Italy	7	12	3	4	United Kingdom	68	1	4	36

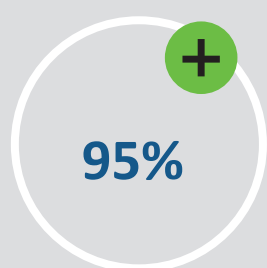
Table 2 Response rate of patients (N=385), physicians (N=209), nurses (N=149) and other healthcare professionals (N=289) to EAHP's 2019 Medicines Shortages Survey grouped by country.

Nurses that responded to the 2019 Medicine Shortages Survey work in a wide range of hospital departments, including but not limited to the intensive care unit, the emergency department, the unit responsible for paediatrics and neonatology, the operating room and the oncology department. Similarly to nurses, the participating physicians covered a wide range of specialities, including but not limited to anaesthesiology, dermatology, general medicine, gynaecology, internal medicine, paediatrics, oncology and urology.

The 289 other healthcare professionals do not only work in the hospital environment, but also in the community pharmacy sector, for the pharmaceutical industry or as wholesalers. Hospital managers, laboratory personnel, pharmacy technicians and midwives were among the groups of professionals working in the hospital. In addition, pharmacy and medical trainees that are currently interning in a hospital participated in the survey.

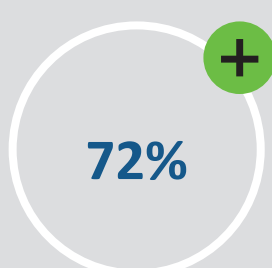
PREVALANCE OF SHORTAGES IN EUROPEAN HOSPITALS

FACTS



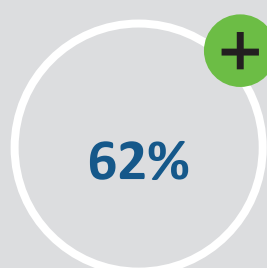
Hospital Pharmacists

There is a statistically significant increase in the percentage of countries where hospital pharmacists reported shortages to be a problem from the 2018 survey and the 2019 survey.



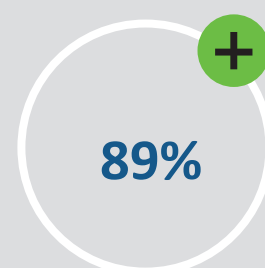
Physicians

Most physicians stated that medicines shortages are causing a problem in delivering the best possible care to patients.



Nurses

More than half of nurses also believe that medicines shortages are a problem in their hospital.



Other Healthcare Professionals

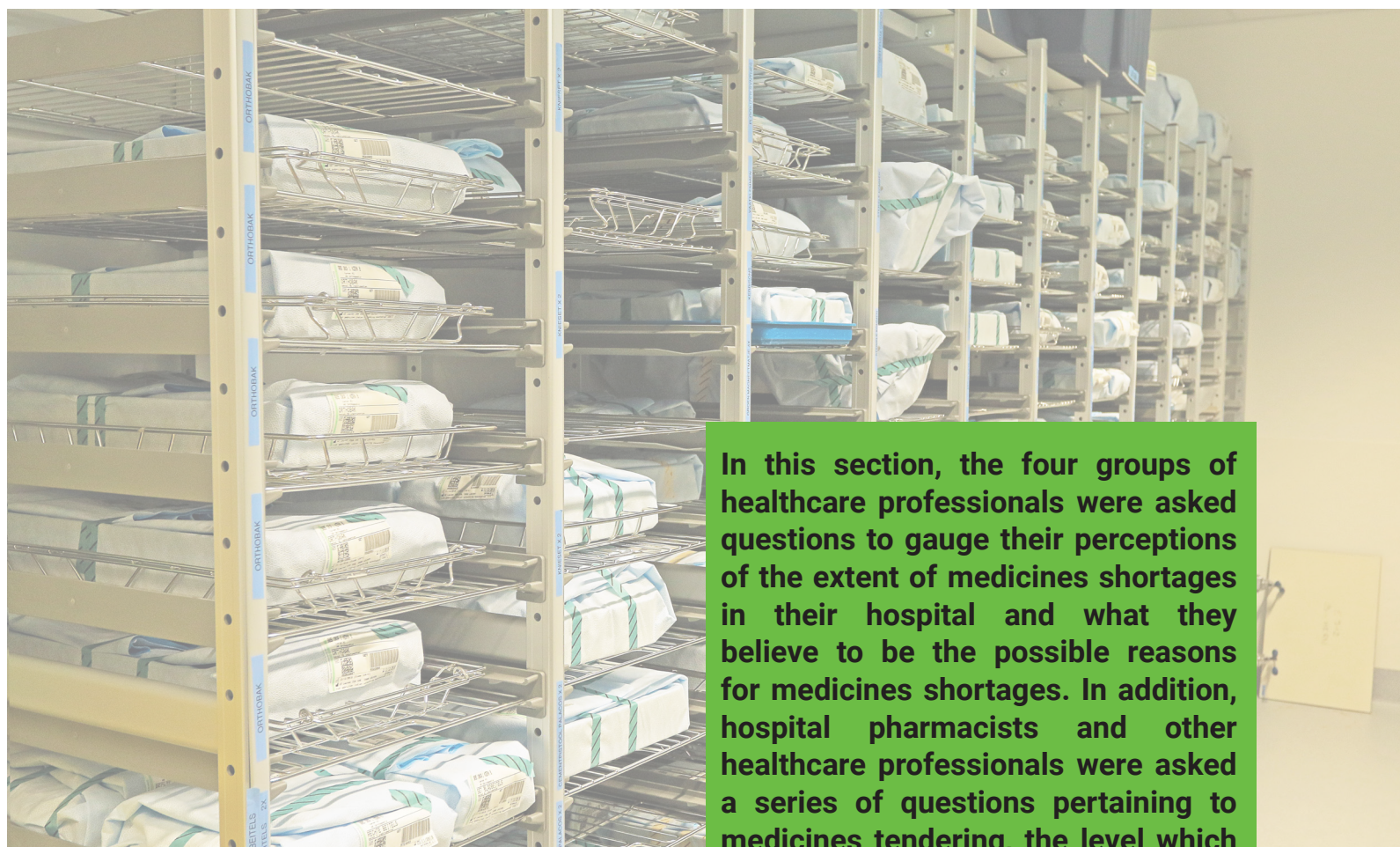
A significant majority of other healthcare professionals agree that medicines shortages are currently an issue for them and for patient care.

HIGHLIGHTS

The four groups of healthcare professionals surveyed agreed that medicines shortages are preventing the delivery of the best care to patients and comparisons with the 2018 EAHP Medicines Shortages Report demonstrates that the problem has worsened. However, the responses differed when it came to the question of possible reasons, with hospital pharmacists being more likely

to lay the blame on global shortages of APIs, manufacturing and supply chain problems than physicians or nurses. This section also looked at hospital pharmacist's involvement in tendering, and the differences in medicines tendering depending on the level of which it is conducted was also highlighted.

PREVALANCE OF SHORTAGES IN EUROPEAN HOSPITALS



In this section, the four groups of healthcare professionals were asked questions to gauge their perceptions of the extent of medicines shortages in their hospital and what they believe to be the possible reasons for medicines shortages. In addition, hospital pharmacists and other healthcare professionals were asked a series of questions pertaining to medicines tendering, the level which they are conducted, the criteria used and whether they are involved in the process.

Question 3 (hospital pharmacists) | question 32 (physicians) | question 53 (nurses) | question 83 (other healthcare professionals):
Are shortages of medicines a current problem in the hospital you are working in, in terms of delivering the best care to patients and/or operating the hospital pharmacy?

A large majority (95%|N=2036) of the hospital pharmacists that answered this question agreed that medicines shortages are frequently encountered in their hospital, while only 5% (N=100) believed that medicines shortages are not a current problem for delivering the best care to patients and/or operating the hospital pharmacy.

Compared to the results of EAHP's 2018 Medicines Shortages Survey in which 90% of respondents answered affirmative to the question 'Are shortages of medicines a current problem in the hospital you are working in, in terms of delivering the best care to patients and/or operating the hospital pharmacy?', the problems posed by medicines shortages seem to have grown. This trend becomes even more obvious when going back to data collected by EAHP's 2014 Medicines Shortages Survey

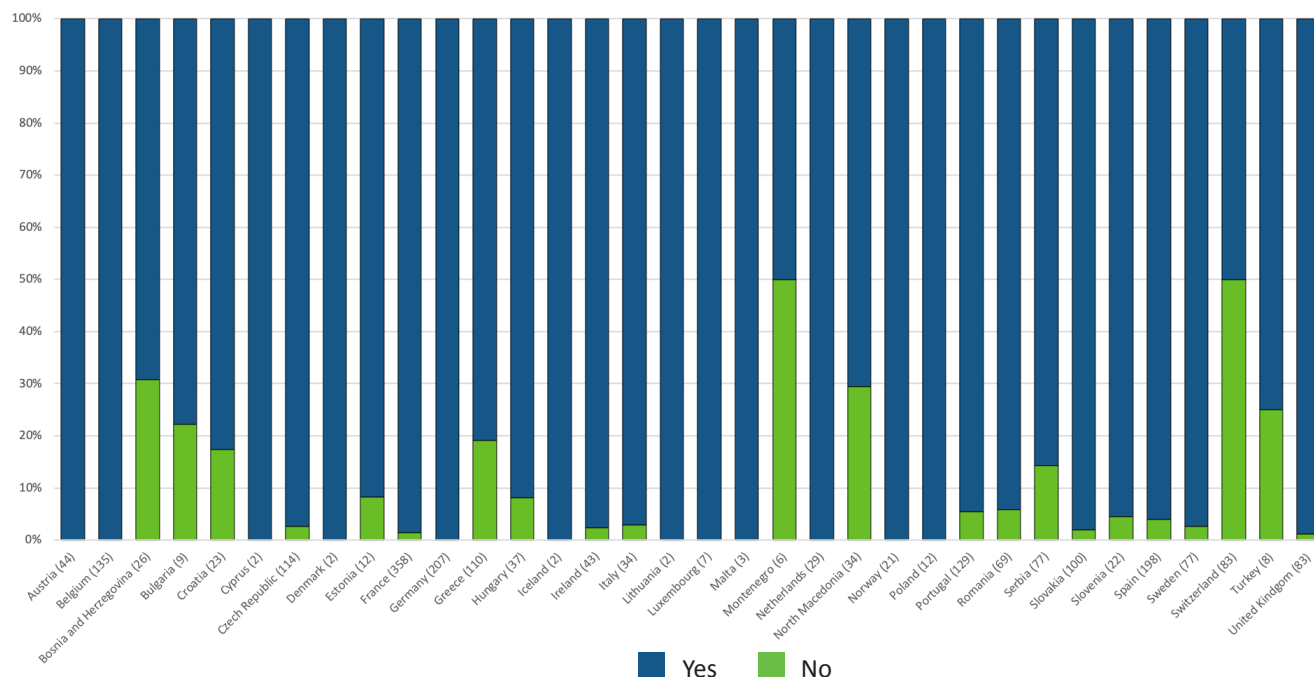


Figure 1 Percentage of responses by hospital pharmacists (N=2136) for question 3 'Are shortages of medicines a current problem in the hospital you are working in, in terms of delivering the best care to patients and/or operating the hospital pharmacy?', grouped by country.

which showed that 86% of hospital pharmacists believed that shortages were a current problem in their pharmacy at that time.

The responses, in particular of nurses and physicians paint a different picture. While the majority of other healthcare professionals (89% | N= 258) agreed that medicines shortages are a problem, only 62% of nurses (N= 92) and 72% (N= 150) of physicians shared this view.

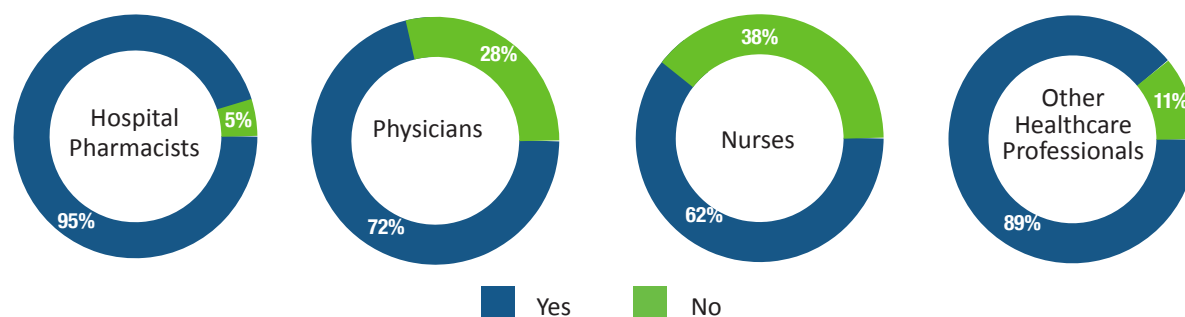


Figure 2, 3, 4 and 5 Percentage of responses by hospital pharmacists (N=2316) for question 3, physicians (N=209) for question 32, nurses (N=149) for question 53 and other healthcare professionals (N=289) for question 83 'Are shortages of medicines a current problem in the hospital you are working in, in terms of delivering the best care to patients?', grouped by profession.

An analysis was carried out which aimed at detecting statistical significant differences in the percentage of respondents in a country reporting shortages to be "a problem in terms of delivering the best care to patients and/or operating the hospital pharmacy" in the 2018 and the 2019 Medicines Shortages Survey. The analysis was performed considering only countries that answered to both surveys. The 2019 survey foresaw two answers possibilities for question 3: 'yes' and 'no'. While in the 2018 survey participants could choose between 'yes', 'no' and 'unsure'. For this reason, the calculation of the percentage of 'yes' answers for each country in 2019 was based on the division of the number of 'yes' answers by the sum of the number of 'yes' and 'no' answers. For the results of the 2018 survey, the percentage of 'yes' replies was obtained by dividing the number of 'yes' responses by the sum of all responses from hospital pharmacists.

Data obtained was cleaned for outliers and tested with a paired student's t-test. The t-test results showed a statistical significant increase in the percentage of countries that reported shortages to be a problem in terms of delivering the best care to patients and/or operating the hospital pharmacy in 2019 compared to 2018 (T= 3,959; df= 27; p= 0,0005; d= 1.024).

Question 4 (hospital pharmacists) | question 33 (physicians) | question 54 (nurses) | question 84 (other healthcare professionals): What do you see as possible reasons of shortages in your hospital? Tick all that apply.

When asked what they believed to be the possible reasons for medicines shortages in their hospital the top three answers for hospital pharmacists were, global shortage of an active pharmaceutical ingredient (API) (72%), manufacturing (72%) and supply chain problems (49%). The top three answers were the same for other healthcare professionals, with 55% choosing global shortage of API as one of the possible causes of medicines shortages in their hospital, 58% choosing manufacturing problems and 44% opting for supply chain problems. For physicians, the top three responses were the price of a medicine (either too low or too high) with 40%, supply chain problems (33%) and issues related to parallel export (32%). For nurses, the top three responses were similar to those of physicians, with the price of a medicine (either too low or too high) with 37%, manufacturing problems (33%) and supply chain problems (32%).

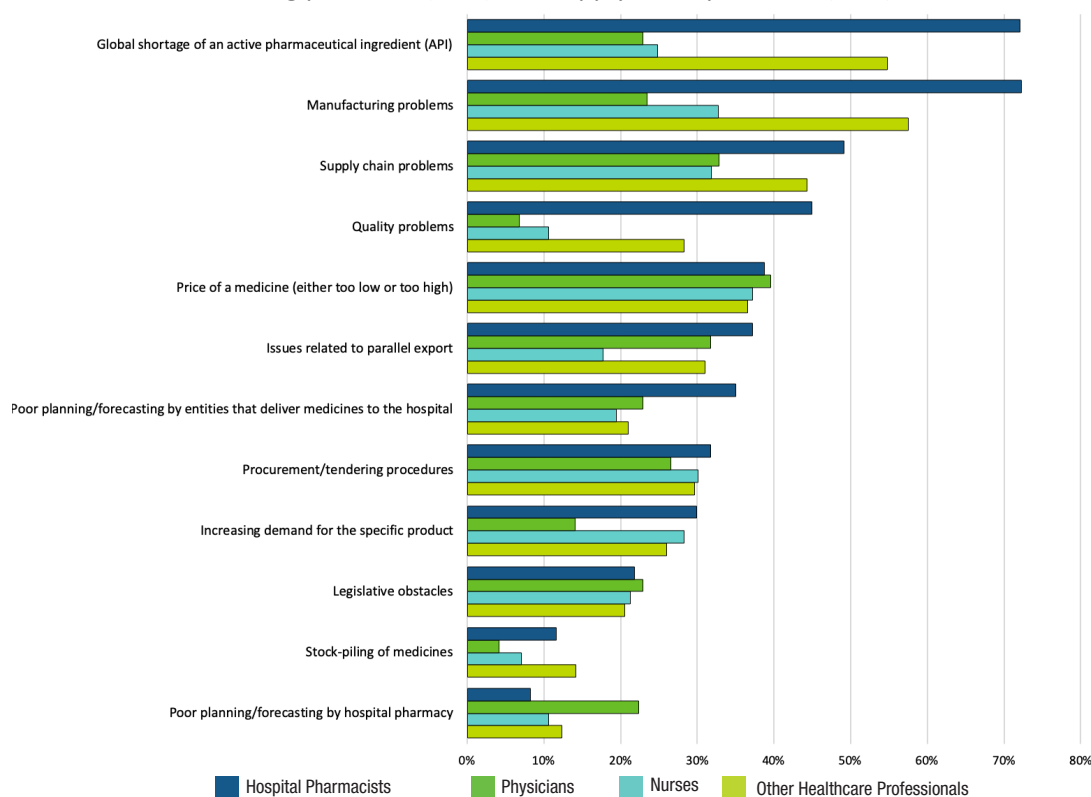


Figure 6 Percentage of responses by hospital pharmacists (N=2075) for question 4, physicians (N=192) for question 33, nurses (N=113) for question 54 and other healthcare professionals (N=219) for question 84 'What do you see as possible reasons of shortages in your hospital?', grouped by profession. (Note that this was a tick all that apply question).

The results reveal considerable differences in the perception, between the four groups of healthcare professionals, on the possible reasons for medicines shortages. The biggest divergence can be seen at the top of the graph which demonstrates that while 72% of hospital pharmacists believed that a global shortage of an API was the reason behind medicines shortages in their hospital, only 23% of physicians and 25% of nurses answered the same. Similarly, 72% of hospital pharmacists replied that manufacturing problems were causing medicines shortages in their hospital, compared to only 23% of physicians and 33% of nurses. Physicians were also more likely to believe that poor planning/forecasting by the hospital pharmacy was causing medicines shortages in their hospital, with 22% of physicians choosing that answer possibility, when only 8% of hospital pharmacists, 11% of nurses and 12% of other healthcare professionals chose that option.

These results demonstrate that although the four groups of healthcare professionals do have very similar perceptions on some of the possible causes of medicines shortages, such as the price of medicines, procurement/tendering procedures and legislative obstacles for example, there are also significant differences. Hospital pharmacists are noticeably more concerned with issues related to the manufacturing process and the supply chain which might reflect the differences in the tasks and responsibilities of the healthcare professions surveyed.

Question 5 (hospital pharmacists) | question 85 (other healthcare professionals): At which level is medicines tendering carried out in your country?

Hospital pharmacists and other healthcare professionals were then asked at which level medicines tendering is carried out in their country. Other healthcare professionals (32%) were significantly more likely to answer that they didn't know than hospital pharmacists (11%). For hospital pharmacists, the answers were fairly diverse with 25% stating that medicines tendering is conducted both nationally and at hospital level, 22% stating that it was done at the hospital level and 19% stating that it was done via purchasing group.

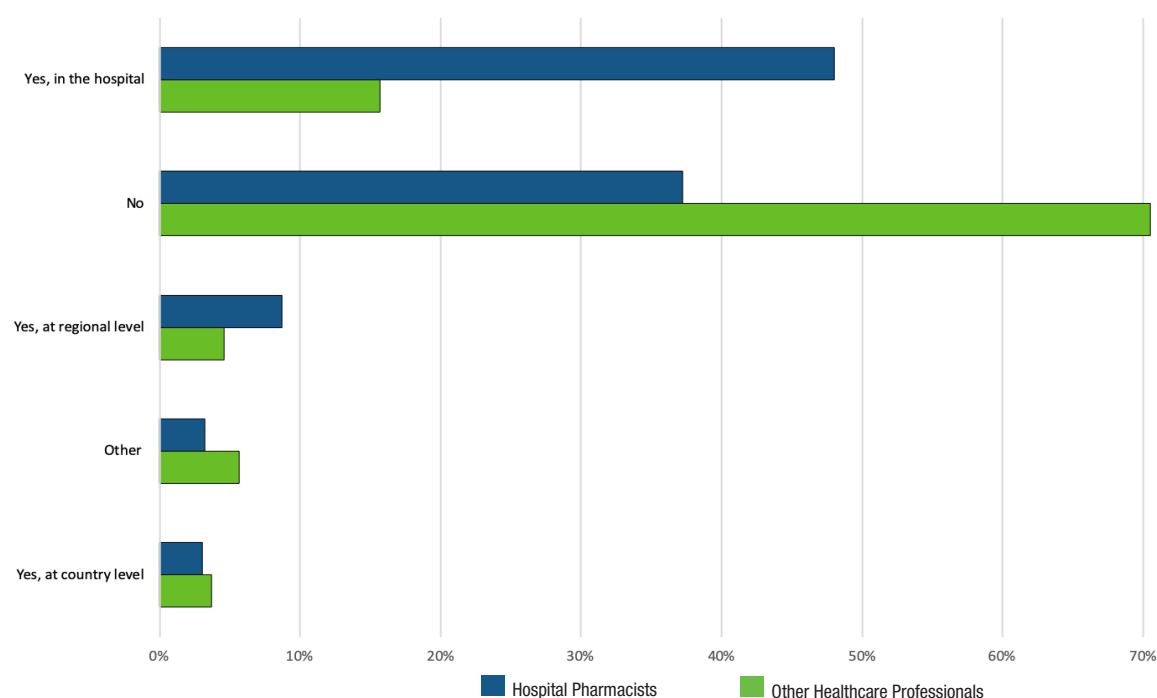


Figure 7 Percentage of responses by hospital pharmacists (N=2034) for question 5 and other healthcare professionals (N=199) for question 85 'At which level is medicines tendering carried out in your country?', grouped by profession.

As highlighted in EAHP's position paper on procurement the procedures for medicines tendering vary significantly across Europe and are conducted at different levels in different countries. The answers to question 5 therefore reflect the diverse procurement landscape in Europe.

Question 6 (hospital pharmacists) | question 86 (other healthcare professionals): Are you involved in medicines tendering? Tick all that apply.

Hospital pharmacists and other healthcare professionals were asked whether they are involved in medicines tendering. Hospital pharmacists were significantly less likely to answer ‘no’, with 37% of hospital pharmacists stating that they were not involved in medicines tendering compared to 71% of other healthcare professionals. Most of the participating hospital pharmacists who take part in medicines tendering are involved on the hospital level (48%), with some participating in the tendering process on the regional level (9%). This demonstrates that hospital pharmacists play a substantial role in medicines tendering, especially in hospitals.

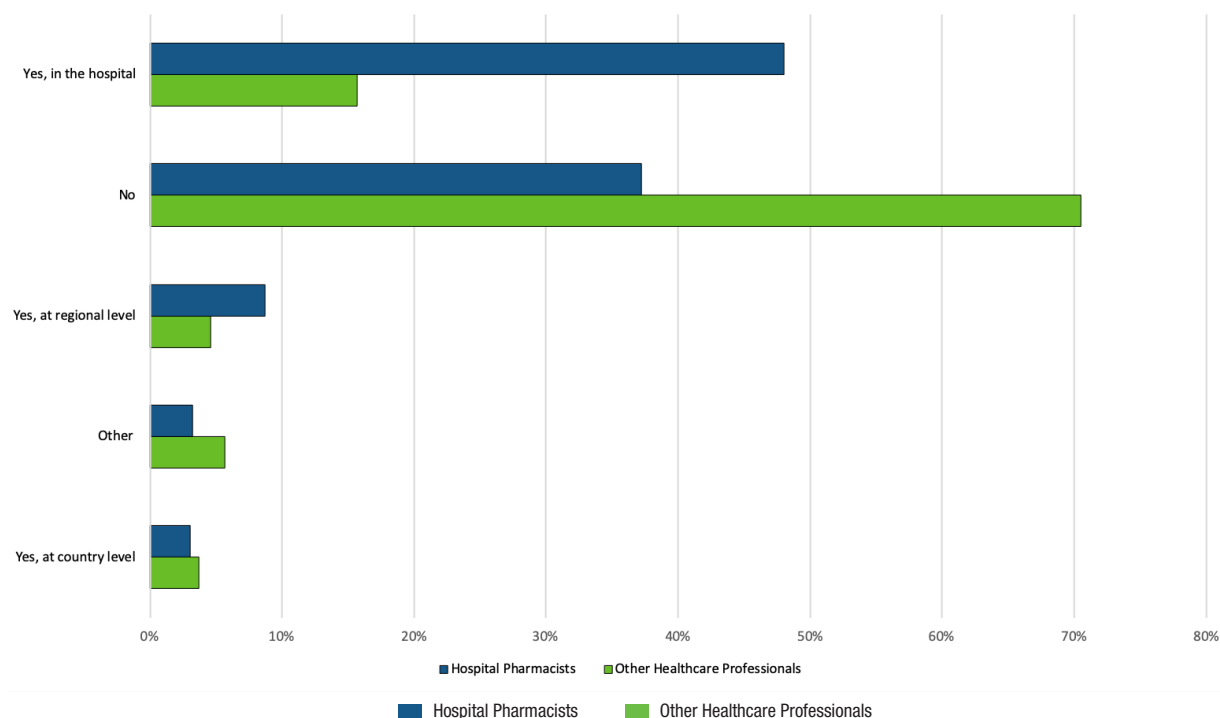


Figure 8 Percentage of responses by hospital pharmacists (N=2034) for question 6 and other healthcare professionals (N=217) for question 86 ‘Are you involved in medicines tendering?’, grouped by profession.

Respondents who ticked the answer possibility ‘other’ were given the option to specify in a free text response. Of those who did many stated that they were involved in medicines tendering on several different levels, such as medicines tendering on the hospital level with regional cooperation. Several respondents highlighted that the level of the medicines tendering varied depending on the medicine. With some medicines being tendered on the hospital level while others on the regional or country level. The most frequent free text response to the ‘other’ answer option was that of purchasing groups or syndicates:

“Mainly in the hospital but some in co-operation at regional level/purchasing group” – Hospital pharmacist, Finland

“Our hospital is part of a purchasing group, this purchasing group is acting for a group of hospitals, not only regional and not valid for the whole country. Furthermore, not all medicines are tendered by this purchasing” – Hospital pharmacist, Germany

Question 7 (hospital pharmacists) | question 87 (other healthcare professionals): Please mark all criteria relevant for the tendering procedure.

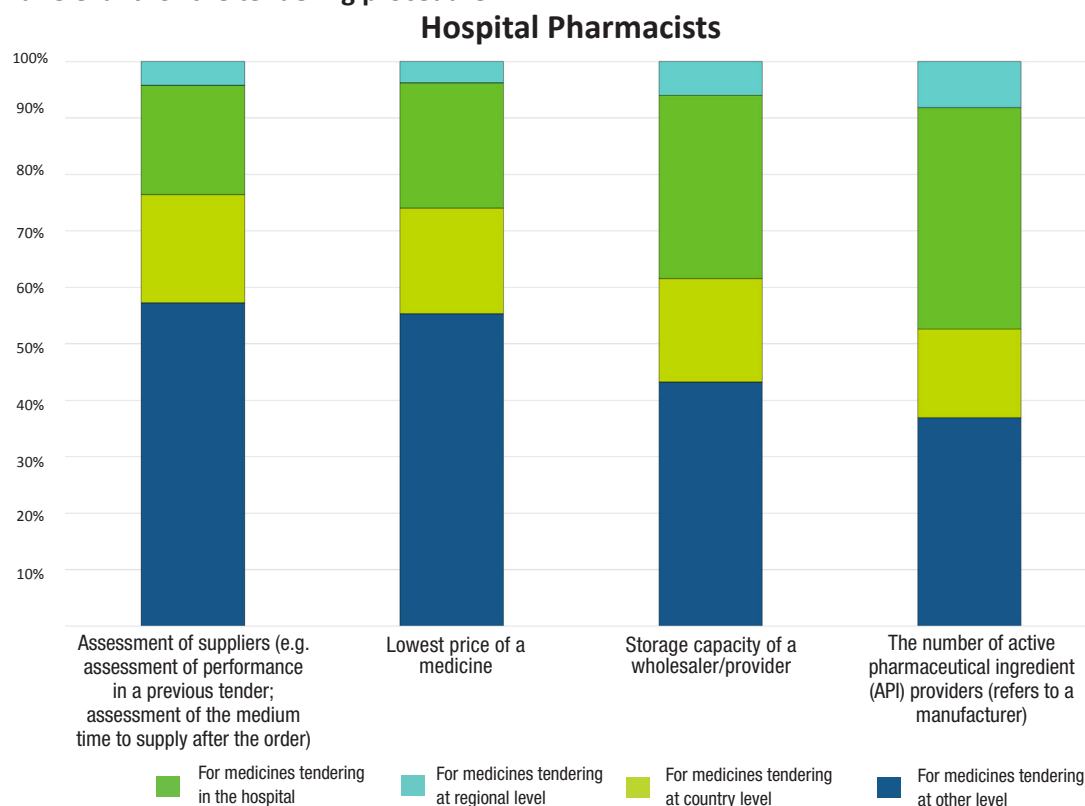


Figure 9 Percentage of responses by hospital pharmacists (N=1182) for question 7 'Please mark all criteria relevant for the tendering procedure'. Grouped by profession. (Note that this was a tick all question).

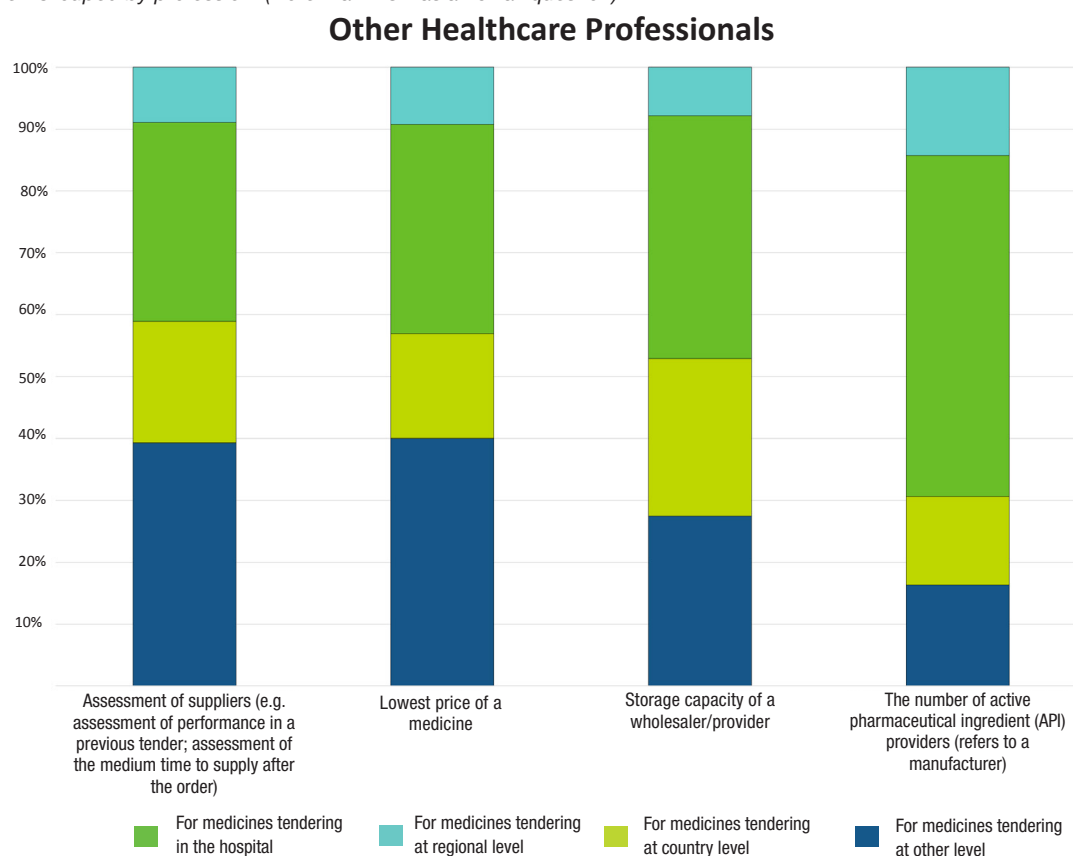


Figure 10 Percentage of responses by other healthcare professionals (N=66) for question 87 'Please mark all criteria relevant for the tendering procedure'. Grouped by profession. (Note that this was a tick all question).

In order to ascertain whether the criteria for medicines tendering differ depending on which level the tendering is conducted at, the hospital pharmacists and other healthcare professionals who had stated in question 6 that they were involved in medicines tendering, were asked to choose which criteria were the most relevant to the different levels of tendering. 59% of hospital pharmacists and 39% of other healthcare professionals stated that the assessment of suppliers was the most relevant criteria for medicines tendering in the hospital, as well as the lowest price (55% of hospital pharmacists and 40% of other healthcare professionals) and the storage capacity of a wholesaler/provider (42% of hospital pharmacists and 27% of other healthcare professionals). The number of API providers was deemed to be more significant for medicines tendering at the country level for both groups, with all four criteria being deemed almost equally as important for medicines tendering at the regional level. Indicating that the tendering procedure does vary depending on the level which it is conducted at.

Question 8 (hospital pharmacists) | question 88 (other healthcare professionals): In your experience, how many times have you experienced a shortage for a medicine in 2019, which is provided by a single pharmaceutical company?

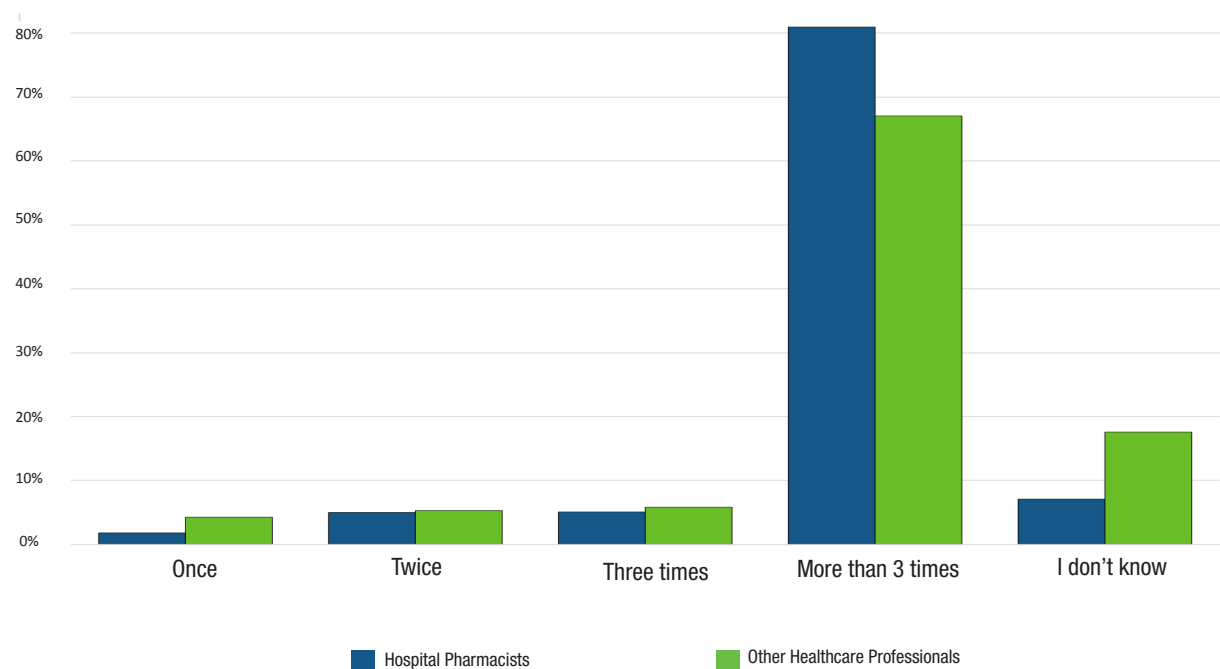


Figure 11 Percentage of responses by hospital pharmacists (N=1944) for question 8 and other healthcare professionals (N=188) for question 88 'In your experience, how many times have you experienced a shortage for medicine in 2019, which is provided by a single pharmaceutical company?', grouped by profession.

The vast majority of both hospital pharmacists (N=1806) and other healthcare professionals (N=155) stated that they have experienced a shortage for a medicine in 2019, which was provided by a single pharmaceutical company. With 81% of hospital pharmacists and 67% of other healthcare professionals answering that this has occurred in their hospital more than three times in 2019. This indicates that one possible solution to address medicines shortages would be to ensure a diverse set of suppliers for medicines.

Question 9 (hospital pharmacists) | question 89 (other healthcare professionals): Is parallel trade prohibited in your country by law under certain circumstances (e.g. in case of a shortage of a particular medicine)?

For this question, 29% of hospital pharmacists and 20% of other healthcare professionals stated that there are laws in their country to restrict or prohibit parallel trade in certain circumstances. However, in both groups a significant portion of respondents answered, 'I don't know', which might suggest that hospital pharmacists and respondents who identified as other healthcare professionals, are either unaware of or unconcerned with legislative instruments such as those which restrict parallel trade.

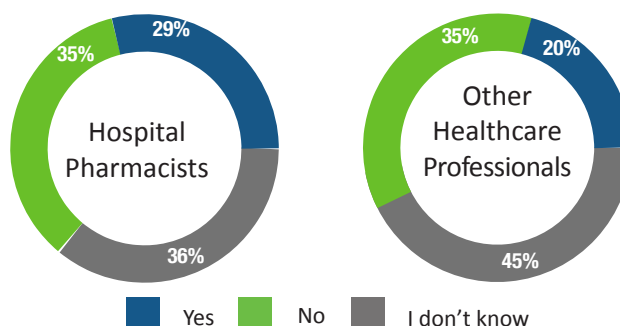


Figure 12 and 13 Percentage of responses by hospital pharmacists (N=1961) for question 9 and other healthcare professionals (N=198) for question 89 'Is parallel trade prohibited in your country by law under certain circumstances (e.g. in case of a shortage of a particular medicine)?', grouped by profession.

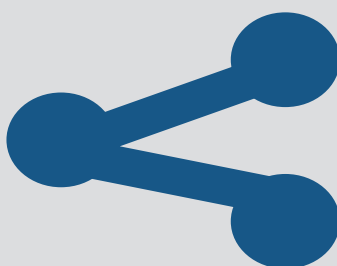
Respondents who answered 'yes' were given the option to specify the national legislation. Several free text responses from Hungary referenced to "449/2017. (XII. 27.) Government Decree on the authorisation of wholesale and parallel import activities with medicinal products". Replies from the United Kingdom mentioned "Regulation 43(2) of the Human Medicines Regulations 2012" which mandates the creation of a list of medicines which cannot be exported. There were also several free text responses from the Czech Republic which quoted "Act No. 378/2007 about medicines" and from Germany which referred to "§73 Medicinal Products Law".

FACTS

The top three proposals put forward by hospital pharmacists to help alleviate the problem of medicines shortages:



Improving communication.



Obliging manufacturers to share information about medicines shortages in a timely manner.



Applying prudent tendering/procurement mechanisms that ensure that there is more than one supplier per medicines/API in Europe.

HIGHLIGHTS

Hospital pharmacists, physicians, nurses and other healthcare professionals prefer proposals which aim to tackle the cause of medicines shortages and to strengthen European wide cooperation and communications to manage shortages when they do occur. The results also reveal gaps in medicines shortages management. With 70% of hospital pharmacists stating that the medicine prescribing/

dispensing IT system is not automatically fed with information on shortages and potential alternatives and 61% answering that they do not have a protocol/contingency plan on managing medicines shortages in their hospital.

MEDICINES SHORTAGES MANAGEMENT



Question 10 (hospital pharmacists) | question 34 (physicians) | question 55 (nurses) | question 90 (other healthcare professionals): Who is managing the public shortages reporting system in your country?

Respondents were then asked who manages the public shortages reporting system in their country. The most common answer for both hospital pharmacists and other healthcare professionals was 'medicines agency' with 64% (N=1254) of hospital pharmacists and 58% (N=109) of other healthcare professionals choosing that option. In contrast, the most common answer for physicians (N=96) and nurses (N=86) with 54% each was 'I don't know'.

The four groups of healthcare professionals were asked questions regarding the communication of and management strategies for medicines shortages in their hospitals. Including questions regarding the national public shortages reporting system, who is able to report shortages to these systems, whether they are updated and useful and whether they receive feedback from their national competent authorities. Respondents were also asked to rank the usefulness of several suggested proposals to address and/or manage medicines shortages in Europe.

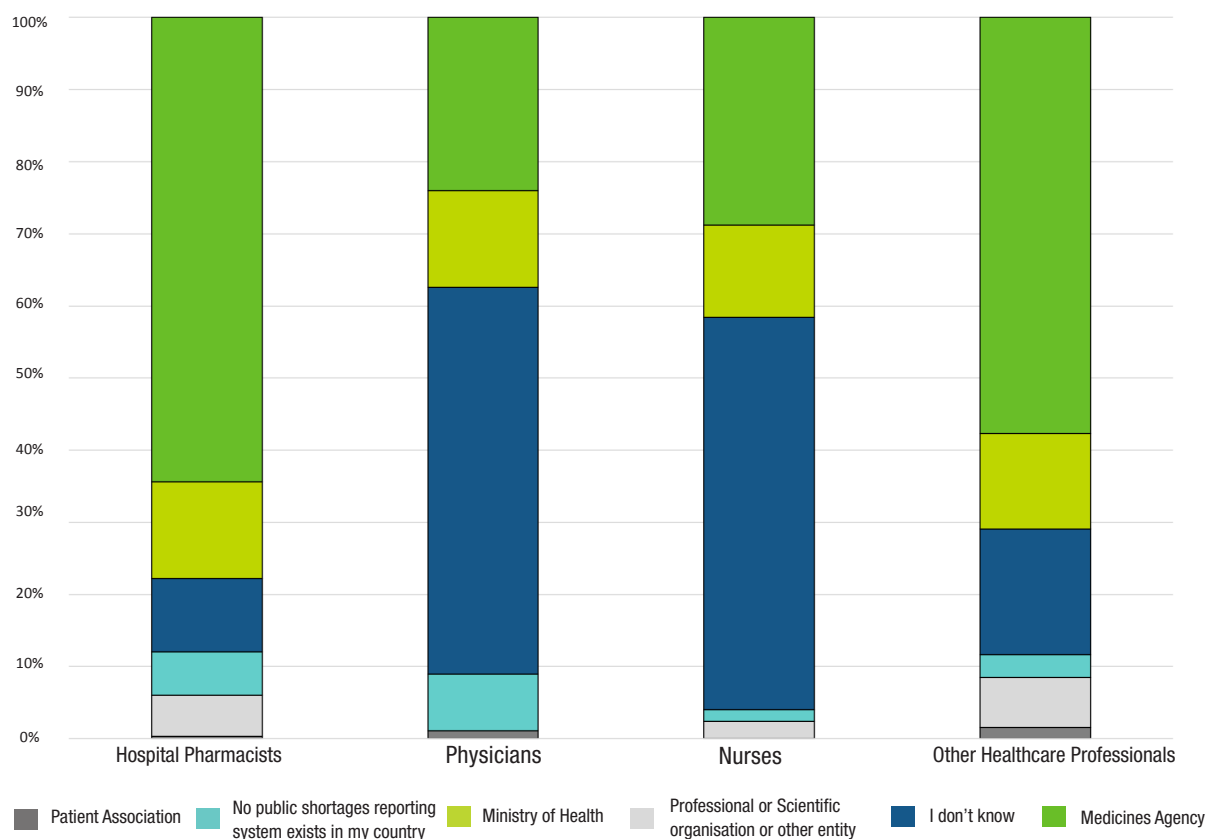


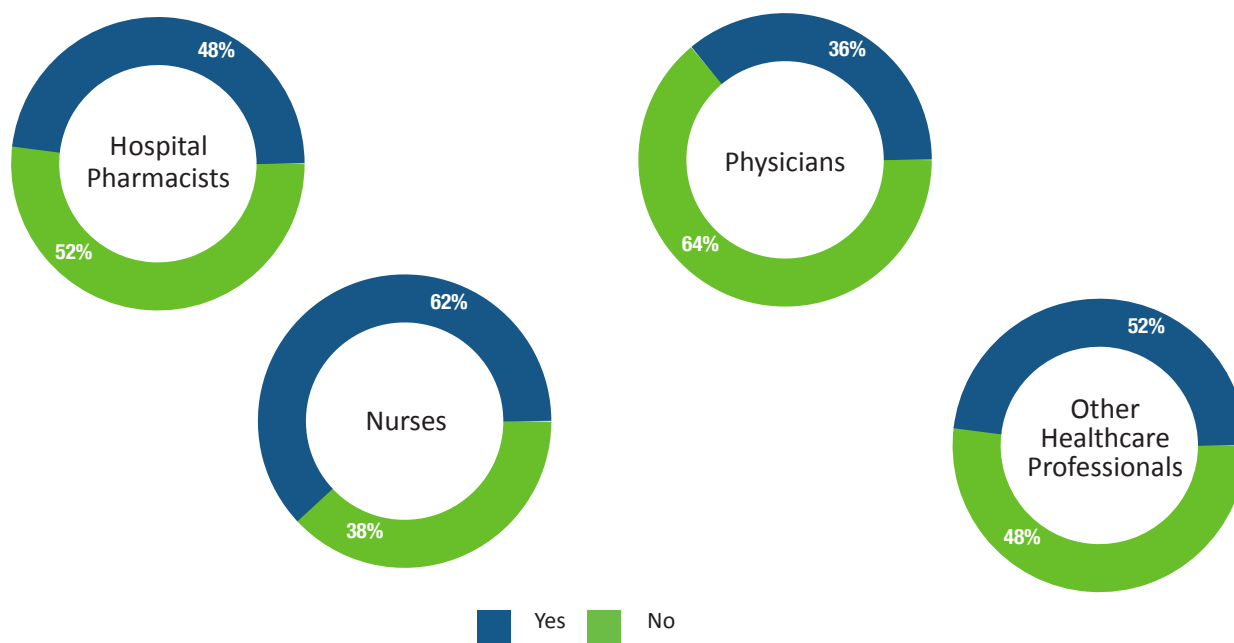
Figure 14 Percentage of responses by hospital pharmacists (N=1948) for the question 10, physicians (N=179) for the question 34, nurses (N=125) for the question 55 and other healthcare professionals (N=189) for question 90 'Who is managing the public shortages reporting system in your country?', grouped by profession.

The differences between the healthcare professions are again demonstrated in the responses to question 10. Physicians and nurses were significantly more likely to state that they didn't know who was managing the public shortages reporting system in their country, compared to only 10% of hospital pharmacists and 17% of other healthcare professionals. This does suggest that awareness of the public shortages reporting system is often not extended to those healthcare professionals who are not directly involved in the tendering or dispensing of medicine in the hospital.

Respondents were given the option to specify their answer with a free text response. Several hospital pharmacists from the Netherlands highlighted that there it is the Dutch Association of Pharmacists who manages the public shortages reporting system. Several hospital pharmacists from Switzerland also identified a private initiative called www.drugshortage.ch, which is used for monitoring shortages in addition to the public system.

Question 11 (hospital pharmacists) | question 35 (physicians) | question 56 (nurses) | question 91 (other healthcare professionals): Do you find that your national public reporting system on shortages is useful and regularly updated?

Those who didn't answer 'I don't know' to question 10 were asked whether they found their national public reporting system on shortages to be useful and regularly updated. Of the four groups, nurses were the most positive, with 62% (N=36) answering 'yes', along with other healthcare professionals of which 52% (N=79) answered 'yes'. In comparison, only 36% (N=32) of physicians and 48% (N=762) of hospital pharmacists found their national public reporting system on shortages to be useful and regularly updated.



Figures 15, 16, 17 and 18 Percentage of responses by hospital pharmacists (N=1594) for question 11, physicians (N=90) for question 35, nurses (N=58) for question 56 and other healthcare professionals (N=152) for question 91 'Do you find that your national public reporting system on shortages is useful and regularly updated?', grouped by profession.

A similar question was included in EAHPs 2018 Medicines Shortages Survey where hospital pharmacists were asked 'do you judge [public reporting system for shortages] it as effective/working/functional?', to which 56% of hospital pharmacists (N=663) replied that they regarded their reporting system to be effective/working/functional. This does indicate that satisfaction with the national public reporting systems has decreased among hospital pharmacists between 2018 and 2019.

Question 12 (hospital pharmacists) | question 37 (physicians) | question 57 (nurses) | question 92 (other healthcare professionals): Please name the database and share the link of the website.

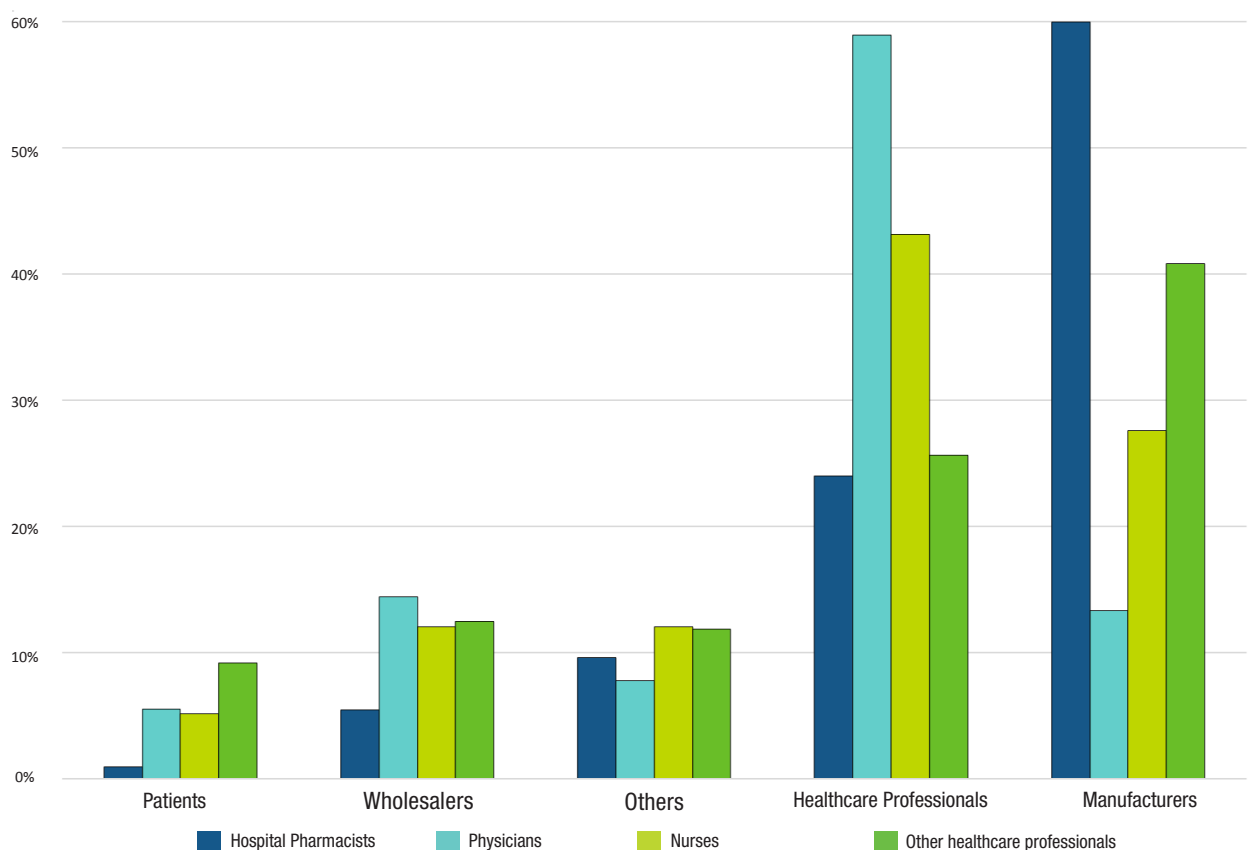
This question inquired about existing national public reporting system via which medicines shortages can be reported in each country. A summary of the responses is included in Annex 1.

Question 13 (hospital pharmacists) | question 37 (physicians) | question 58 (nurses) | question 93 (other healthcare professionals): Who can report medicines shortages via the public shortages reporting system?

When asked the question ‘who can report medicines shortages via the public shortages reporting system’ the four groups of respondents varied in their responses. 60% of hospital pharmacists (N=950) answered that manufacturers can report medicines shortages, while only 13% of physicians (N=12) and 28% of nurses (N=16) answered the same. Physicians (59%) and nurses (43%) were more likely to state that healthcare professionals are able to report via the public shortages reporting system, in comparison only 24% of hospital pharmacists and 26% of other healthcare professionals said the same. Of those hospital pharmacists who responded with ‘other’ 62 respondents specified in a free text response that anyone can report to the medicines shortages via the public shortages reporting system:

“Manufactures, wholesaler and healthcare professionals. The Medicines Agency also has a phone where the patients can ask questions regarding shortages.” – Hospital pharmacist, Norway

“Marketing authorisation holders and their offices, and any other including the public (anonymously on the website).” – Hospital pharmacist, Iceland



Figures 19 Percentage of responses by hospital pharmacists (N=1584) for question 13, physicians (N=90) for question 37, nurses (N=58) for question 58 and other healthcare professionals (N=152) for question 93 ‘Who can report medicines shortages via the public shortages reporting system?’, grouped by profession.

This variance in the responses from the four groups of healthcare professionals is most likely due to the fact that a significant portion of physicians and nurses are not aware of their national public shortages reporting system. The large difference between the answers from the physicians and nurses on the one hand and the hospital pharmacists on the other might simply indicate that physicians and nurses are more likely to be aware and informed of such systems if they have the ability to contribute and report to the public shortages reporting systems.

Question 14 (hospital pharmacists) | question 38 (physicians)| question 59 (nurses)| question 94 (other healthcare professionals): Do you get feedback from your national competent authority/ authorities when you report a medicine shortage?

The difference between the groups was lesser in comparison to the results from question 13 when asked whether they received feedback from their national competent authority when they reported a medicine shortage. A significant portion of each group, 45% of hospital pharmacists (N=839), 45% of physicians (N=61), 50% of nurses (N=45) and 40% of other healthcare professionals (N=61) answered that they didn't know. Of the four groups, physicians were most likely to report that they do get feedback, with 40% saying yes, with nurses being least likely with only 16% saying 'yes'.

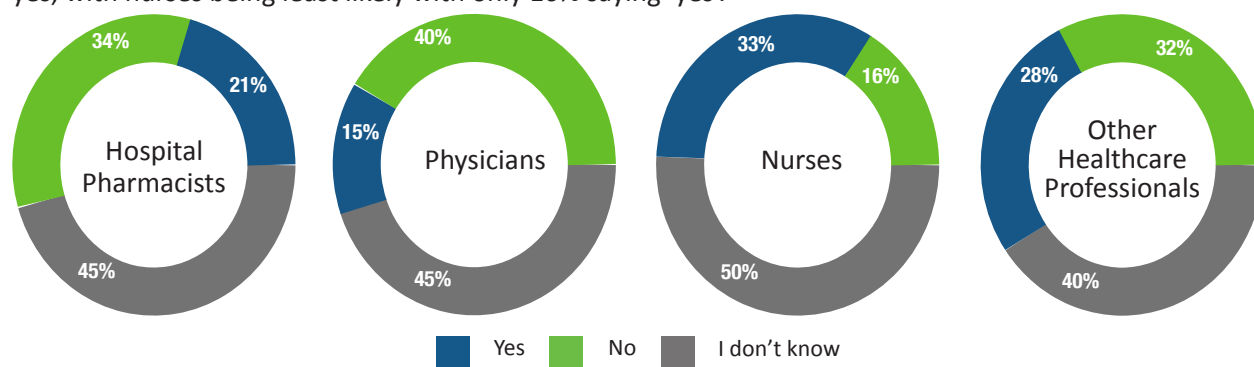


Figure 20, 21, 22 and 23 Percentage of responses by hospital pharmacists (N=1854) for question 14, physicians (N=137) for question 38, nurses (N=89) for question 59 and other healthcare professionals (N=153) for question 94 'Do you get feedback from your national competent authority/authorities when you report a medicine shortage?', grouped by profession.

Question 15 (hospital pharmacists) | question 95 (other healthcare professionals): Do manufacturers communicate the shortage of a medicine independently of or based on legal obligations?

Both hospital pharmacists (N=1854) and other healthcare professionals (N=153) were asked to provide feedback on the reporting obligations of manufacturers. The responses were quite mixed. The majority of hospital pharmacists (38%) and other healthcare professionals (37%) indicated that the notification by manufacturers is based on legal obligations. 28% of hospital pharmacists and 24% of other healthcare professionals believed that reporting is carried out independently. The remaining survey participants were unsure and therefore opted for the answer possibility 'I don't know'.

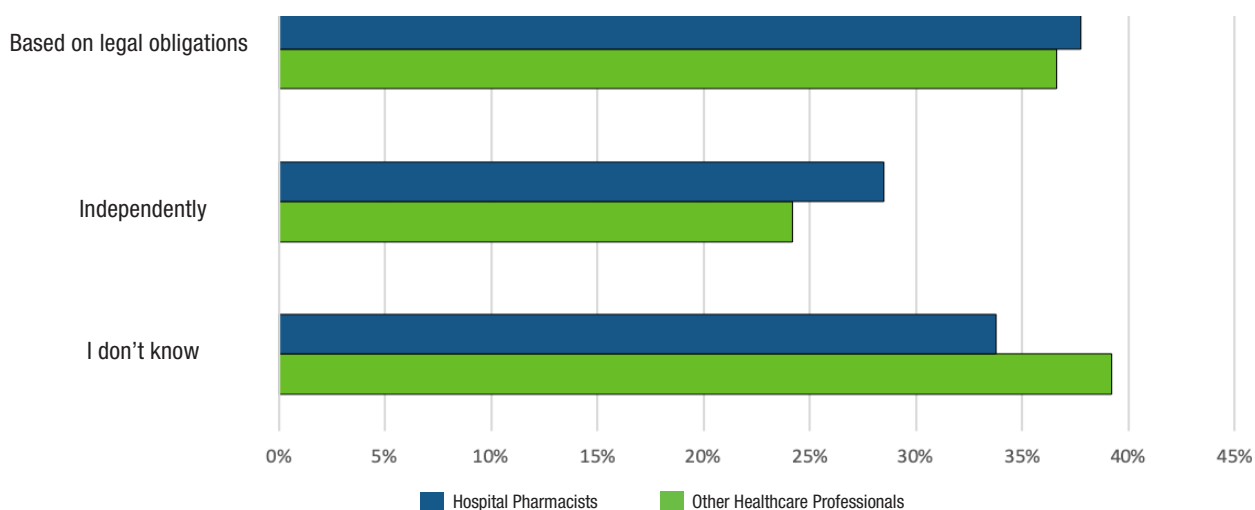


Figure 24 Percentage of responses by hospital pharmacists (N=1854) for question 15 and other healthcare professionals (N=153) for question 95 'Do manufacturers communicate the shortage of a medicine independently of or based on legal obligations?', grouped by profession.

The disparities between the answers of both hospital pharmacists and other healthcare professionals show that information in relation to the reporting obligation under Article 23a of Directive 2001/83/EC, which requires the holder of a marketing authorisation to notify the competent authority if a medicinal product ceases to be placed, either temporarily or permanently, on the market, is not widely known among practitioners.

Question 16 (hospital pharmacists) | question 39 (physicians) | question 60 (nurses) | question 96 (other healthcare professionals): Do you have a medicine shortages task force group or dedicated team?

Given the importance of coordinating responses on medicines shortages question 16 inquired about the existence of a task force group or team dedicated to this topic. Task forces and/or dedicated teams are mostly situated in the hospital or at national level. Only a small percentage of professionals (8% of other healthcare professionals | 5% of hospital pharmacists | 1% of physicians | 0% of nurses) are aware that such groups are organised regionally. From the answers, it can be deduced that other healthcare professionals seem to be most aware of the existence or non-existence of dedicated shortage discussion groups since only 14% (N=34) of hospital pharmacists and 22% (N=226) of other healthcare professionals could not provide feedback.

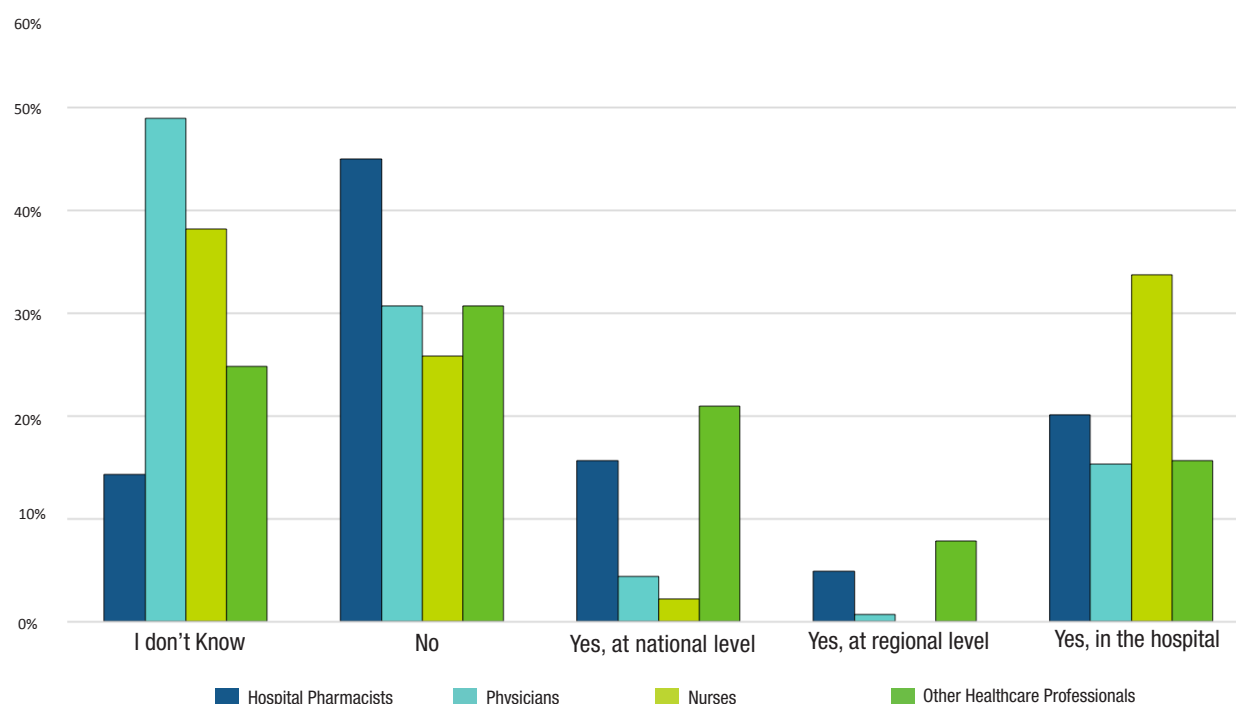


Figure 25 Percentage of responses by hospital pharmacists (N=1854) for question 16, physicians (N=137) for question 39, nurses (N=89) for question 60 and other healthcare professionals (N=153) for question 96 'Do you have a medicine shortages task force group or dedicated team?', grouped by profession.

Despite the fact that the question did not investigate the involvement of different professionals in the task force or dedicated team, it is notable that nurses and physicians are rarely aware of the existence of such groups at national or regional level. This difference in response rate could be linked to the fact that nurses and physicians are more often involved in medicines shortages task forces set up at hospital level, while hospital pharmacists and other healthcare professionals are in general more active in task forces set up at all levels, including the national level.

Question 17 (hospital pharmacists) | question 40 (physicians) | question 61 (nurses) | question 97 (other healthcare professionals): How do you communicate information on shortages/alternatives with other healthcare professionals in your hospital?

Email and phone communication were identified by all four groups of professionals as the most commonly used mediums through which information on medicines shortages and alternatives is shared with the different professionals in their hospitals. Hospital pharmacists (62% | N=1145) and other healthcare professionals (55% | N=84) most frequently resorted to email communication, while physicians preferred phone communication (28% | N=38). For nurses, both mediums ranked equally with 36% (N=39) using either email or the phone.

Apps such as WhatsApp, Viber and other social media programmes were the least favoured means of communication among hospital pharmacists (2% | N=31) and nurses (2% | N=2). Print materials in open space were identified by physicians (1% | N=1) and other healthcare professionals (3% | N=5) as the least frequently used means to communicate with colleagues. Exchanges within the Drug and Therapeutics Committee was listed as an infrequently used medium by all professionals. 2% of hospital pharmacists, 8% of nurses, 14% of other healthcare professionals and 17% of participating physicians chose not to provide feedback to the question on how shortages are communicated.

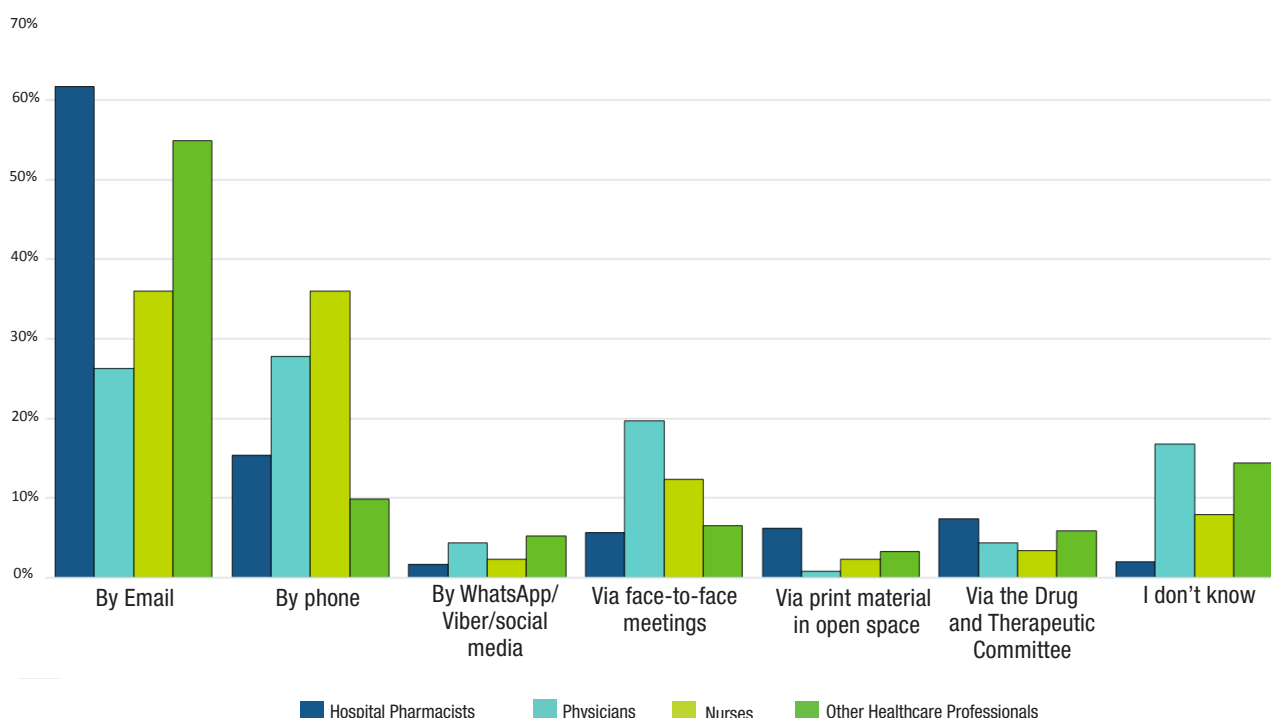


Figure 26 Percentage of responses by hospital pharmacists (N=1854) for question 17, physicians (N=137) for question 40, nurses (N=89) for question 61 and other healthcare professionals (N=153) for question 97 'How do you communicate information on shortages/alternatives with other healthcare professionals in your hospital?', grouped by profession.

Question 18 (hospital pharmacists) | question 98 (other healthcare professionals): Is the medicine prescribing/dispensing IT system automatically fed with information on ongoing shortages and potential alternatives in your hospital?

Hospital pharmacists (N= 1854) and other healthcare professionals (N=153) were asked whether the medicine prescribing/dispensing IT system automatically fed with information on ongoing shortages and potential alternatives in their hospital. The difference between the two groups was minimal with 70% of hospital pharmacists and 59% of other healthcare professionals answering 'no'.

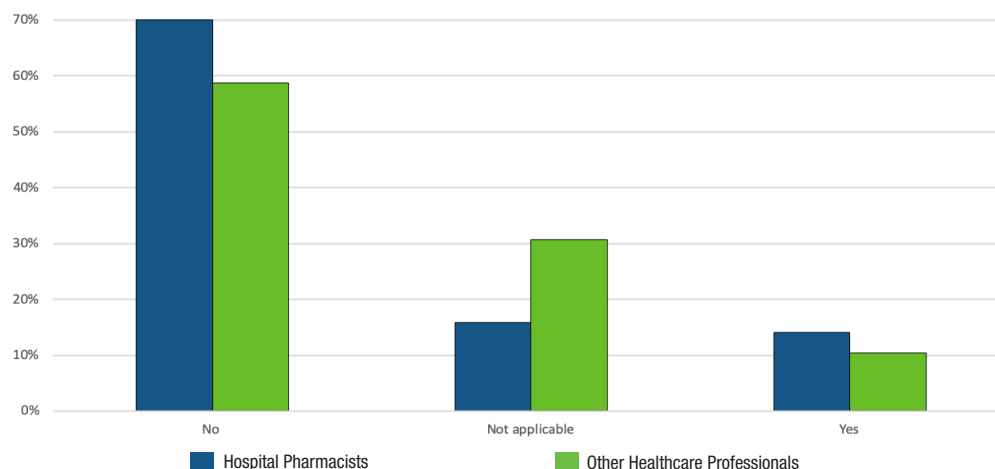


Figure 27 Percentage of responses by hospital pharmacists (N=1854) for question 18 and other healthcare professionals (N=153) for question 98 'Is the medicine prescribing/dispensing IT system automatically fed with information on ongoing shortages and potential alternatives in your hospital?', grouped by profession.

Question 19 (hospital pharmacists) | question 99 (other healthcare professionals): Do you have a protocol/contingency plan on managing medicines shortages in your hospital?

Hospital pharmacists (N=1854) and other healthcare professionals (N=153) were then asked whether they have a protocol/contingency plan on managing medicines shortages in their hospital. Other healthcare professionals were more likely to answer that they didn't know with 35% choosing that option compared to only 9% of hospital pharmacists. However, in both groups, a sizable portion of respondents answered that there are no protocols or contingency plans on managing medicines shortages in their hospital. With 61% of hospital pharmacists and 37% of other healthcare professionals answering 'no' to the question.

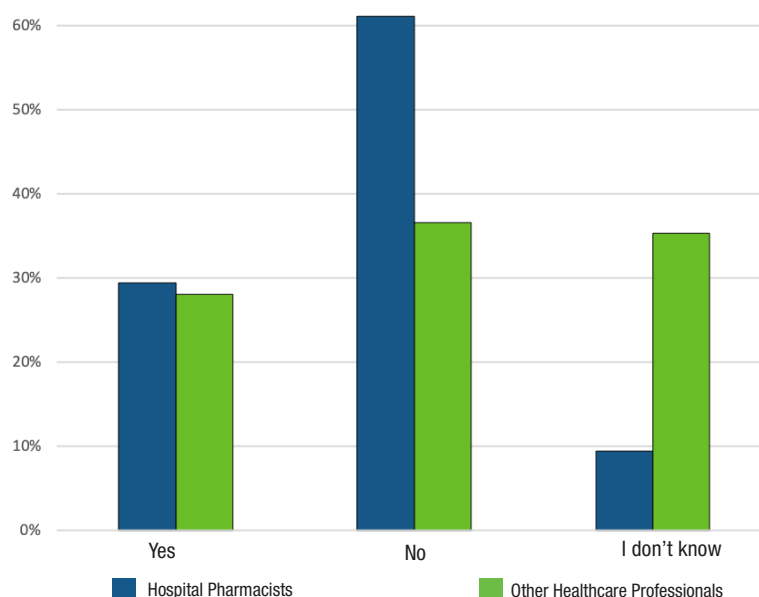


Figure 28 Percentage of responses by hospital pharmacists (N=1854) for question 19 and other healthcare professionals (N=153) for question 99 'Do you have a protocol/contingency plan on managing medicines shortages in your hospital?', grouped by profession.

Question 20 (hospital pharmacists) | question 43 (for physicians) | question 64 (for nurses) | question 100 (for other healthcare professionals): How would you rank the usefulness of the following proposals? (0 = not useful | 1 = rarely useful | 2 = sometimes useful | 3 = unsure | 4 = useful | 5 = very useful)

In order to explore not only the problems, but possible solutions as well, the four groups of healthcare professionals were asked to rank the usefulness of five different proposals. The answers provided demonstrate that the four groups have very similar opinions on which solutions are most likely to be effective and useful in addressing medicines shortages. The five proposals were well received by all four groups of professionals, with 5 being the favoured rank for all but one of the proposals. The least preferred suggestion was to 'ensure appropriate staffing levels in order to lower the impact that medicines shortages currently have on the overall patient services'. This suggests that appropriate staffing levels cannot mitigate the impact of medicines shortages on patients. Health professionals preferred proposals which aim to tackle the root of the problem of medicines shortages on the European level and improve communications.

Better enforcing the mandatory early notification of a medicine shortage

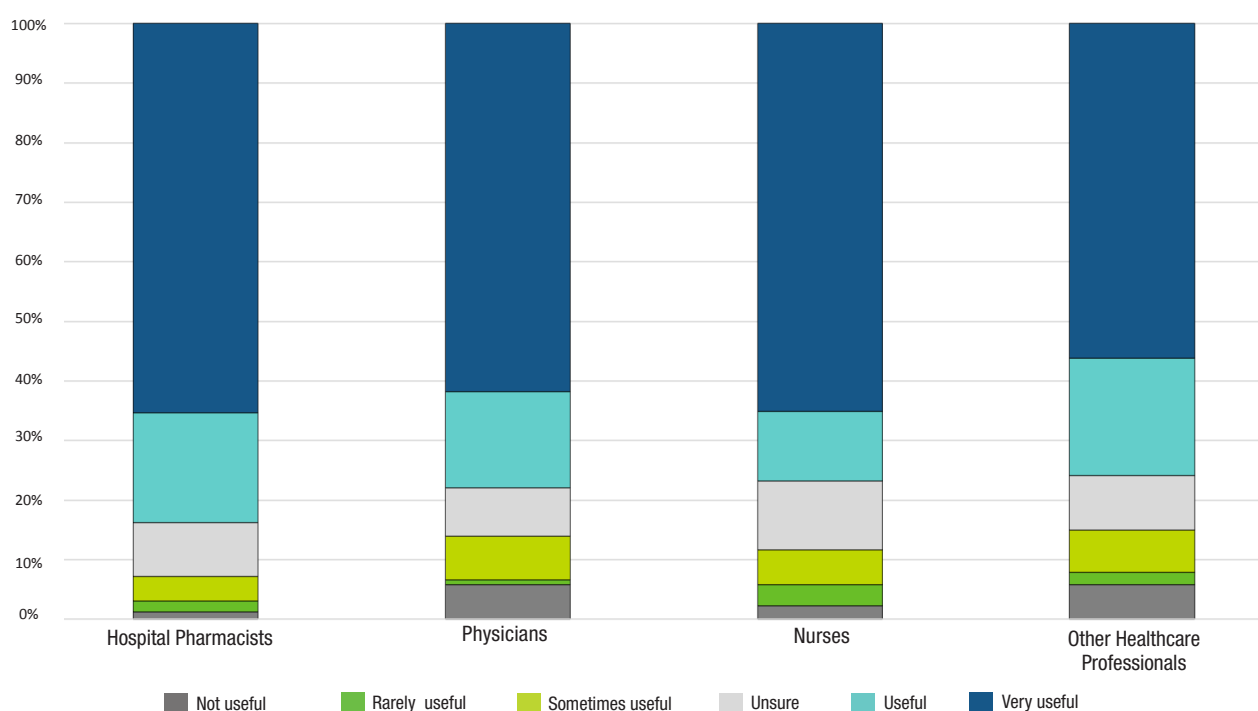


Figure 29 Percentage of responses by hospital pharmacists (N=1845) for question 20, physicians (N=136) for question 43, nurses (N=86) for question 64 and other healthcare professionals (N=153) for question 100 'How would you rank the usefulness of the following proposals? (0 = not useful | 5 = very useful)' proposal 'Better enforcing the mandatory early notification of a medicine shortage', grouped by profession.

65% of hospital pharmacists (N=1205), 62% of physicians (N=84), 65% of nurses (N=56) and 56% of other healthcare professionals (N=86) gave the proposal 'better enforcing the mandatory early notification of a medicine shortage' a ranking of 5 (very useful).

Ensuring appropriate staffing levels in order to lower the impact that medicines shortages currently have on the overall patient services

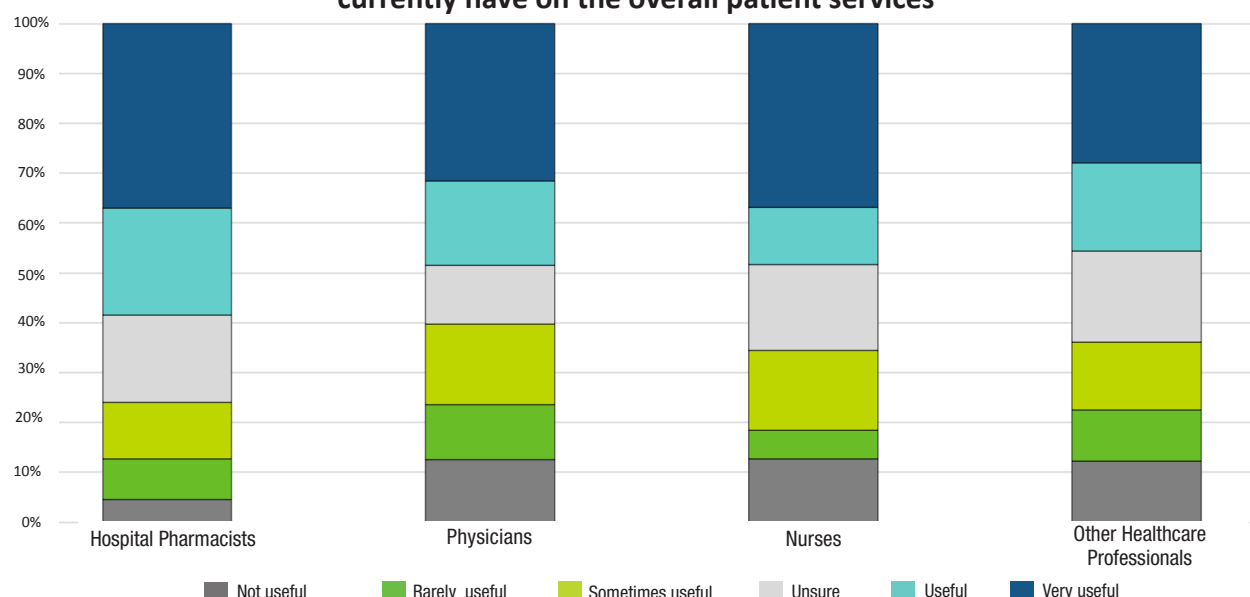


Figure 30 Percentage of responses by hospital pharmacists (N=1820) for question 20, physicians (N=136) for question 43, nurses (N=87) for question 64 and other healthcare professionals (N=147) for question 100 'How would you rank the usefulness of the following proposals? (0 = not useful | 5 = very useful)' proposal 'Ensuring appropriate staffing levels in order to lower the impact that medicines shortages currently have on the overall patient services', grouped by profession.

The proposal 'ensuring appropriate staffing levels in order to lower the impact that medicines shortages currently have on the overall patient services' was not as well received by respondents. With only 37% of hospital pharmacists (N=674), 32% of physicians (N=43), 37% of nurses (N=32) and 28% of other healthcare professionals (N=41) giving it a ranking of 5.

Conducting a European wide analysis of the causes to provide targeted solutions

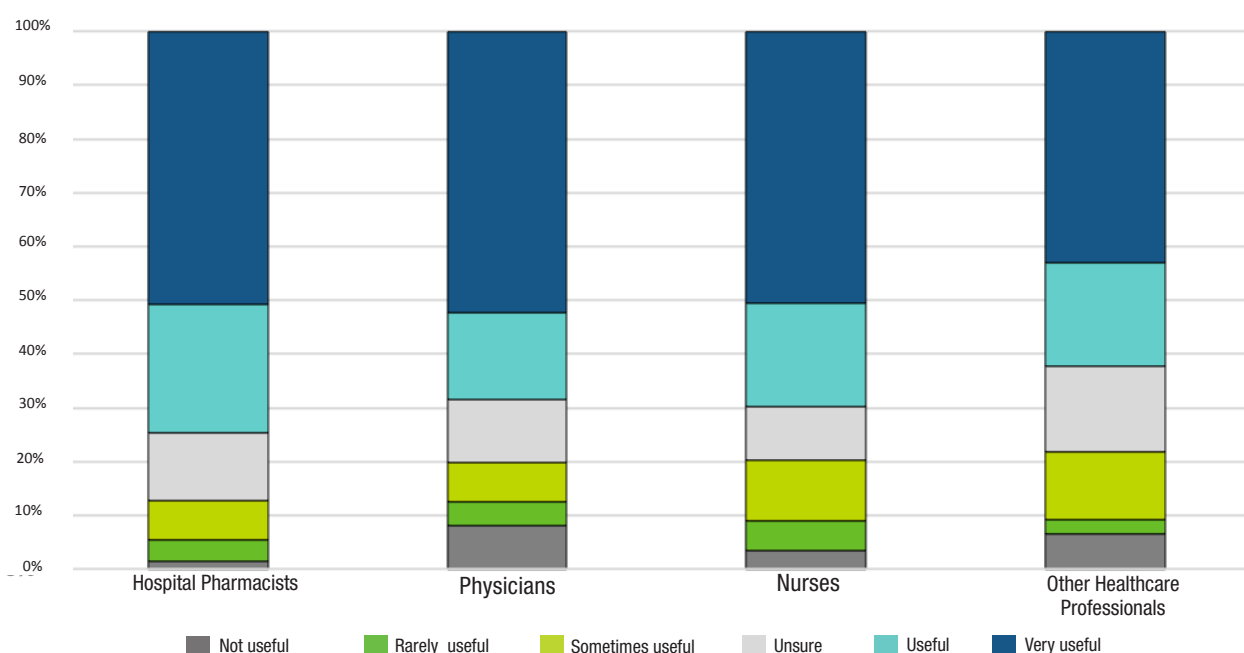


Figure 31 Percentage of responses by hospital pharmacists (N=1834) for question 20, physicians (N=136) for question 43, nurses (N=89) for question 64 and other healthcare professionals (N=151) for question 100 'How would you rank the usefulness of the following proposals? (0 = not useful | 5 = very useful)' proposal 'Conducting a European wide analysis of the causes to provide targeted solutions', grouped by profession.

The proposal 'conducting a European wide analysis of the causes to provide targeted solutions' was better received. With 51% of hospital pharmacists (N=930), 52% of physicians (N=71), 51% of nurses (N=45) and 43% of other healthcare professionals (N=65) giving this proposal the highest ranking of 5. Confirming that respondents prefer proposals which aim to tackle the causes of medicines shortages.

Strengthening collaboration between the European countries and the European institutions

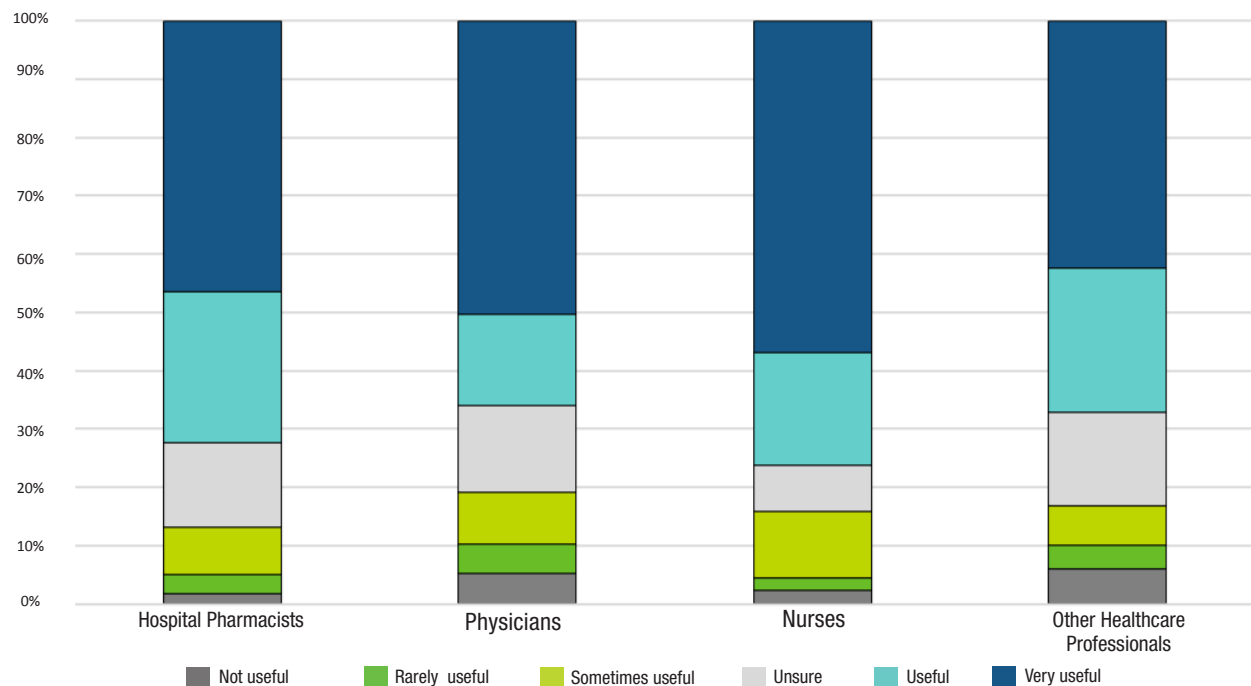


Figure 32 Percentage of responses by hospital pharmacists (N=1830) for question 20, physicians (N=135) for question 43, nurses (N=88) for question 64 and other healthcare professionals (N=149) for question 100 'How would you rank the usefulness of the following proposals? (0 = not useful | 5 = very useful)' proposal 'Strengthening collaboration between the European countries and the European institutions', grouped by profession.

The proposal of 'strengthening collaboration between the European countries and the European institutions' received slightly less positive feedback compared to the previous statement. With 46% of hospital pharmacists (N=848), 50% of physicians (N=68), 37% of nurses (N=50) and 47% of other healthcare professionals (N=63) giving the proposal a ranking of 5. However, very few respondents were entirely against this proposal, with other healthcare professionals being the group with the least favourable opinion on the proposal with 7% giving it a ranking of 0.

Mandating improved communication among all stakeholders (manufacturers, parallel traders, wholesalers and healthcare professionals)

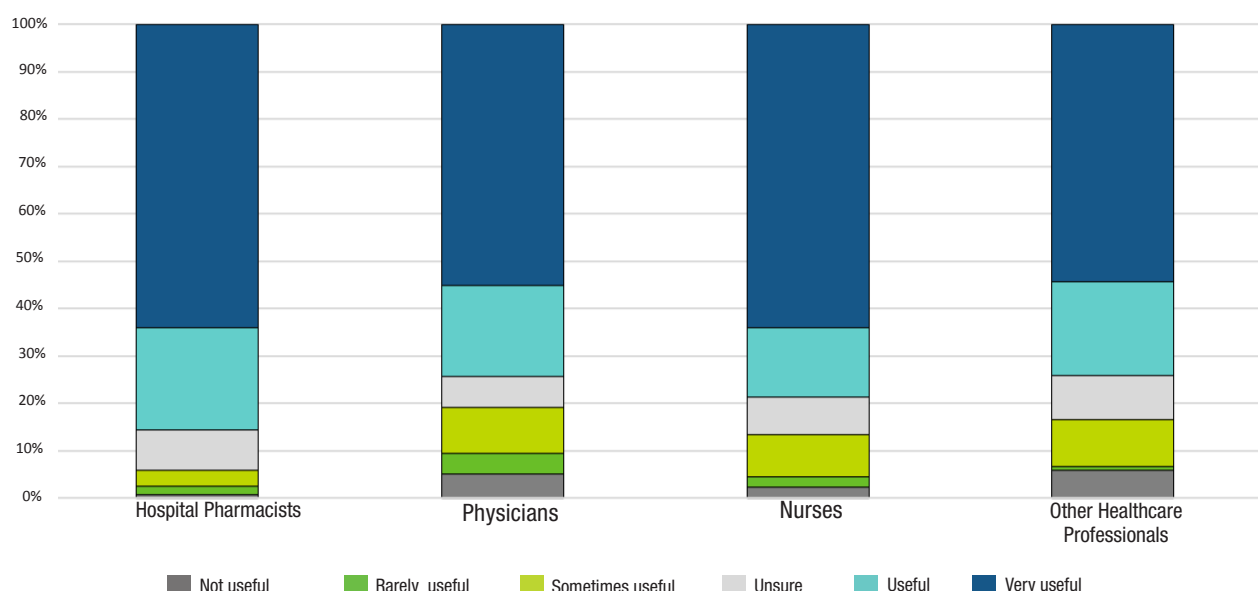


Figure 33 Percentage of responses by hospital pharmacists (N=1840) for question 20, physicians (N=136) for question 43, nurses (N=89) for question 64 and other healthcare professionals (N=151) for question 100 'How would you rank the usefulness of the following proposals? (0 = not useful | 5 = very useful)' proposal 'Mandating improved communication among all stakeholders (manufacturers, parallel traders, wholesalers and healthcare professionals)', grouped by profession.

The proposal ‘mandating improved communication among all stakeholders (manufacturers, parallel traders, wholesalers and healthcare professionals)’ received a very positive response. With 64% of hospital pharmacists (N=1176), 55% of physicians (N=75), 64% of nurses (N=57) and 54% of other healthcare professionals (N=82) giving the proposal a ranking of 5 (very useful).

Question 21 (hospital pharmacists) | question 44 (physicians) | question 65 (nurses) | question 101 (other healthcare professionals): Do you have another proposal that is currently being applied in your hospital/ your country that could help alleviate the problem of medicines shortages? (free text)

The 235 proposals submitted by hospital pharmacists in relation to question 21 were diverse. Suggestions ranged from improvements within the supply chain towards adjustments inside the hospital. Some of the most common themes which emerged from the free text responses of hospital pharmacists to question 21 are listed below:

Improving communication (46 responses):

“Improve communication at all levels to solve the problem of medicines shortages.” – Hospital pharmacist, Bosnia and Herzegovina

“The problem could be solved by improving communication at all levels and updating the development of the shortage on a day-to-day basis at all levels (national and hospital).” – Hospital pharmacist, Belgium

Obliging manufacturers to share information about medicines shortages in a timely manner (42 responses):

“Requiring manufacturers to do fast notifications via the on-line web application of the Medicine Agency within a maximum to 3-5 days.” – Hospital pharmacist, Czech Republic

“Real-time platform to track problems where healthcare institutions can also report that they are experiencing shortages. There should be tripartite management: regulator, manufacturer and end user (hospitals).” – Hospital pharmacist, Portugal

“Timely information and alternative therapeutic suggestions.” – Hospital pharmacist, Greece

Applying prudent tendering/procurement mechanisms that ensure that there is more than one supplier per medicine/API in Europe (36 responses):

“Legislative requirement to have an acceptable number of API producers and/ or manufacturers of required medicines.” – Hospital pharmacist, Germany

“Tendering procedures shall be constructed in a way that they inherently counteract shortages by maintaining a healthy market diversity and competition.” – Hospital pharmacist, Hungary

“Procurement should not only be focused on one supplier, but two alternative suppliers must be safeguarded from the outset.” – Hospital pharmacist, Portugal

Centralising the monitoring of shortages at national and/or European level and making sure that information on alternatives is being made available by the authorities (31 responses):

“Create a European database in which the data of the individual EU countries is shown.” – Hospital pharmacist, Italy

“I propose to connect the database of the Spanish Agency of Medicines (AEMPS) with the database of contingencies in the supply of the General Council of Pharmacists (CISMED), and that both open automatic alerts in the electronic prescription in both Primary Care of the Sistema Nacional de Salud, as in the hospital. CISMED detects supply problems before the total shortage alert goes off.” – Hospital pharmacist, Spain

Mandating manufactures to stop ‘just in time production’ and to increase stocks at national level, especially for those products that are essential and/or regularly out of stock (29 responses):

“Make it mandatory that pharmaceutical companies built up stock for at least 4 months of normal demand, the just in time delivering and producing should be forbidden.” – Hospital pharmacist, Germany

“Implementation of a risk-based stock quantity of medicines, that means augmentation of stock in case of medicines with a high risk of drug shortage” – Hospital pharmacist, Switzerland

“Oblige manufacturers to have sufficient stock to supply the countries concerned.” – Hospital pharmacist, France

Imposing/enforcing penalties for the non-communication of a medicine shortage (24 responses):

“I have no idea that is already being implemented in Germany, but only the obligation to deliver security with very high penalties for the industry will solve the problem.” – Hospital pharmacist, Germany

“Enforcement of penalties (depending on the reason for the supply shortage, the company’s annual turnover and the availability of alternatives.” – Hospital pharmacist, Austria

“We should have an estimated time when the product is available again. Anything too long should incur a fine from the authority.” – Hospital pharmacist, United Kingdom

Moving the production of active pharmaceutical ingredients (APIs)/medicines back to Europe (22 responses):

“This should be solved by increasing the number of drugs and API produced in well-developed countries in Europe.” – Hospital pharmacist, Norway

“To regain autonomy in the production of medicines in France or in Europe concentrating the manufacturing of APIs and medicines should be stopped.” – Hospital pharmacist, France

“More production in the EU instead of in Asia.” – Hospital pharmacist, the Netherlands

Fewer responses were received from the other professional groups. The majority of the 5 nurses that made suggestions, proposed to limit exports. For the 12 physicians that provided feedback, improving and centralising the reporting were the main suggestions. Out of the 26 other healthcare professionals that responded, the majority proposed stockpiling, local production/compounding and improving communication as solutions that could help tackle shortages.

FACTS



Risk assessments are still far from being routine for hospital pharmacists.



Shortages impacted patient care for more than half of the participating physicians.



Non-recognition of the replacement medicine is only a problem for nurses in 1/3 of the cases.



Other healthcare professionals identified oncology medicines as the medicine most frequently in shortage.

HIGHLIGHTS

More than half of all hospital pharmacists, physicians and other healthcare professionals that participated in the survey indicated that they had experienced shortages having an impact on patient care in their hospital. Delays in care or therapy were for all professionals the type of impact that was chosen the most.

MEDICINES SHORTAGES

PATIENT IMPACT



Question 22 (hospital pharmacists) | question 45 (physicians) | question 66 (nurses) | question 102 (other healthcare professionals): In which area of medicine does your hospital experience shortages most commonly? Please refer to the year 2019. Tick all that apply.

More than half of the hospital pharmacists (N=1158) that responded to this question selected antimicrobial agents as the area of medicine which is most commonly in short supply in their hospitals. With 47% of hospital pharmacists listing them in short supply, oncology medicines ranked second. Followed by anaesthetic agents which 38% of hospital pharmacists found most commonly in shortage.

This section investigated how medicines shortages affect patients. The four groups of professionals were asked about the medicines most frequently in shortage and how the problem impacted patients. Concerning patient care on prioritisation and admission rate increases caused by medicines shortages. Patients provided feedback on their experience with medicines shortages.

The findings for physicians, nurses and other healthcare professionals differed from those for hospital pharmacists. While physicians (43%) and nurses (31%) identified antimicrobial agents as the area of medicine that is most commonly in short supply, other healthcare professionals have observed more shortages for oncology medicines (39%). For them antimicrobial agents together with cardiovascular medicines (both 37%) ranked second. For 31% of physicians' preventive medicines, such as vaccines, were the type of medicines that is second most commonly in shortage. Nurses had identified analgesics and oncology medicines (both 29%) as areas of medicines that are frequently in shortage.

Hospital Pharmacists

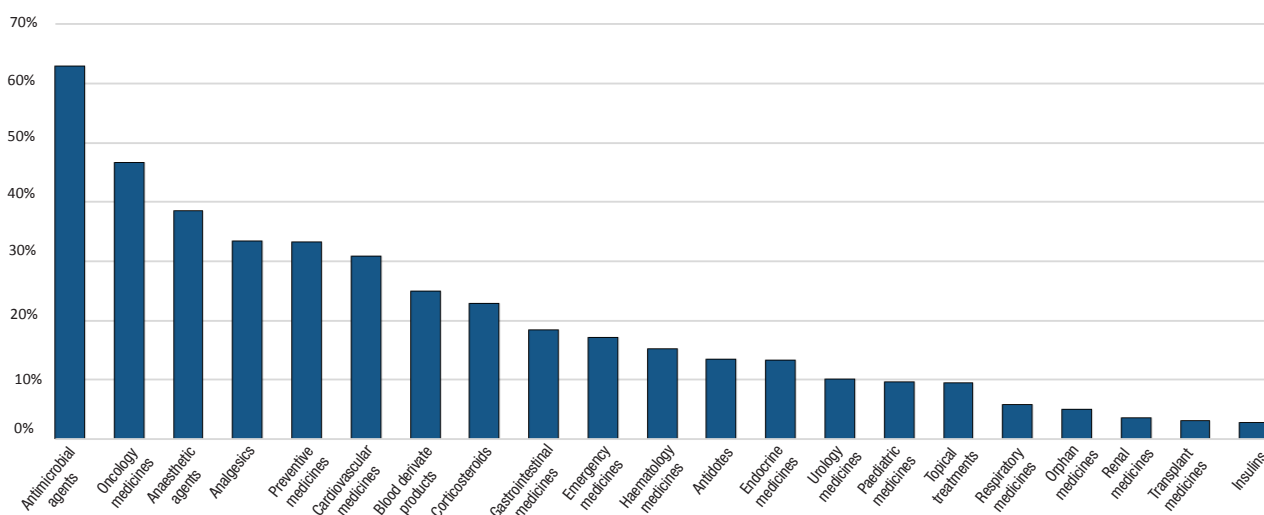


Figure 34 Percentage of responses by hospital pharmacists (N=1837) for question 22 'In which area of medicine does your hospital experience shortages most commonly? Please refer to the year 2019.' (Note that this was a tick all question)

Physicians

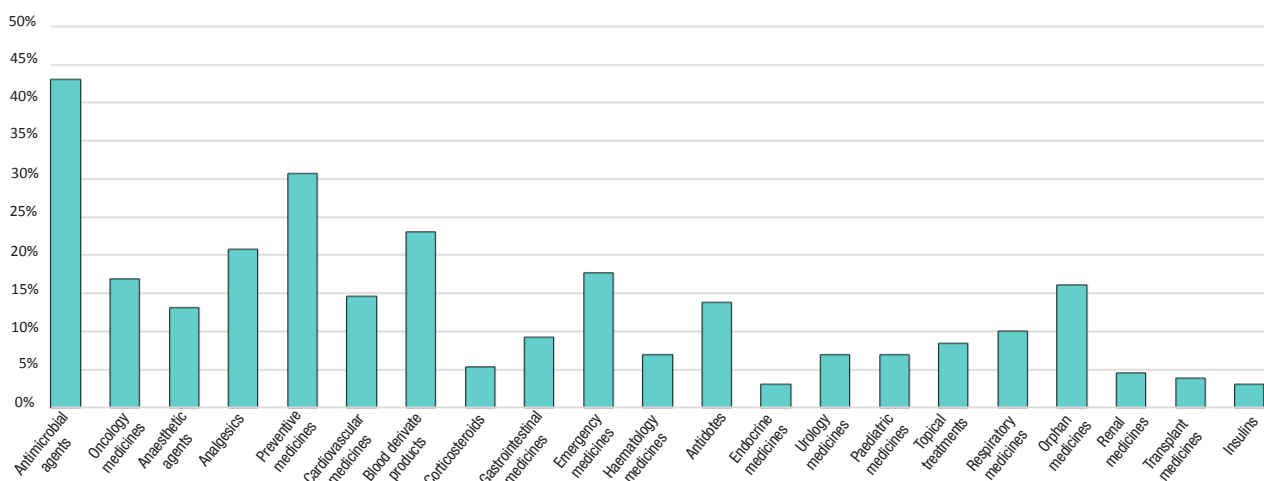


Figure 35 Percentage of responses by physicians (N=130) for question 45 'In which area of medicine does your hospital experience shortages most commonly? Please refer to the year 2019.' (Note that this was a tick all question)

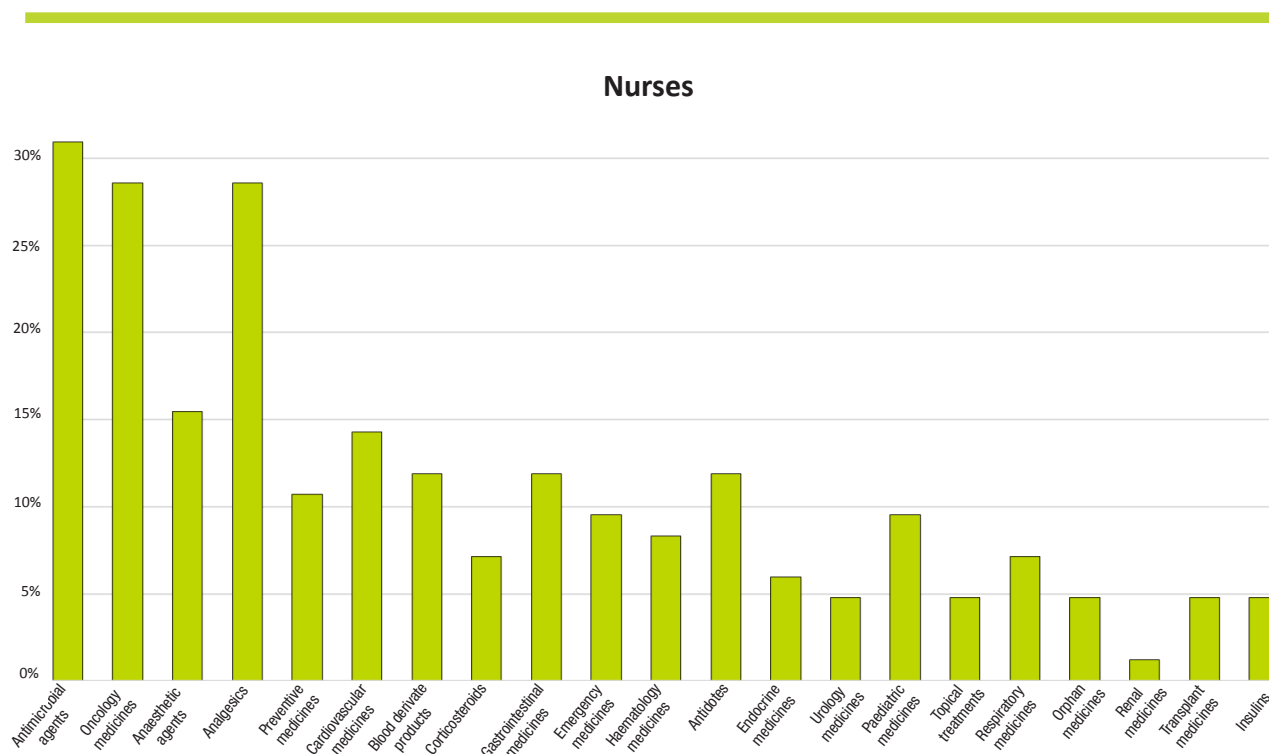


Figure 36 Percentage of responses by nurses (N=84) for question 66 'In which area of medicine does your hospital experience shortages most commonly? Please refer to the year 2019.' (Note that this was a tick all question)

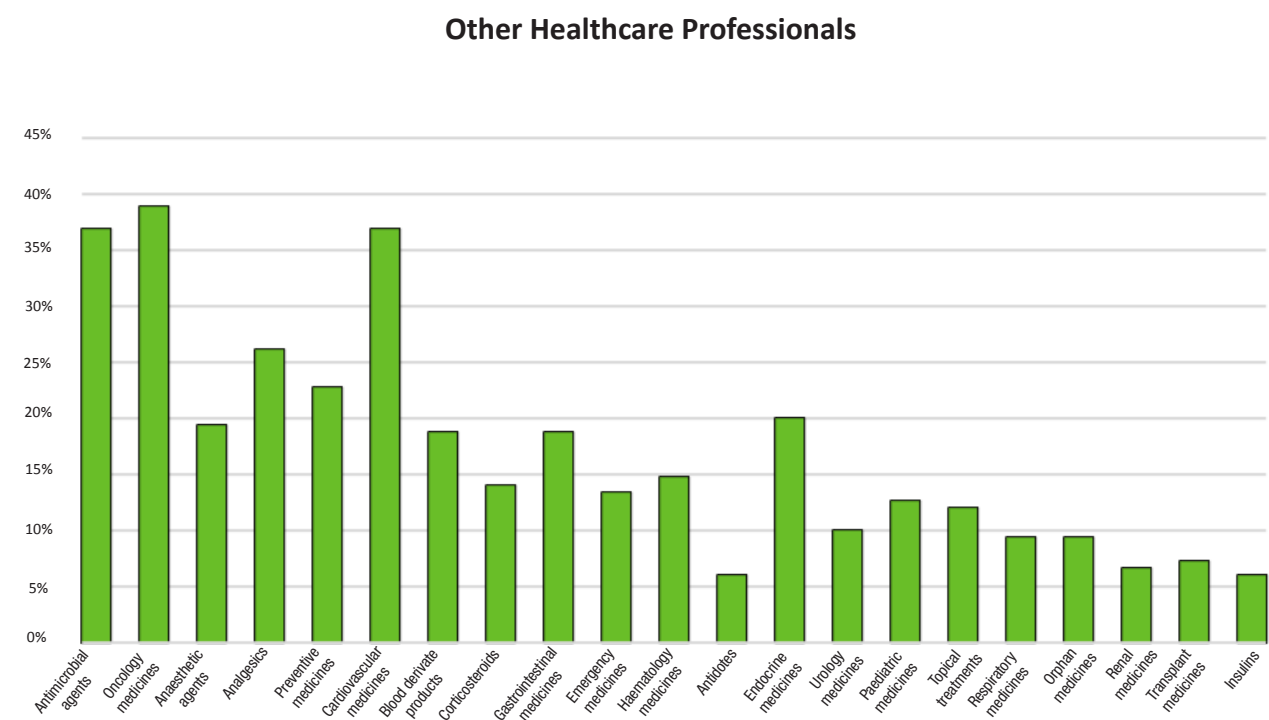


Figure 37 Percentage of responses by other healthcare professionals (N=149) for question 102 'In which area of medicine does your hospital experience shortages most commonly? Please refer to the year 2019.' (Note that this was a tick all question)

Compared to the 2018 Medicines Shortages Survey results, shortages for oncology medicines increased from 39% in 2018 to 47% in 2019, while those for anaesthetic agents remained stable with 39% in 2018 and 38% in 2019. After the increase to 77% in 2018 from 57% in 2014, the reports for antimicrobial agents decreased to 63%.

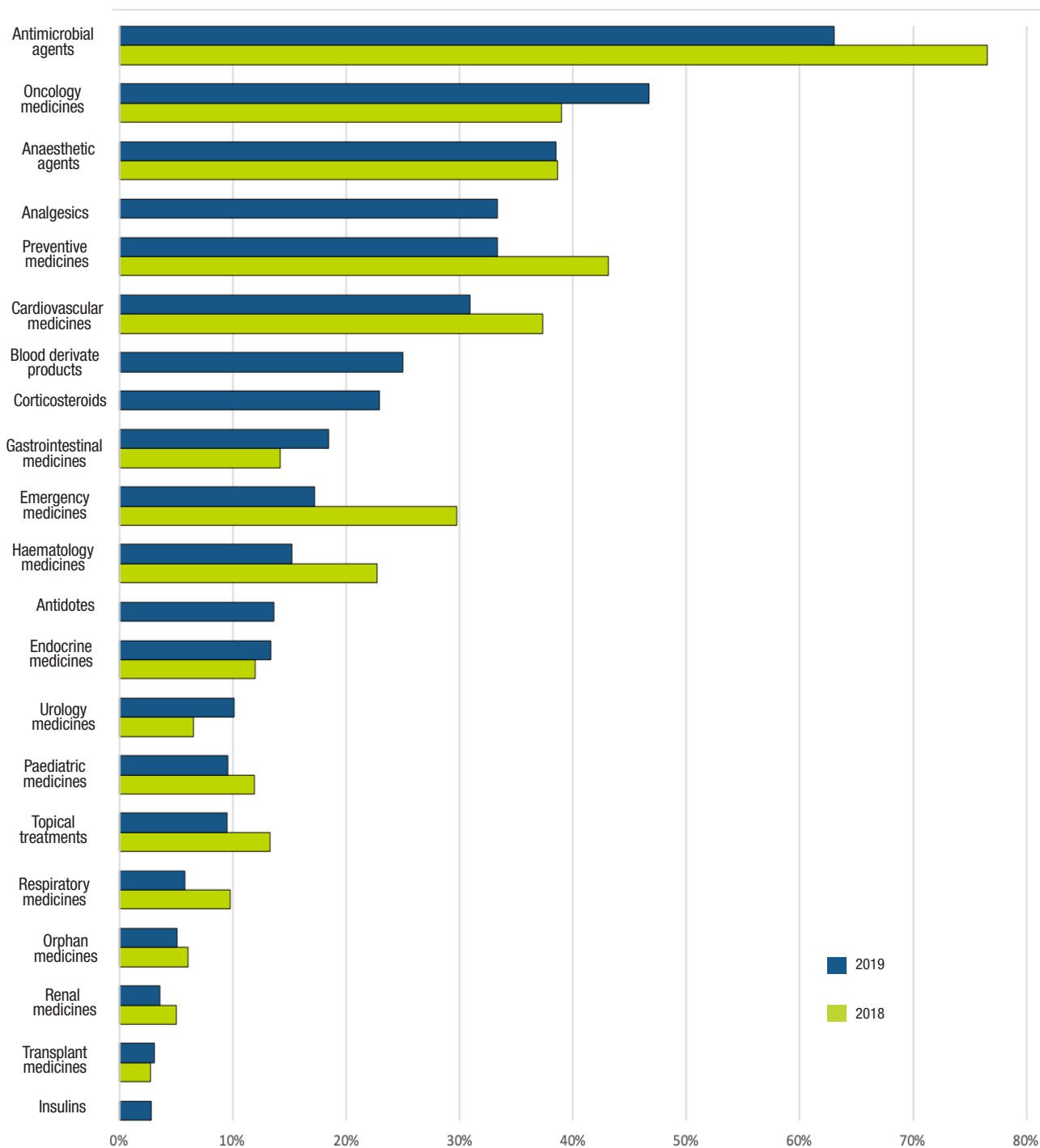


Figure 38 Percentage of responses by hospital pharmacists (N=1837) for question 22, 'In which area of medicine does your hospital experience shortages most commonly? Please refer to the year 2019.' compared to responses by hospital pharmacists (N=1348) to the question 'In which area of medicine does your hospital experience shortage most commonly?' from the 2018 Medicines Shortages Survey. (Note that this was a tick all question)

Question 23 (hospital pharmacists) | question 46 (physicians) | question 68 (nurses) | question 103 (other healthcare professionals): Are you aware if the shortage/the shortages you have experienced had an impact on patient care in your hospital?

More than half of the hospital pharmacists (63 % | N= 1153) that participated in the survey indicated that they had experienced shortages having an impact on patient care in their hospital. A similar response rate was observed for physicians (58% | N=75) and other healthcare professionals (52% | N=78). For nurses the picture was more homogenous with a third of the respondents either having experienced shortages that had a patient impact, having noted no impact or not being able to respond to the question.

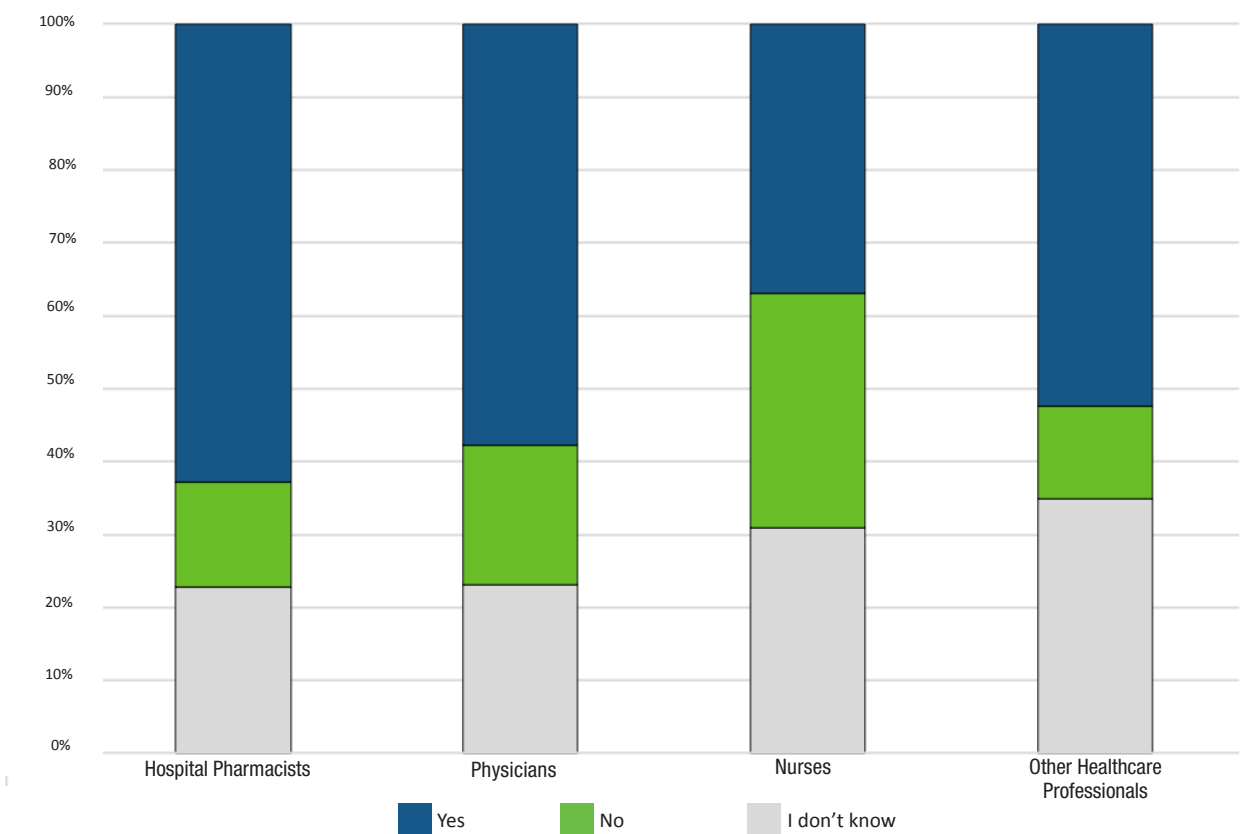


Figure 39 Percentage of responses by hospital pharmacists (N=1837) for question 23, physicians (N=130) for question 46, nurses (N=84) for question 68 and other healthcare professionals (N=149) for question 103 'Are you aware if the shortage/the shortages you have experienced had an impact on patient care in your hospital?', grouped by profession.

Question 24 (hospital pharmacists) | question 47 (physicians) | question 69 (nurses) | question 104 (other healthcare professionals): Please choose the type of impact medicines shortages had on patient care in your hospital. Tick all that apply.

Question 24 analysed the effect that medicines shortages had on patient care from the perspective of the four different groups of professionals that participated in the survey. Hospital pharmacists identified delays in care or therapy (42% | N=771), suboptimal treatment, as well as including inferior efficacy (28% | N=512) and cancellation of care (27% | N=488) as the main consequences of medicines shortages in the hospitals that they practice in. Physicians and other healthcare professionals named the same consequences as their top three, with physicians providing 47 (delays in care or therapy), 44 (suboptimal treatment) and 33 (cancellation of care) responses and other healthcare professionals providing 56 (delays in care or therapy), 37 (suboptimal treatment) and 32 (cancellation of care) responses. For nurses, the increased length of stay in the hospital was the second most common cause identified (19% | N=16), which ranked fourth for hospital pharmacists (18% | N=326) and physicians (23% | N=30) and fifth for other healthcare professionals (12% | N=18).

Readmission due to treatment failure received the third lowest amount of responses from hospital pharmacists (5% | N=88), while it ranked in the top five for physicians and nurses. Death and adverse events/greater toxicity were named as the least common consequences by all four groups of professionals.

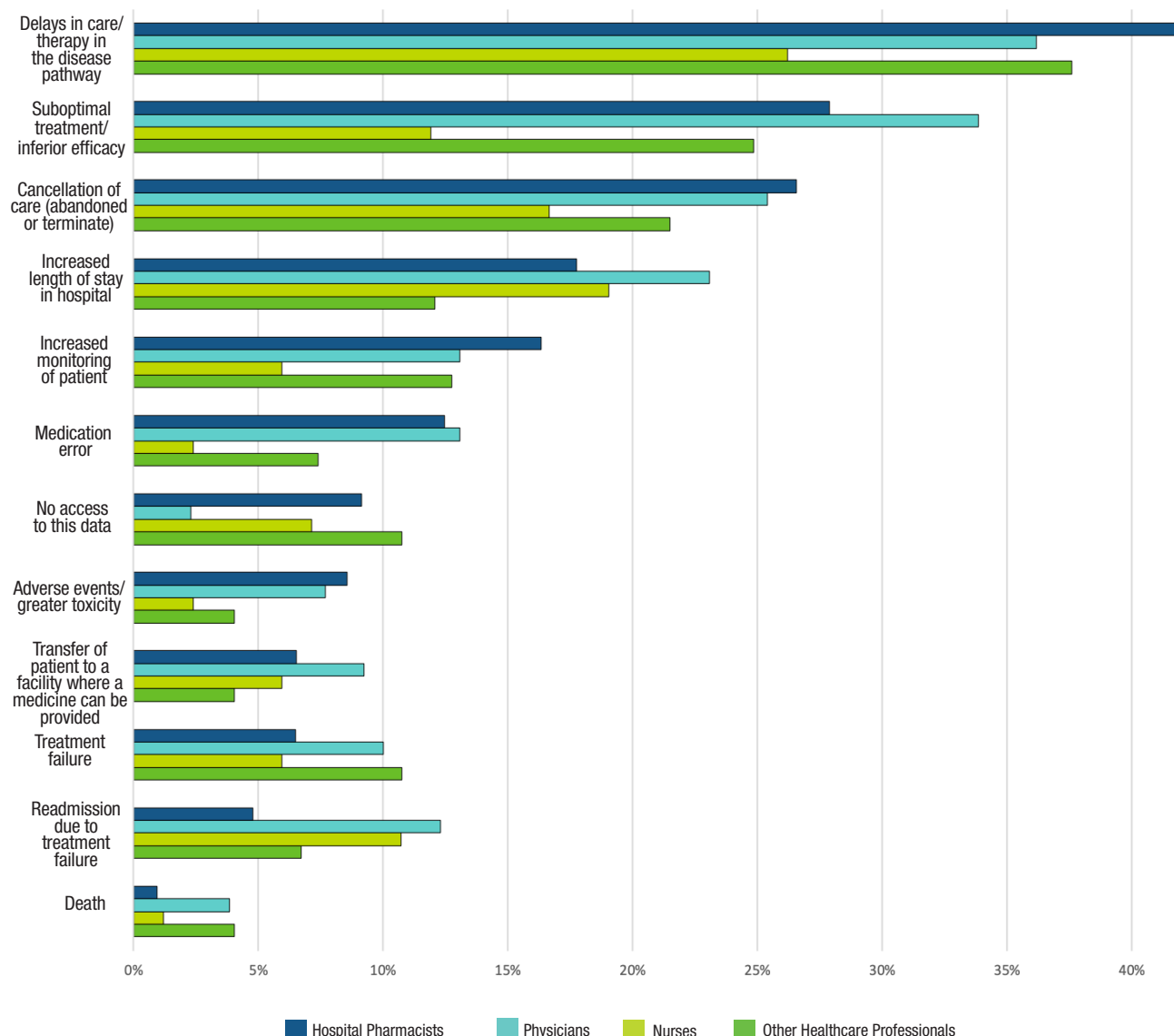


Figure 40 Percentage of responses by hospital pharmacists (N=1837) for question 24, physicians (N=130) for question 47, nurses (N=84) for question 69 and other healthcare professionals (N=149) for question 104 'Please choose the type of impact medicines shortages had on patient care in your hospital', grouped by profession. (Note that this was a tick all question)

A similar question was asked to hospital pharmacists that answered to the 2018 Medicines Shortages Survey. The 946 hospital pharmacists that responded to the 2018 Medicines Shortages survey, also included delays of care or therapy (59% | N=555) and cancellation of care (31% | N=297) among the main consequences of a medicine shortage that have had an impact on patient welfare. Suboptimal treatment ranked fourth (25% | N=239), while medication errors (25% | N=241) were listed as the third most common problem. The latter ranked sixth in the 2019 Medicines Shortages Survey, with 12% (N=229) of hospital pharmacists naming medication errors as a consequence that medicines shortages had on patient care in their hospital.

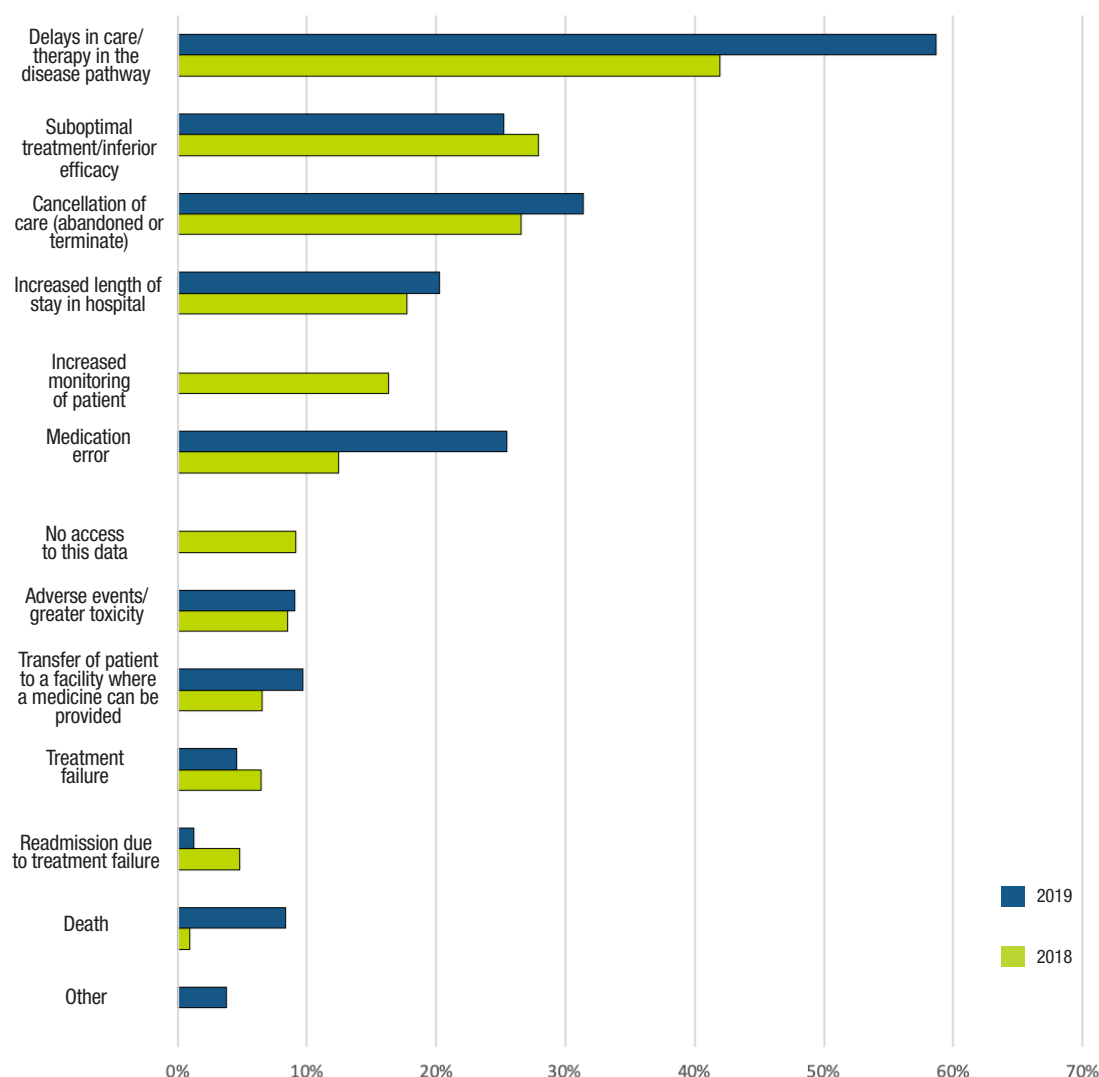


Figure 41 Percentage of responses by hospital pharmacists (N=1837) for question 24, 'Please choose the type of impact medicines shortages had on patient care in your hospital' compared to responses by hospital pharmacists (N=1348) to the question 'Please provide any relevant examples from your hospital over the past year of the impact medicines shortages have had on patient safety welfare.' from the 2018 Medicines Shortages Survey. (Note that this was a tick all question)

Question 25 (hospital pharmacists) | question 48 (physicians) | question 70 (nurses) | question 105 (other healthcare professionals): Were you in a position to prioritise provision of medicines to the patients based on their disease/clinical status when it comes to medical treatment affected by shortages?

For medical treatment affected by medicines shortages, half of the hospital pharmacists (50% | N= 910) that participated in the survey were able to prioritise the provision of medicines to patients based on their disease/clinical status in 2019. Nurses were able to prioritise in 58% of the cases, while both physicians and other healthcare professionals could do so in only 41% of the cases.

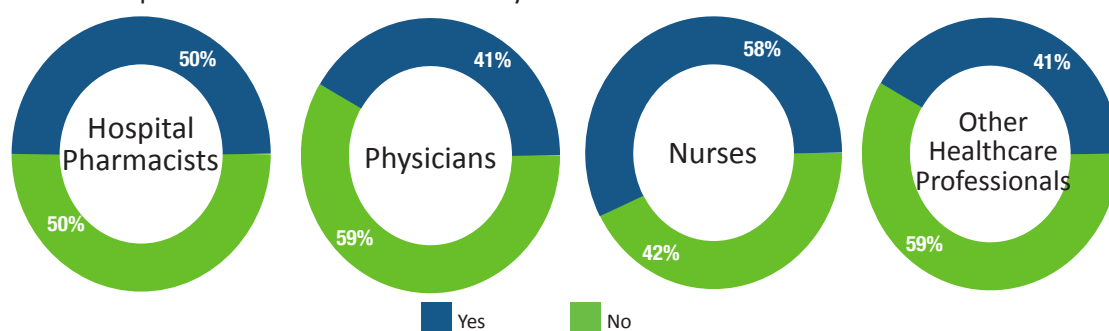
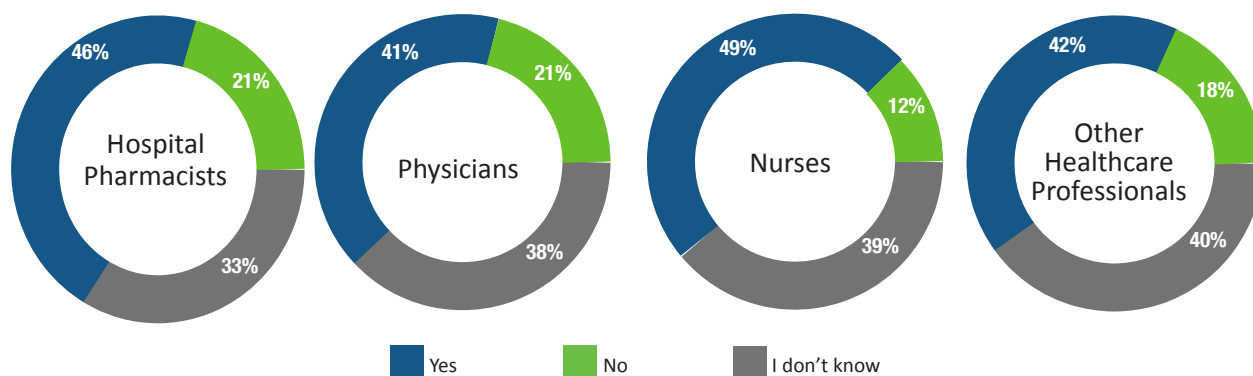


Figure 42, 43, 44 and 45 Percentage of responses by hospital pharmacists (N=1825) for question 25, physicians (N=128) for question 48, nurses (N=84) for question 70 and other healthcare professionals (N=147) for question 105 'Were you in a position to prioritise provision of medicines to the patients based on their disease/clinical status when it comes to medical treatment affected by shortages?', grouped by profession.

Question 26 (hospital pharmacists) | question 49 (physicians) | question 71 (nurses) | question 106 (other healthcare professionals): Did this prioritisation affect a larger group of patients who might benefit from the treatment?

Those that responded positively to the previous question were asked if the prioritisation affected a larger group of patients. The responses by the different professionals that participated in the survey were mixed. Out of the 910 hospital pharmacists, 3 choose not to answer the question while 46% indicated that prioritisation affected a larger group of patients. The remaining 54% of respondents either could not provide feedback (33%) or confirmed that only a small group of patients was affected (21%). Similar to the previous question the responses for physicians and other healthcare professionals were closely aligned. Prioritisation was possible for both of these groups in 41% (physicians) and 42% (other healthcare professionals) of the cases. Nurses reported that almost half (49%) of the cases affected a larger patient group.

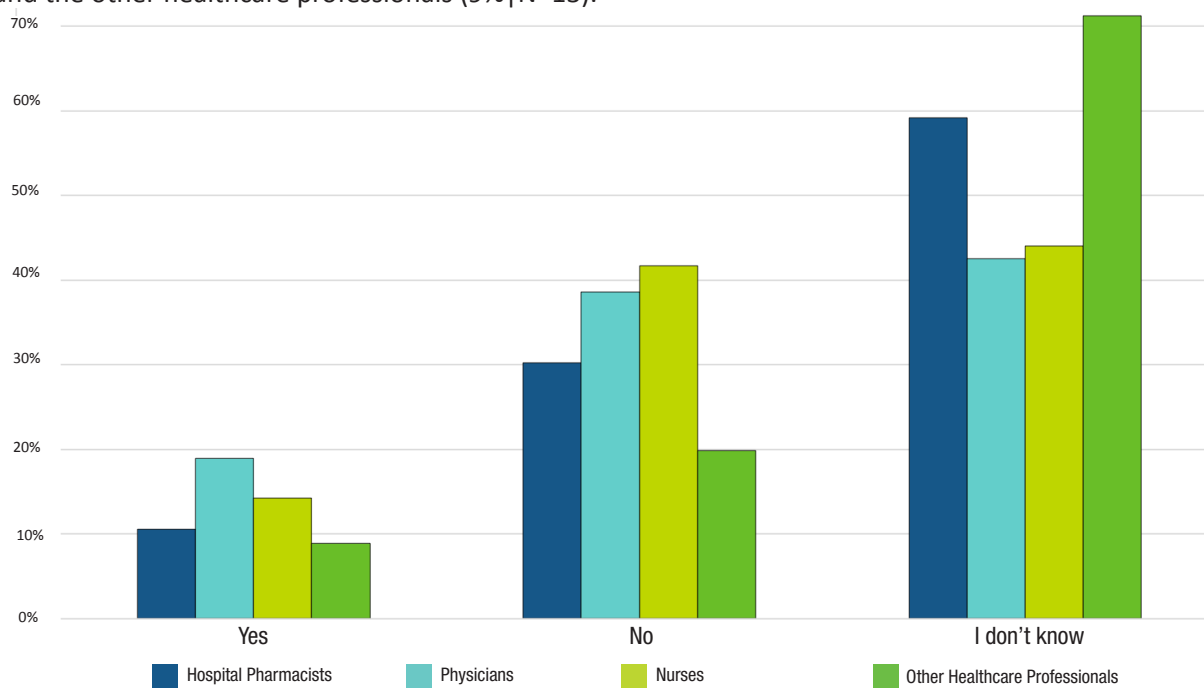


Figures 46, 47, 48 and 49 Percentage of responses by hospital pharmacists (N=910) for question 26, physicians (N=53) for question 49, nurses (N=49) for question 71 and other healthcare professionals (N=60) for question 106 'Did this prioritisation affect a larger group of patients who might benefit from the treatment?'; grouped by profession.

Question 27 (hospital pharmacists) | question 50 (physicians) | question 72 (nurses) | question 107 (other healthcare professionals): Did you experience higher admission rates at your hospital as a consequence of shortages?

More than half of the hospital pharmacists and other healthcare professionals stated that they didn't know whether they had experienced higher admission rates at their hospital as a consequence of shortages. With 59% (N=1076) of hospital pharmacists and 71% (N=104) of other healthcare professionals choosing that answer. In comparison, physicians and nurses were less likely to say that they didn't know with only 43% (N=54) of physicians and 44% (N=37) of nurses answering so.

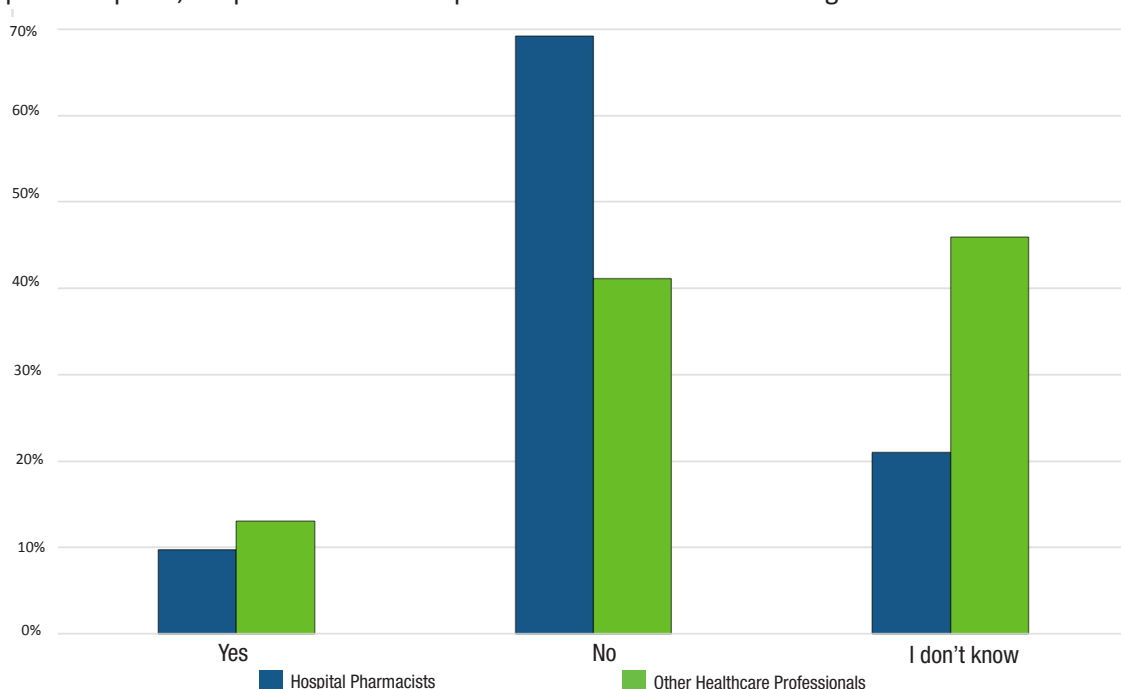
The graph shows that the highest percentage of health professionals that didn't experience higher admission rates were the nurses (42% | N=35) and physicians (39% | N=49). Hospitals pharmacist presented a lower percentage, (30% | N=549) compared to other healthcare professionals (20% | N=29). 19% (N=24) of physicians and 14% (N=12) of nurses answered yes, followed by the hospital pharmacists, (11% | N=192) and the other healthcare professionals (9% | N=13).



Figures 50 Percentage of the responses by hospital pharmacists (N=1817) for question 27, physicians (N=127) for question 50, nurses (N=82) for question 72 and other healthcare professionals (N=145) for question 107 'Did you experience higher admission rates at your hospital as a consequence of shortages?', grouped by profession.

Question 28 (hospital pharmacists) | question 108 (other healthcare professionals): Are you carrying out risk assessments in case of a shortage?

Figure 51 shows that only 10% (N=177) of hospital pharmacists and 13% (N=19) of other healthcare professionals are carrying out risk assessments in case of a shortage. 69% (N=1258) of hospital pharmacists and 41% (N=60) of other healthcare professionals are not carrying out risk assessments. 21% (N=382) and 46% (N=67) of hospital pharmacists and other healthcare professionals answered that they didn't know. This demonstrates that the conducting risk assessments in case of a shortage is not widely done in European hospitals, despite the increased prevalence of medicines shortages.



Figures 51 Percentage of the responses by hospital pharmacists (N=1817) for question 28 and the other healthcare professionals (N=146) for question 108 'Are you carrying out risk assessments in case of a shortage?', grouped by profession.

Question 29 (hospital pharmacists) | question 109 (other healthcare professionals): If yes, which tool do you use?

Hospital pharmacists and other healthcare professionals had the option to give a free text response to specify what tool they use if they answered 'yes' to question 26. There were 123 free text responses and the answers provided focused not only on the tools but also on the strategies used by their hospitals. The following tools were provided in the answers: In House, Datix, FMEA, AMDEC, Excel, SOP, Brexit reporting tool, ad hoc risk assessment and email. Several respondents stated that their hospital used national agencies in case of risk assessment such as NHS England and HPRA.

Below are some of the strategies shared on how hospitals tackle medicines shortages. The strategies focus on analysing the information from previous years, having interprofessional working groups on shortages, the development of their own tool and searching for possible replacements to the medicine experiencing shortages.

"Internal records about shortages in my hospital's pharmacy service." – Hospital pharmacist, Spain

"Market analyses including statistics on need and use of products by different providers." – Hospital pharmacist, Switzerland

"Professional meetings and shared thinking for access to therapy and replacement with complementary therapy." – Hospital pharmacist, North Macedonia

"We have developed a risk assessment and monitoring application integrated to the hospital IT system" – Hospital pharmacist, Greece

“In-house developed in conjunction with our internal SOPs.” – Other healthcare professional, United Kingdom

“Direct communication through regular meetings at hospital wards.” – Hospital pharmacist, Bosnia and Herzegovina

“For the shortage of a parenteral nutrition product (sulmetin) we assessed how it affected service management, clinic and service economy. We collected the data of patients administered with the drug and the alternatives and evaluated the clinical part with the statistical program SPSS. The rest was with unit price data and excels that we exported from the nutrition program.” – Hospital pharmacist, Spain

Question 67 (nurses): Have medicines shortages in your hospital led to non-administration/ delays of administration due to non-recognition of the replacement medicine?

Nurses were asked whether medicines shortages had affected the administration of medicines in their hospital. Nurses are the healthcare professionals responsible for the administration of the drugs, as they are the ones in contact with the patient on the moment of administration. 83 nurses responded to this question, with 27% (N=22) of them reporting that shortages had led to non-administration/delays of administration due to non-recognition of the replacement medicine. 42% (N=35) of respondents stated that medicines shortages had not affected the administration of treatment and 31% (N=26) answered that they didn't know.

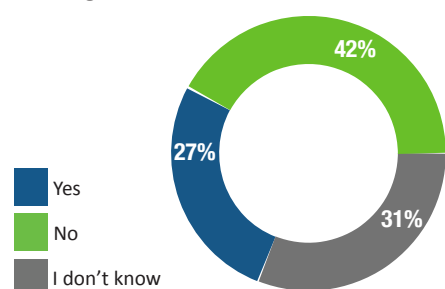
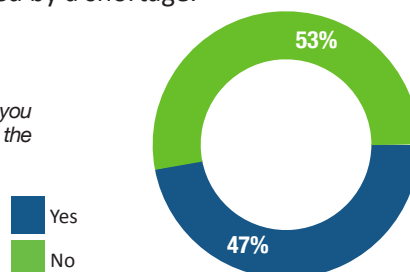


Figure 52 Percentage of responses by nurses (N=83) for question 67 'Have medicines shortages in your hospital led to non-administration/ delays of administration due to non-recognition of the replacement medicine?'.

Question 74 (patients): Did you or one of your family members during treatment at a hospital ever experience the shortage of medicines?

Patients were given their own set of questions beginning with question 74. This question had 357 respondents, with 47% (N=169) of them reporting that they had experienced medicines shortages to their own person or by a family member. 53% (N=188) of the patients that answered to this question said that neither they nor a member of their family had been affected by a shortage.

Figure 53 Percentage of responses by patients (N=357) for question 74 'Did you or one of your family members during treatment at a hospital ever experience the shortage of medicines?'.



Question 75 (patients): Did you receive information about the reasons of the medicines shortage from your hospital pharmacist/nurse/physician or any other healthcare professional working in the hospital?

This question was only answered by those patients who had responded 'yes' to question 74. This question had 160 responses from patients, with 46% (N=74) answering positively when asked if they had been informed of the reasons behind the shortage of their medicine, while 54% (N=86) gave a negative answer.

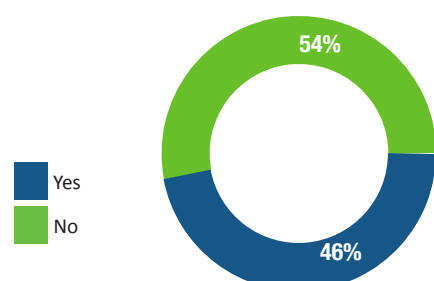


Figure 54 Percentage of responses by patients (N=160) for question 75 'Did you receive information about the reasons of the medicines shortage from your hospital pharmacist/nurse/physician or any other healthcare professional working in the hospital?'.

Question 76 (patients): What solution was offered to you?

This question was only answered by those patients that responded 'yes' to the question 74. 158 responses were received from patients of which 40% (N=63) reported that they were offered a substitution as a solution for a medicines shortage, 13% (N=20) were advised to miss one dose and 3% (N=5) were told to take a lower dose. 9% (N=15) didn't know the answer to this question and 35% (N=55) of patients chose "Other" meaning that the solutions offered was not listed as one of the options.

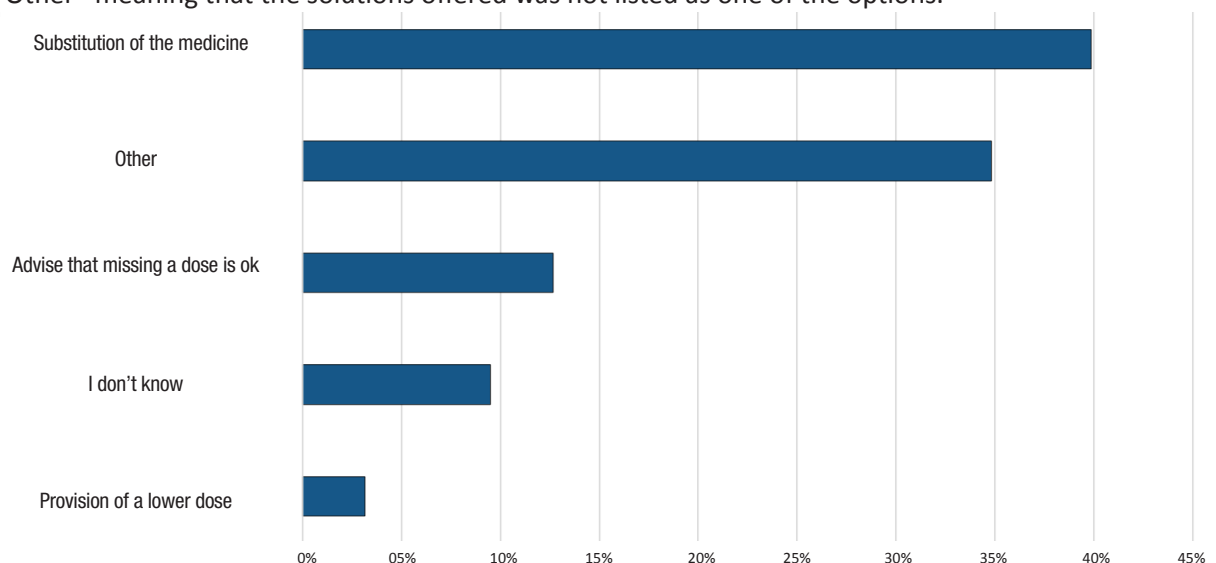


Figure 55 Percentage of responses by patients (N=158) to question 76 'What solution was offered to you?'.

Three themes emerged from the free text responses included by patients that selected the option 'other'. These included taking medicines from home to the hospital, buying medicines and treatment delay. A common answer provided by the Romanian patient was to purchase the medicine outside of the country. Some of the 52 free text responses related to the main themes are displayed below:

Patients bringing the medicines from home to the hospital :

"Had to wait a day until my wife brought the drug from home." – Patient, United Kingdom

"Taking my own treatment with me to the hospital." – Patient, France

"Asked me to bring my own treatment for my 1 month hospital stay." – Patient, France

Patients buying the medicines themselves:

"Independent procurement abroad." – Patient, Serbia

"Purchase on own account." – Patient, Romania

"Purchase of the drug outside the hospital." – Patient, Romania

Treatment delay:

"Non-administration of drug treatment and monitoring at three months." – Patient, France.

In some cases, there was no solution provided, the patients were just informed that the medicines were not available in the country. There were patients that were advised to take more pills from a lower dose. Viewing this data it is possible to see that the patients are not always receiving proper solutions in case of shortages.

Question 77 (patients): Do you feel that the problem was correctly handled?

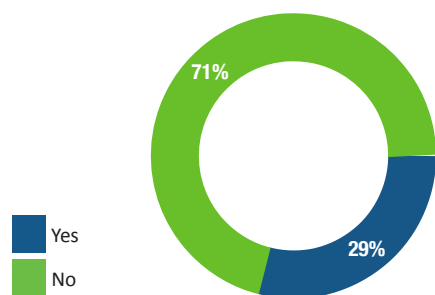


Figure 56 Percentage of responses by patients (N=158) for question 77 'Do you feel that the problem was correctly handled?'.

This question was only answered by those patients which had responded 'yes' to question 75 which inquired if patients received information about the reasons of the medicines shortage from their hospital pharmacist, nurse, physician or any other healthcare professional working in the hospital. There were 158 responses to this question, with only 29% (N=46) of respondents stating that they felt that the problem had been correctly handled. In contrast, 71% (N=112) of the patients that answered to this question stated that they did not feel that their problem was correctly handled.

Question 78 (patients): Since you felt that the problem was not correctly handled, please tell us what went wrong and should be improved.

There were 71 free text responses to this question. Patients were asked to give recommendations on how to improve the solutions offered to patients and their families in the event of a medicine shortage. In general, the patients used this opportunity to share the issues that they had experienced with medicines shortages. Despite not being within the scope of the question, one Slovakian patient also commented on the practice of parallel trade, while another urged to stop the sale of overpriced, ineffective drugs at all costs. Some common themes which emerged from the responses are listed below:

Reason behind not receiving the prescribed treatment:

"I should have been given a reason why there was a shortage and that reason should have come from a pharmacist and no one else." – Patient, United Kingdom

"They should have told me about the problem and I would have tried to find the drug from a drugstore." – Patient, Greece

"Lack of information. Impression of abandonment. Long and fruitless wait." – Patient, France

"After 4 days, I was told that my medicines were ordered but that no information on the delivery date could be given and I found myself without medicines." – Patient, France

Substitution medicine had more adverse effects or was less effective:

"The medicine suggested as a substitute was less effective than the originally proposed treatment." – Patient, Greece

"The alternatives offered did not have the same effect as the original drug. The problems worsened." – Patient, Romania

"The drug replacement did not work for me as the original medicine should improve the health system should improve because I think those doctors were not responsible for the fact that the medicine was not available in pharmacies." – Patient, Slovakia

Solutions or replacements were not found/were not possible or no solution was offered:

"They didn't have several of the medications I needed and they just said they were sorry that they didn't stock those items. No substitutes were offered and they did nothing to get them." – Patient, United Kingdom

"I did not receive the medicine resulting in deregulation of end-stage heart failure." – Patient, Greece

“No solution untreated for 3 months and I needed to be operated on again.” – Patient, France

Advised to bring or buy their own medicines to the hospital:

“Hospital’s should not have to ask patients to bring in their own tablets.” – Patient, United Kingdom

“Medications should exist in the hospital, the patient’s family has enough worries, should not run through pharmacies.” – Patient, Romania

“A common drug should not be missing from the hospital pharmacy, the patient should not be sent to buy the necessary medicines.” – Patient Romania

Bigger stocks or a better planning from the hospital:

“ If there was a centralized list of how many doses there are and how many patients they need then the problem would not have appeared.” – Patient, Romania

“Given that the drug was inaccessible to immunotherapy - targets (erlotinib), its pausing led to a certain degree of exacerbation of malignant changes and the progression of the tumour, which was stably kept under control during therapy. It is necessary to develop a better organization and prevent it from happening.” – Patient, Serbia

“ Recurrent lack of common and less common medicines, incorrect / inadequate information from pharmacies, avoiding the emergence drug ordering system – Patient, Slovakia

Question 79 (patients): Do you believe that the shortage/the shortages that you or one of your family members experienced impact your/the family members’ care in the hospital?

This question had 104 responses from patients, with 65% (N=68) of them reporting that the care provided at the hospital was affected by the medicines shortages, while 35% (N=36) stated that they did believe that the shortage had an impact on the care provided in the hospital.

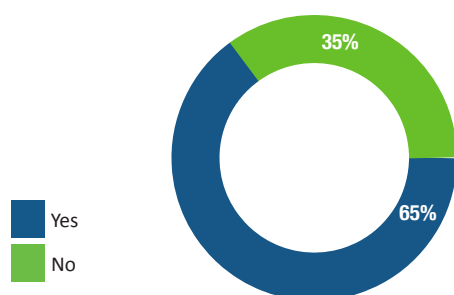


Figure 57 Percentage of responses by patients (N=104) for question 79 ‘Do you believe that the shortage/the shortages that you or one of your family members experienced impact your/the family members’ care in the hospital?’.

Question 80 (patients): Please choose the type of impact medicines shortages had on your care/the care of your family member. Tick all that apply.

The impact resulting from medicines shortages to the patients are shown in Figure 58, which highlights the magnitude of this problem. 30% (N=48) of the respondents have seen care delayed as a consequence of medicine shortages, 12% (N=20) experienced a failure of treatment, 11% (N=18) had an increased length of stay in the hospital. 10% (16) of the patients had their treatment cancelled while 8% (N=13) experienced adverse events or greater toxicity. Readmission due to treatment failure and increased monitoring was presented by 6% (N=8) of the population, in addition, 3% (N=5) of the patients were transferred to a facility where the medicine could be provided. 2% (N=4) of respondents answered that they knew of instances where death had occurred as a result of medicines shortages. 11% (N=17) stated that they didn't know what type of impact the medicines shortage had on their treatment.

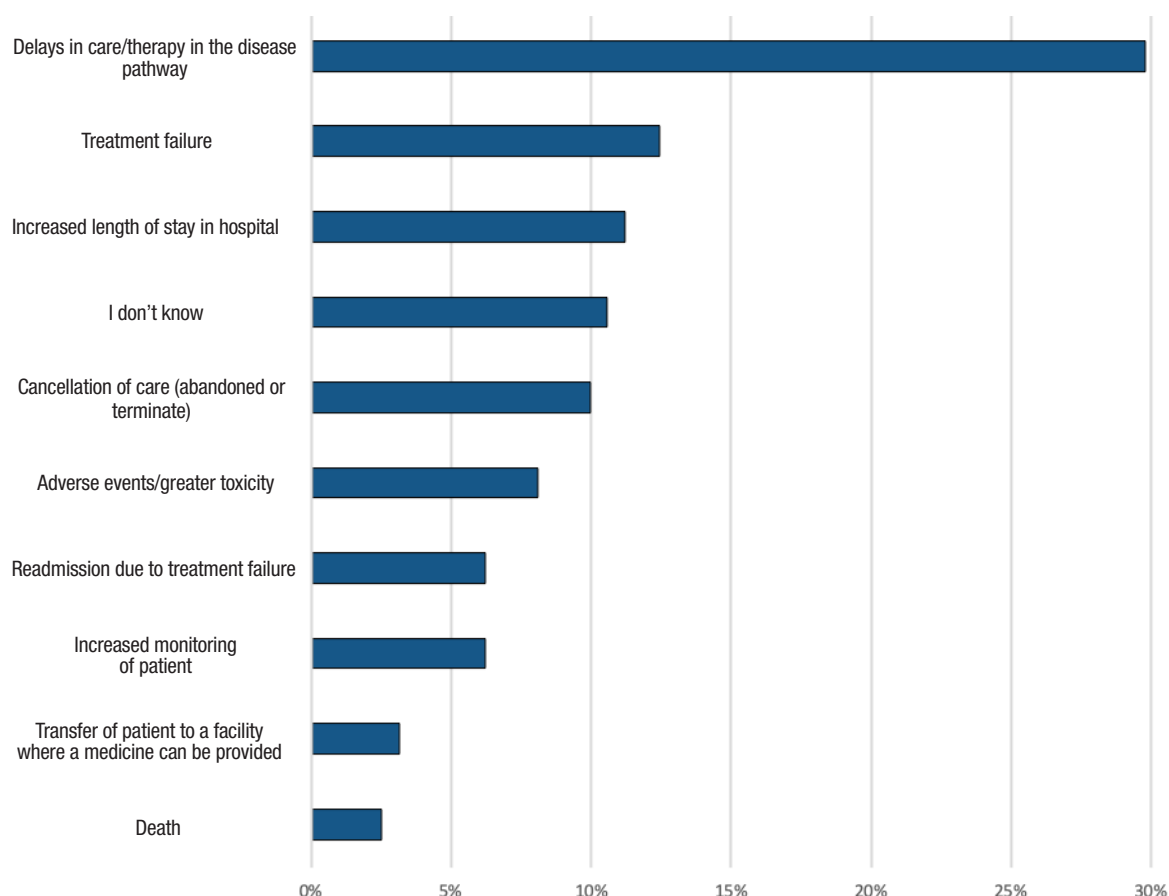


Figure 58 Percentage of responses by patients (N=161) for question 80 'Please choose the type of impact medicines shortages had on your care/the care of your family member.' (Note that this was a tick all question).

The table below gives a summary the medicines shortages reporting websites named by respondents in relation to question 12 (hospital pharmacists), question 37 (physicians), question 57 (nurses) and question 92 (other healthcare professionals).

Country	Website of the reporting system	Feedback provided in relation to the reporting system
Albania		<i>No information provided.</i>
Andorra		<i>No information provided.</i>
Austria	https://www.basg.gv.at	The BASG (Bundesamt für Sicherheit im Gesundheitswesen Austrian Federal Office for Safety in Health Care) has made available information that is shared by pharmaceutical companies regarding shortages of their products, managed by the public health institution.
Belgium	www.bcfi.be	An overview of out of stock medication is available via the website the Belgian Centre for Pharmacotherapeutic Information, the Federal Agency for Medicines and Health Products and the Belgian Pharmacy Association.
	www.afmps.be	
	www.apb.be	The Pharmastatus website of the Federal Agency for Medicines and Health Products contains an overview of the human and veterinary medicines in shortage. It is possible to search by medicine.
	https://pharmastatus.be	
Bosnia and Herzegovina	http://www.almbih.gov.ba/	Manufacturers or wholesalers inform the Medicine Agency which provides information on their website.
Bulgaria	https://www.bda.bg/	-
Croatia	http://www.halmed.hr/	There is a list available for download at HALMED (Agency for Medicinal Products and Medical Devices of Croatia). There are no proposed solutions for therapy substitution. It is unclear how often this list is being updated.
Cyprus	https://www.gesy.org.cy/	The information on the website of the General Health System is not often used by hospital pharmacists.
Czech Republic	http://www.sukl.cz/	The State Institute for Drug Control (SUKL) makes available information about shortages and (if available) about reimbursement.
	http://www.mzcr.cz/dokumenty/seznam-lecivych-pripavkujejichz-distribucio-zahranici-maji-distributori-povi_14530_883_1.html	An Excel list of the Ministry of Health is providing the information on reported shortages.
	https://www.lekarnici.cz/Pro-cleny/Aktualni-temata-(1)/Nedostatkov-LP.aspx	-

Country	Website of the reporting system	Feedback provided in relation to the reporting system
Denmark	<i>No information provided.</i>	
Estonia	https://ravimiamet.ee/#tab_3-tab	The Agency of Medicines of the Republic of Estonian has a list for shortages of medicines. It is updated with new information every day.
Finland	https://www.fimea.fi/web/en/databases_and_registers/shortages	The Finnish Medicine Agency (FIMEA) has a website where medicine companies can inform about common shortages and proposed solutions, and where pharmacies can get the information.
France	https://ansm.sante.fr/	The National Agency for the Safety of Medicines and Health Products (ANSM) shares information on shortages and sometimes also on replacement possibilities. The system is not very efficient because shortage information is not given early enough (sometimes several weeks without news).
Germany	https://www.abda.de/	The German Hospital Pharmacy Organisation shares information on shortages.
	https://www.bfarm.de/	Companies report shortages. These are listed by the Federal Institute for Drugs and Medical Devices. The list is often not up to date, and not all shortages are included since notification is not mandatory and there are different limitations for the inclusion of a shortage in the list.
developed a risk assessment and monitoring application	https://www.eof.gr/web/guest/shortage	There is an on-line reporting system for medicine shortages on the website of the National Organisation for Medicines (EOF). The tool is supervised by EOF and hospital pharmacists can report any relevant problem. EOF provides quick responses by e-mail or via phone calls that inform about the existing level of information for a shortage.
Hungary	https://www.ogyei.gov.hu/gyogyszeradatbazis	There is a list by the National Institution of Pharmacy and Nutrition that is being updated frequently. It is based on the notification by manufacturers.
Iceland	https://www.lyfjastofnun.is/efirlit/lyfjaskortur/	The Iceland Medicines Agency has an overview of the medicines shortages.
Ireland	http://www.hpra.ie/homepage/medicines/medicines-information/medicinesshortages	The Health Products and Regulatory Authority shares information on medicines shortages on its website.
Lithuania	https://www.vvkt.lt/Vaistu-tiekimo-sutrikimai	The State Medicines Control Agency of Lithuania shares information on medicines shortages via an excel table.

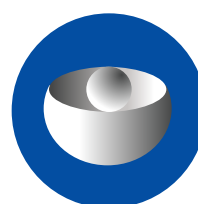
Country	Website of the reporting system	Feedback provided in relation to the reporting system
Luxembourg		No information provided.
Malta		No information provided.
Montenegro		No website available. Shortages are reported by email.
Netherlands	https://farmanco.knmp.nl/	The Farmanco reporting site is run by the Royal Dutch Society of Pharmacy. Manufacturers and wholesalers can report shortages on this website.
	https://www.meldpuntgeneesmiddelenkortendefecten.nl/	The Ministry of Health hosts a response form on its website via which shortages can be reported.
North Macedonia	www.malmed.gov.mk	An overview on medicines shortages is provided.
Norway	https://legemiddelverket.no/legemiddelmangel	The Norwegian Medicine Agency shares information on medicines shortages via its website.
Poland	http://dziennikmz.mz.gov.pl/compatible/KeywordsSearch/55	The Official Journal of the Health Ministry provides an overview of the medicines shortages in the country.
	http://wif.poznan.ibip.pl/public/	Chef Pharmaceutical Inspectorate of Poznan collects data reported by pharmacies regarding drug shortages and produces a list of medicines at risk of being illegally exported. Pharmacists are obliged to report shortages online giving details of nature of shortage. The reporting system is web based but considered by many not user friendly which may hinder the reporting system.
Portugal	https://www.infarmed.pt/web/infarmed/gestao-da-disponibilidade-domedicamento	The Portuguese Medicines Agency runs a reporting system for medicines shortages.
Romania	http://medicamentelipsa.ms.ro/	The website provides an overview on medicines shortages in Romania.
Russia		No information provided.
Serbia	http://site.zus.rfzo.rs/def	The National Insurance Fund runs a website where pharmacists can report shortages. No access is provide to the databases with all reported shortages from other institutions.

Country	Website of the reporting system	Feedback provided in relation to the reporting system
Slovakia	https://portal.sukl.sk/PreruscheniePublic/?act=PreruschenieOznList&mId=2	The State Institute for Drug control has a website with information. This website does not provide feedback on alternatives and manufacturers often don't want to inform about the length of a shortage.
Slovenia	https://www.jazmp.si/humana-zdravila/podatki-o-zdravilih/zdravila-na-trgu/	A system exists run by the Public Agency of the Republic of Slovenia for Medicines and Medical Devices, but manufacturers don't report consistently to the system.
	http://www.cbz.si/cbz/bazazdr2.nsf/Search/\$searchForm?SearchView	Via the Central Medicines Database, it is possible to search for all the medicines on the Slovenian market. The website uses a colour system to categorize the medicine (no colour – no information on shortages; green – medicine available; yellow – shortage might happen; red – medicine shortage). It is also possible to search for the list of medicines shortages per fields.
Spain	https://cima.aemps.es/cima/publico/home.html	The Spanish Medicines Agency provides information via e-mail and on its website. There is also a webpage via which it is possible for hospital to obtain medicines from abroad.
Sweden	https://lakemedelsverket.se/OVRIGA-SIDOR/Restnoteringar/	The Swedish Medical Products Agency has a residual list which shares information on temporary shortages.
	https://docetp.mpa.se/LMF/Reports/Restnoteringar.xlsx	An excel list with the all the information on shortages reported in the country is also available.
Switzerland	https://www.bwl.admin.ch/bwl/fr/home/themen/heilmittel/meldestelle.html	The Federal Office for National Economic Supply hosts an information system which does not contain the most up-to-date information.
	https://www.drugshortage.ch/index.php/uebersicht/	A hospital pharmacist launched the site to provide manufacturers with a place where they can voluntarily report shortages. Other healthcare professionals can also report shortages.
	https://www.swissmedic.ch/swissmedic/fr/home/medicaments-a-usagehumain/surveillance-du-marche/out-of-stock.html	The Swiss Agency for Therapeutic Products has a list of the medicines in shortage in the country.
Turkey	<i>No information provided.</i>	
United Kingdom	<i>No website available. Information on shortages is circulated via an email list.</i>	



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CONTACT

European Medicines Agency
Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

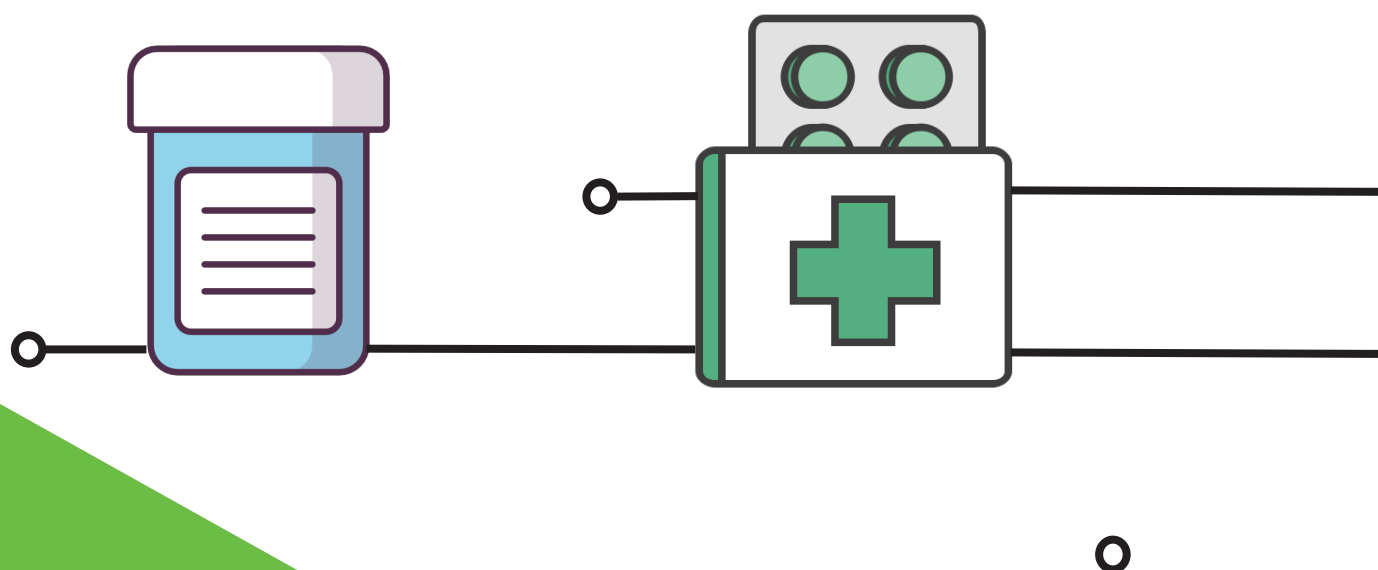
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EAHP's 2018 Survey on Medicines Shortages to improve patient outcomes



MEDICINES SHORTAGES IN EUROPEAN HOSPITALS

Results of the largest pan-European survey on medicines shortages in the hospital sector, an overview of the situation and the key challenges that need to be tackled.

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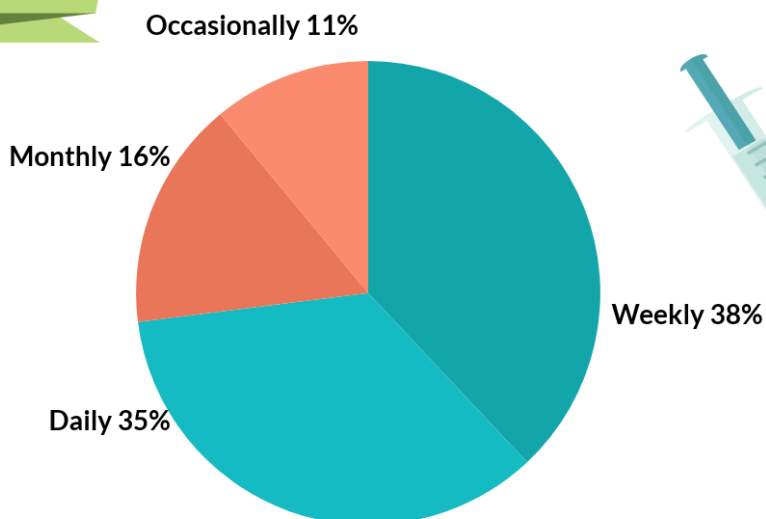
*The 2018 Medicines Shortages Report uses original quotes provided by survey respondents during the consultation period. These quotes have not been altered.

Medicines Shortages Survey results

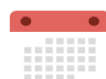
Are medicines shortages a current problem?
91.8% (2018) vs 86.2% (2014)

1.666 responses from 38 countries

How often does your hospital pharmacy experience medicines shortages?



5 Hours per week spent dealing with medicines shortages



2.2 months is the duration of a typical medication shortages

Types of medicines most frequently reported



77%
Antimicrobial agents

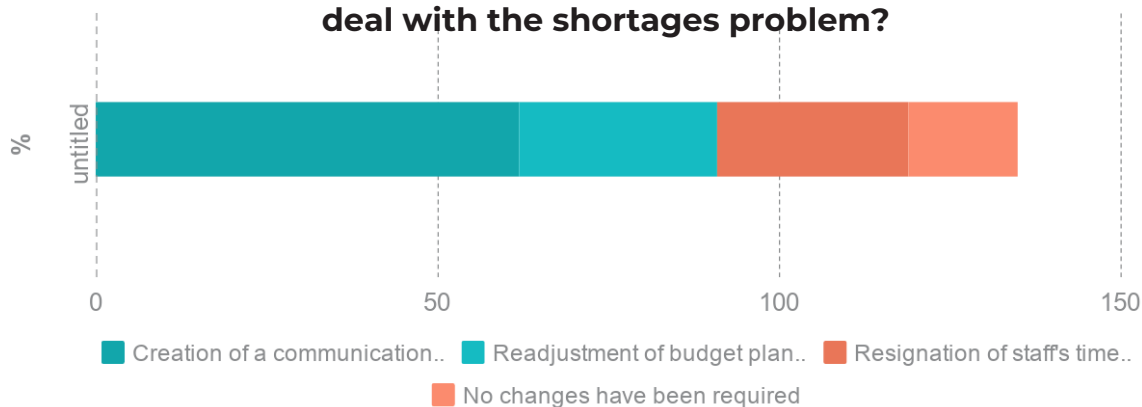


43%
Vaccinations



39%
Oncology medicines

What changes (if any) in practice has your hospital needed to make in order to deal with the shortages problem?



67% of respondents reported their country has a system for reporting shortages, but only 56% of those judge it to be effective



77% responded that generic medicines are most commonly in short supply

1. Foreword by the President

Problems caused by medicines shortages in Europe are a severe threat to patient care and should be addressed through adequate actions on the local, national and European level. The European Association of Hospital Pharmacists (EAHP) started investigating the issue in 2012 due to increased reports from its members expressing the difficulties in sourcing medicines.

In 2014, the first pan-European report on medicines supply shortages in the hospital sector shed more light on the issue. It highlighted that medicines shortages are a serious problem for hospital pharmacists resulting in the unavailability of certain antimicrobial agents, oncology and emergency medicines. To address the issues caused by shortages, such as the increase of staff time needed to solve them, hospital pharmacists urgently called for greater legal clarity regarding the responsibility of suppliers to report supply disruptions at an early stage.



Despite efforts by the supply chain actors, which resulted in the adoption of a joint statement containing recommendations on the provision of information designed to help tackle medicines shortages, the problem of medicines shortages continues to persist as highlighted by the results of the 2018 EAHP Medicines Shortages Survey. EAHP consequently calls on national governments and the European Commission to improve the communication on medicines shortages and to launch an inquiry at the European level into the primary factors causing medicines shortages.

Communication on medicines shortages

A reliable catalogue of medicines in shortage across Europe is needed listing the shortage reason, estimated duration and other advice to pharmacies, prescribers and patients. EAHP acknowledges the efforts by the task force on the availability of authorised medicines for human and veterinary use of the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA). However, in view of the limits of the current catalogue on European medicines shortages, EAHP urges the EMA and the HMA to consider the development of a comprehensive communication strategy on shortages which ensures that all supply chain actors, including hospital pharmacists, receive adequate information on the shortage of medicines.

An inquiry at European level into the primary factors causing medicines shortages

Similar to the findings of the 2014 survey, the result of the 2018 survey underlines again that medicines shortages are a pan-European problem that cannot be solved through national measures alone. Consequently, the EAHP is calling on the European Commission to start an investigation into the factors causing medicines shortages and as a first step to provide solutions that will help to solve preventable shortages.

The first half of 2019 will, in particular, be a crucial time for hospital pharmacists with new regulations coming into effect that aim at combating counterfeit drugs and Brexit. We hope that other stakeholders follow our call to action and help us in securing the necessary solutions to tackle the growing problem of medicines shortages.

EAHP thanks Amgen for supporting the realisation of this report and Keele University for the analysis of the survey results.

Petr Horák

President of the European Association of Hospital Pharmacists

2. Executive summary

Previous work done by the EAHP found that medicines shortages can have a significant impact on patient care. The aim of the 2018 EAHP Medicines Shortages Survey was to provide a clearer and up to date picture on the impact of medicines shortages.

There were 1,666 responses to the 2018 survey from 38 countries, a large increase from the 2014 survey which received 607 responses. Medicines shortages were reported to still be a major issue facing hospitals across Europe. For example, 75% of respondents to the 2018 survey reported that they experienced medicines shortages at least weekly. The reported mean duration of a typical shortage for countries was 2.2 months.

In a number of ways, these issues have become more problematic since the 2014 survey. The percentage of respondents in a country reporting shortages to be a problem in terms of delivering the best care to patients and/or operating the hospital pharmacy saw a statistically significant increase for the 2018 survey ($M = 91.8\%$, $SD = 9.5\%$) compared to the 2014 survey ($M = 82.6\%$, $SD = 17.6\%$), $t(27) = 2.721$, $p = 0.011$, $d = 0.514$. A paired samples t-test also showed a statistically significant increase in the mean percentage of respondents in a country reporting that more than 5 hours per week are spent dealing with medicines shortages for the 2018 survey ($M = 42.0\%$, $SD = 18.7\%$) compared to the 2014 survey ($M = 33.1\%$, $SD = 25.9\%$), $t(26) = 2.275$, $p = 0.031$, $d = 0.438$.

Antimicrobial agents were the type of medicine most frequently reported as having shortage problems, with 77%. Problems were also reported frequently with preventative medicines (vaccinations) (43%) and oncology medicines (39%). The medicine which was reported to be most frequently associated with supply issues was Piperacillin/tazobactam with 272 responses across 18 countries.

Financial issues caused by medication shortages can be due to having to pay more to procure a medicine from another supplier or paying more for an alternative (see Q21). Other issues were having to devote more staff time to the issue (see Q10) or having a direct impact on patient (such as potentially increased length of hospital stay, see Q22). When asked if medicines shortages are having a negative impact on overall budget, most chose either 'agree' (43% of responses) or 'strongly agree' (38% of responses).

When asked about the impact on patients, over half of the respondents have seen patient care delayed as a consequence of medication shortages (59% of respondents). The quality of care received by the patient is also directly affected with cancellations of care (31% of respondents), medication errors (25% of respondents) and suboptimal treatment for patients (25% of respondents) also being frequently reported. There were 12 reports of death as a result of medication shortages (1% of respondents).

When asked how often do you estimate your hospital is able to provide treatment to a patient by providing a therapeutic equivalent or near equivalent medicine, without major disruption to their treatment? 78% of responses were for either 'most of the time' or 'all of the time'. At this point it was questioned if this is sustainable (e.g. *"We have so far always managed to source a timely alternative - but unsure how long this will be sustained"*).

67% of respondents reported their country has a system for reporting shortages, but only 56% of those judged it to be effective. A frequently reported issue was the dependence on manufacturers/suppliers informing authorities of a shortage as this often does not happen or information is flawed (i.e., multiple push backs on restock dates).

Regarding existing policy solutions (Q30), the policy solution with the most support was the medicines shortages catalogue of the EMA, with 43% of respondents answering this question choosing this option. The second most frequent option was 'None of the above' from 42% of respondents, which may cover people who do not support any of the policies, but also people who are not aware of these policies and what they are (e.g. *"not sure what these are and I don't have time to read up on each option"*).

When asked about proposed policy solutions (Q31) it is not surprising to see that 79% of respondents support greater legal clarity on the responsibility of manufacturers to report upcoming supply chain issues at an early stage; in question 10 many comments were observed regarding pharmacists not being aware of supply issues until a delivery did not show up and in question 14 it was observed that the reporting system for medication shortages were weakened by a lack of obligation for manufacturers to share information on supply issues. A comprehensive database run by EMA was also a popular choice with 65% of respondents supporting the proposal, followed by a high level investigation on the causes for shortages and annual reporting on the extent of the problem with 58% and 50% respectively. This is the same order the proposals were ranked in the 2014 survey.

Freetext recommendations from respondents (Q32) include mandatory reporting of shortages by manufacturers, as well as providing accurate information on return dates. Many respondents would like to see manufacturers to have a legal obligation to maintain stock levels and ensure supply of medicines. There are responses calling for a central lead/agency to work on the problem to reduce duplication of efforts in identifying alternatives (either at European, EU, or national level).

Identifying the root cause of shortages is also seen as important – *“A more holistic review needs to be undertaken to understand why shortages occur and try and prevent them. Currently most shortages are managed reactively instead of proactively.”*

3. Background

Work done by the EAHP has already provided evidence on the extent of the problem of medicines shortages, and the impact it has on patient care. EAHP's 2014 Medicines Shortages Survey was designed to provide policy and decision makers with a clearer picture, to adequately assess the nature and available solutions to the problem of medicines shortages ⁽¹⁾. When asked if the shortages of medicines were a problem in the hospital they work in, 86% of the 537 respondents responded 'yes'.

The issue of medicines shortages also appeared in another survey conducted by the EAHP. The primary focus of the 2017 EAHP European Statements of Hospital Pharmacy Survey was to identify the barriers to the implementation of the EAHP European Statements of Hospital Pharmacy (statement 2.5 reads 'Each hospital pharmacy should have contingency plans for shortages of medicines that it procures.'). The results of this survey saw 60% of respondents say they had reason to contact the medicines authority because of a shortage. The survey also showed that the number of fully qualified pharmacists working in a hospital was a significant factor on a hospital having contingency plans to deal with medication shortages ⁽²⁾.

The aim of the 2018 Survey on Medicines Shortages was to provide a clearer picture on the impact of medicines shortages on hospital pharmacists ⁽³⁾. This included:

- the current nature of medicines shortages problems in Europe, including their prevalence;
- the most common types of shortages;
- their impact on patient care and hospital pharmacy services;
- existing national mechanisms for dealing with or monitoring shortages;
- how hospital pharmacists typically manage the problems shortages cause; and,
- hospital pharmacist views on proposed policy solutions.

The 2018 Survey on Medicines Shortages was created using SurveyMonkey, and conducted by the EAHP. Keele University was commissioned to analyse the results. The survey ran from 19th March 2018 to 11th June 2018.

Significance testing was performed to compare the 2018 survey data with the 2014 survey data for questions asked in both surveys. Testing was carried out using IBM SPSS software, and firstly the Shapiro Wilk's test was performed to check for normality. If the differences between the distributions of data were approximately normal and no significant outliers detected, a paired sample t-test was used. If a parametric test was not appropriate, a Wilcoxon signed rank test was used where the distribution of differences between the 2 sets of data was symmetric, and a sign test was used if not ⁽⁴⁾.

Terminology

M	Mean
SD	Standard Deviation
p	p-value
t	t-value
d	Effect size
Z	Test statistic

4. Response rates

There were 1,666 responses to the 2018 survey, a large increase from the 2014 survey which received 607 responses. The table below shows the breakdown of responses by country, compared to the number of responses received in the 2014 survey. Note that the table only includes responses from countries which responded to the 2018 survey. The countries which saw the biggest increase in responses were the UK (+284) and France (+189).

Country	Responses (2018)	Responses (2014)	Country	Responses (2018)	Responses (2014)
Albania	1	0	Latvia	4	2
Austria	29	21	Lithuania	1	8
Belgium	90	94	Luxembourg	3	0
Bosnia & Herzegovina	19	9	Malta	6	11
Bulgaria	3	6	Montenegro	4	0
Croatia	26	25	Netherlands	20	11
Cyprus	2	1	Norway	21	11
Czech Republic	26	4	Poland	32	13
Denmark	10	25	Portugal	85	42
Estonia	17	15	Romania	24	2
Finland	33	1	Russia	1	0
France	192	3	Serbia	20	8
FYROM	14	4	Slovakia	23	16
Germany	78	10	Slovenia	18	5
Greece	84	14	Spain	190	105
Hungary	33	12	Sweden	5	0
Iceland	9	4	Switzerland	67	7
Ireland	51	47	Turkey	61	5
Italy	73	41	UK	291	7

6. Prevalence of shortages in your hospital (Q2-3)

Q2. Are shortages of medicines a current problem in the hospital you work in, in terms of delivering the best care to patients and/or operating the hospital pharmacy?

This question received 1,666 responses, and an overwhelming 90% of respondents answered 'Yes', providing strong evidence that shortages of medicines is an extremely common problem in hospitals today. 7% of respondents answered 'No', and 3% were unsure.

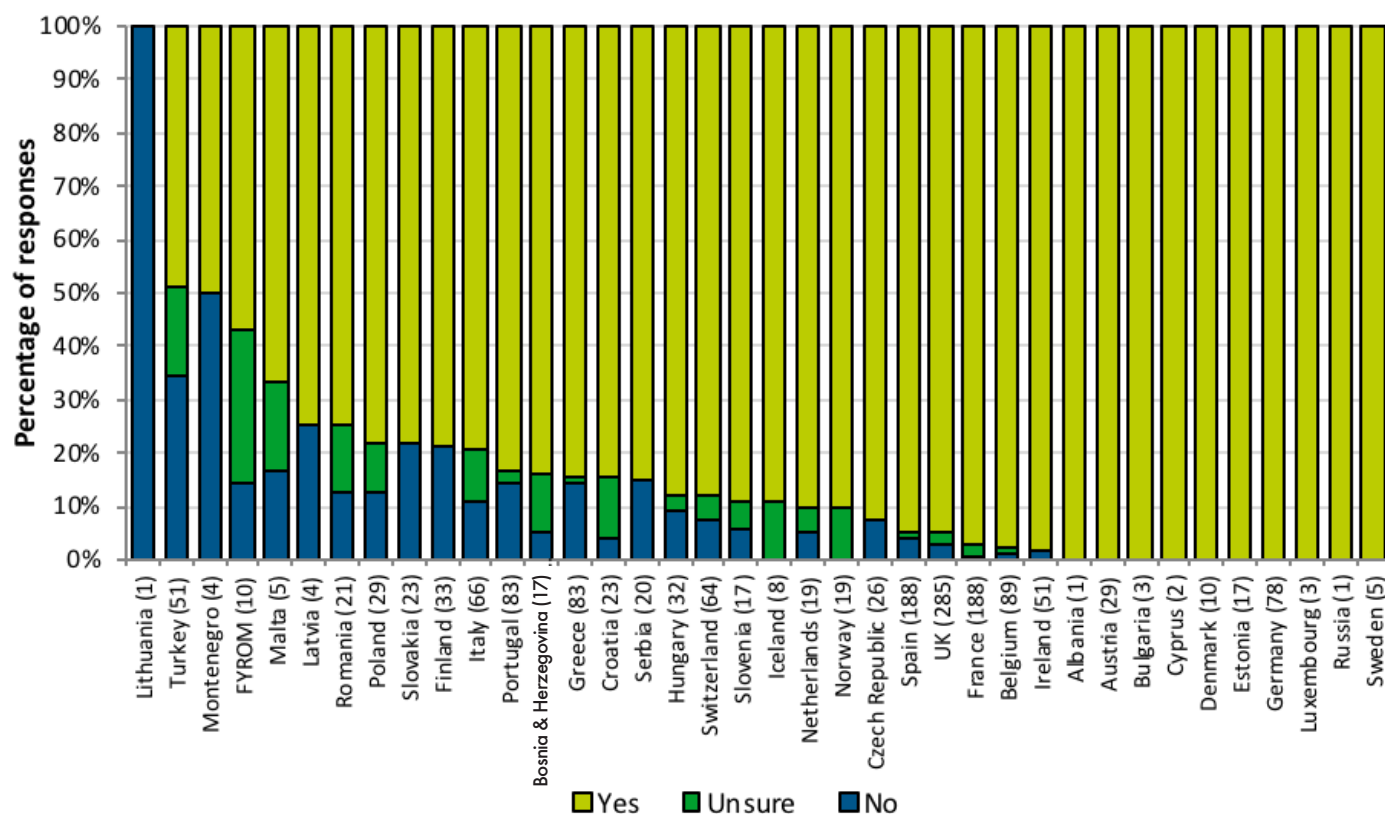


Figure 1 - Percentage of responses for question 2 'Are shortages of medicines a current problem in the hospital you work in, in terms of delivering the best care to patients and/or operating the hospital pharmacy?', grouped by country. Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 1**, where they are sorted by the proportion of respondents answering 'Yes'. In 10 countries, 100% of respondents answered 'Yes'. The only countries where more than 50% of respondents did not answer 'Yes' were Lithuania, Turkey and Montenegro.

The percentage of respondents in a country answering that medicines shortages are a problem in their hospital was compared to data from the 2014 survey where the same question was asked. A paired samples t-test showed a statistically significant increase in the mean percentage of 'Yes' responses for countries for the 2018 survey (M = 91.8%, SD = 9.5%) compared to the 2014 survey (M = 82.6%, SD = 17.6%), $t(27) = 2.721$, $p = 0.011$, $d = 0.514$. This indicates that more people consider this to be an issue today, in terms of delivering the best care to patients and operating the hospital pharmacy, than they did in 2014.

Q3. Approximately how often does your hospital pharmacy experience medicines shortages?

The most frequent response to this question, based on 1,666 responses, was 'weekly' with 39% of the responses, followed by 'daily' (36%), 'monthly' (16%) and 'occasionally' (11%), which shows most hospitals are experiencing shortages on a frequent basis.

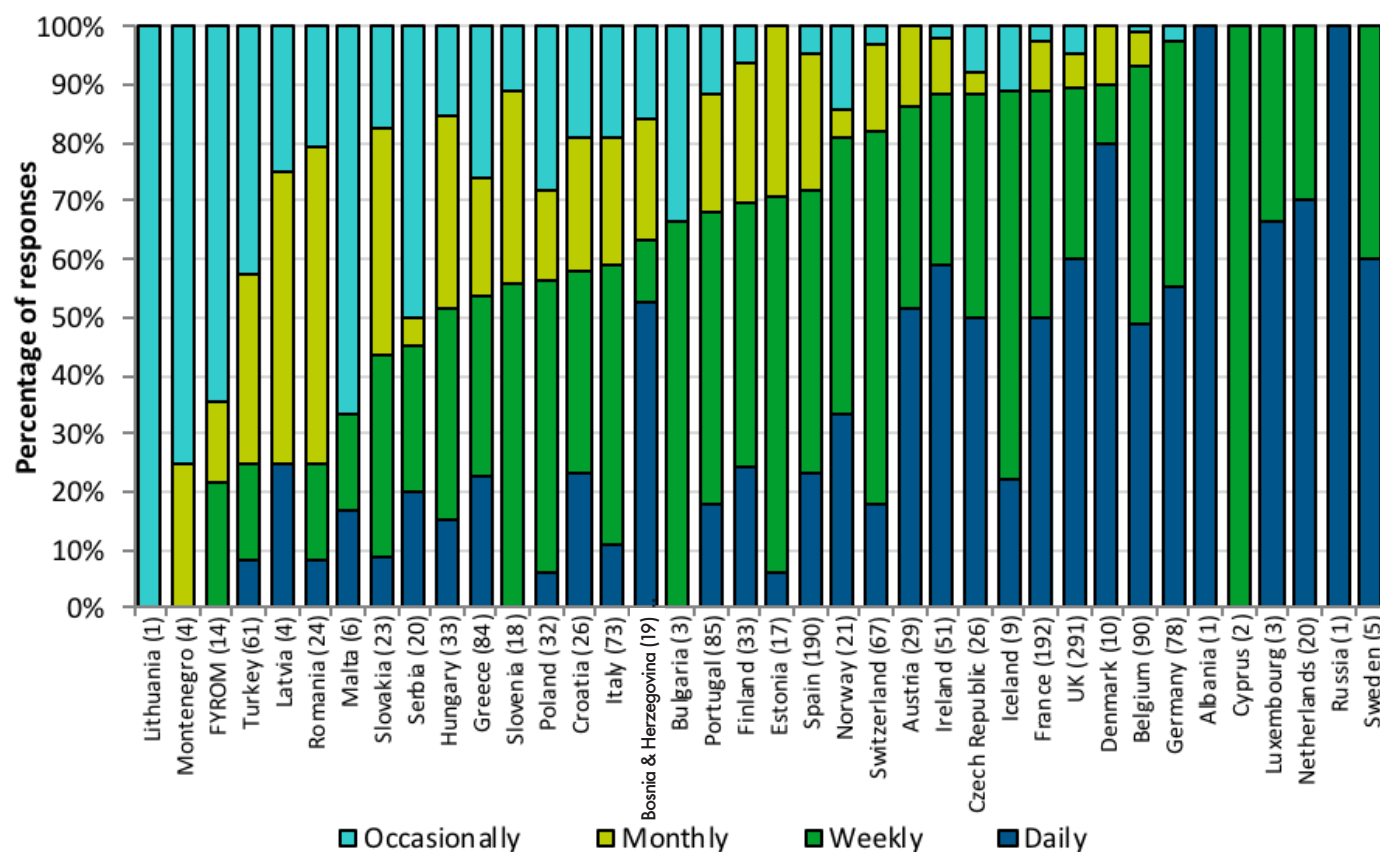


Figure 2 Percentage of responses for question 3 'Approximately how often does your hospital pharmacy experience medicines shortages?', grouped by country. Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 2**, where they are sorted by the percentage of respondents answering at least weekly (aka 'daily' responses + 'weekly' responses). Viewing the data this way helps to show that the frequency medicines shortages are experienced by hospitals varies greatly between countries.

A paired samples t-test indicated that the mean percentage of respondents in a country reporting that their hospital pharmacy experiences shortages at least weekly was not significantly different for the 2014 survey ($M = 70.3\%$, $SD = 21.0\%$) compared to the 2018 survey ($M = 68.4\%$, $SD = 22.2\%$), $t(27) = -0.414$, $p = 0.682$, $d = -0.0782$.

7. Nature of shortages (Q4-6)

Q4. Which type of medicine do you most commonly experience to be in short supply?

This question had 1347 people respond to it, with 77% of them reporting generic medicines to be the most common type in short supply, with originator medicines coming in second with 65% (although note that 46% of respondents selected both options to be most commonly in short supply.)

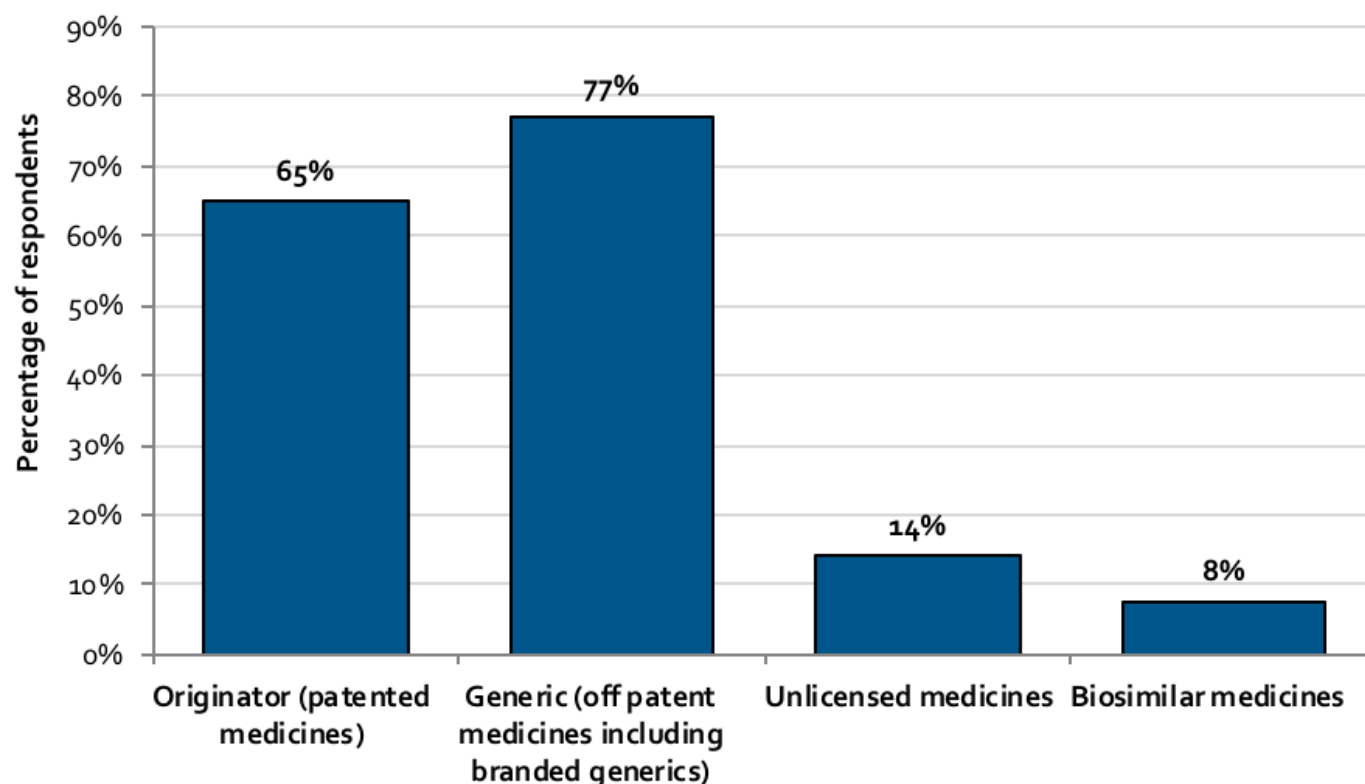


Figure 3 Percentage of participants in the survey who identified this type of medicine to be most commonly in short supply. (N=1,347) (Note that this was a tick all that apply question)

Only 14% of respondents experienced unlicensed medicines to be most commonly in short supply, followed by biosimilars with 8%, although these smaller numbers are likely since these medicines represent a smaller proportion of the total prescribing that occurs.

When this question was asked in the 2014 survey, originator medicines were the most commonly experienced type to be in short supply with 51% of the responses, compared to generic medicines which accounted for 37% of the responses. Note that when the question was asked in the 2014 survey, participants could only choose one of three options. In the 2018 survey the biosimilar medicines option was added, and also participants were able to select multiple options (tick all that apply), which needs to be taken into consideration when comparing the data.

Q5. In which area of medicine does your hospital experience shortage most commonly? Tick all that apply.

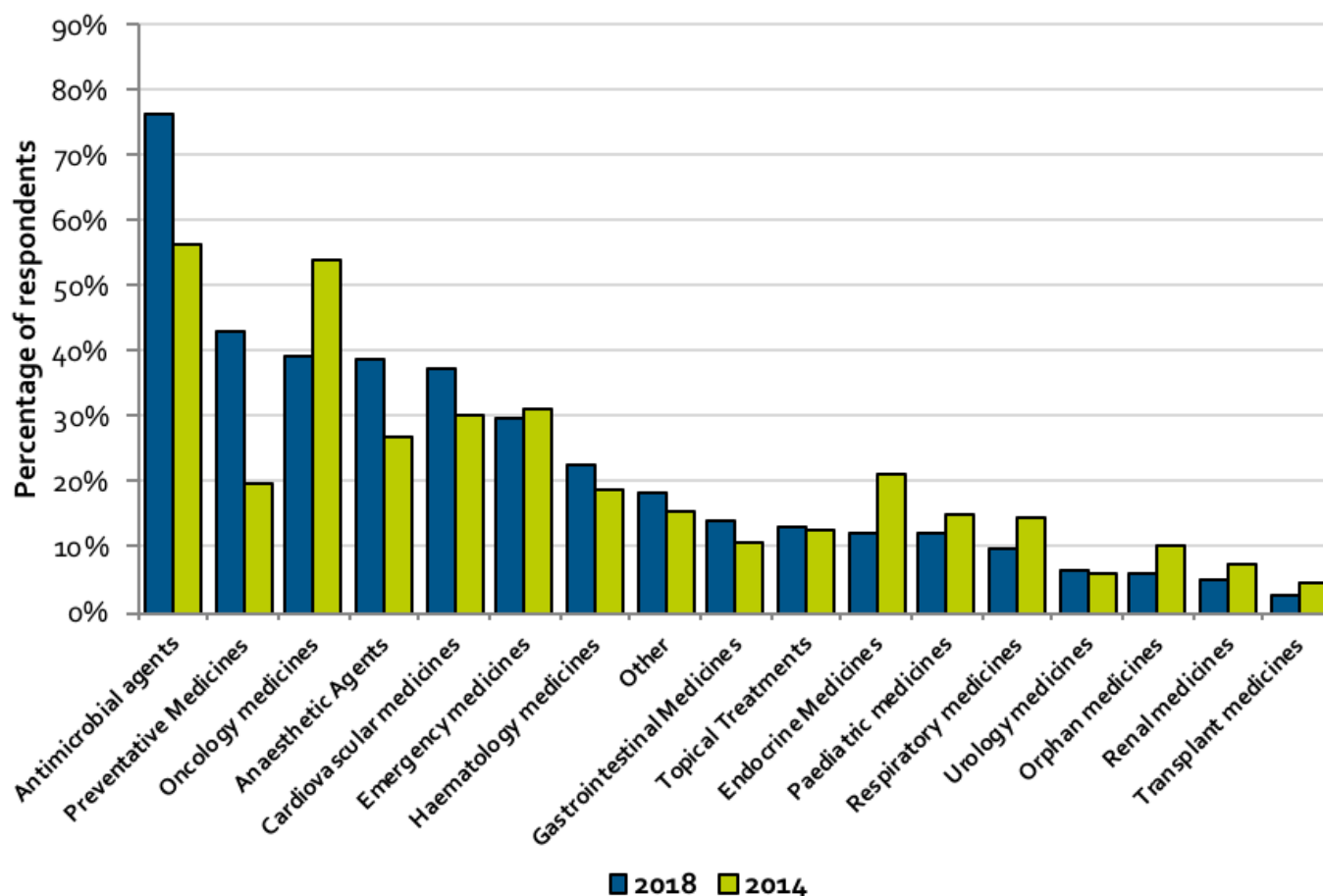


Figure 4 Percentage of participants in the survey who identified this area of medicine to be commonly in short supply. (N=1,348) (Note that this was a tick all that apply question)

Antimicrobial agents were reported to be commonly in short supply by 77% of the 1,348 respondents who answered this question in the 2018 survey.

In 27 countries antimicrobial agents were the area of medicine which received the most reports. However, there was some variation in the most commonly reported area of shortage across countries, with 6 countries (Albania, Estonia, Montenegro, Poland, Romania and Sweden) reporting anaesthetic agents as the most common area of shortage. Bosnia reported oncology medicines, Cyprus reported haematology medicines, FYROM reported emergency medicines, and Slovakia reported cardiovascular medicines as the most common area of shortage within their country. Although preventative Medicines (e.g. vaccines) were the second highest reported area of medicines shortages with 43% of participants reporting them to be an issue, it was not the area of medicine which received the most reports in any country.

The biggest theme of responses from the 'Other' category was drugs related to mental health or antipsychotics (87 responses), followed by contrast/x-ray medicines (25 responses), analgesics (24 responses) and immunoglobulins (24 responses).

Compared to the 2014 survey, the areas with the biggest increase in reports of common shortages are antimicrobial agents (77% of respondents reporting this as an issue in 2018 compared to 57% in 2014), preventative medicines (43% in 2018 compared to 20% in 2014) and anaesthetic medicines (39% in 2018 compared to 27% in 2014), suggesting shortages in these areas have become more frequent. The area with the

biggest decrease in reports of common shortages was oncology medicines (39% of respondents reporting this as an issue in 2018 compared to 54% in 2014).

Q6. Please tell us the medicines in which the experience of shortages was most frequent during the past year. If possible please include their brand name, INN (International non-proprietary name) and common indications as appropriate or available.

There were 948 responses to this freetext question. As the responses were freetext, responses vary from referring to specific medicines to groups or classes of medicines. Some refer to the chemical name, particular brands or abbreviated names. After analysing and aggregating these data, the top 10 most frequently referred to items were:

- 1. Piperacillin/tazobactam** (272 responses across 18 countries) – This drug elicited a huge number of responses and constitutes a big part of the antimicrobial results seen in Q6.
- 2. Vaccinations** (144 responses across 18 countries) – Although referring to an area of medicines, many respondents reported experiencing shortages in all vaccinations without being specific, so these data have been aggregated together. Some of the most frequently specified vaccinations were Hepatitis B (65 responses), Pneumococcal (27 responses), Tuberculosis (25 responses), Tetanus (17 responses) and Hepatitis A (17 responses).
- 3. Immunoglobulins** – (99 responses across 13 countries) – The majority of the responses for immunoglobulins did not specify a brand, so they have counted as a group (Privigen was the most frequent with 28 responses).
- 4. Cephalosporins** (86 responses across 20 countries) – Another group of drugs that were grouped together due to the responses received. The most frequently specified Cephalosporins were Ceftazidime (29), Cefepime (19), Cefuroxime (16), Cefotaxime (15), and Ceftriaxone (7).
- 5. Gentamycin** (80 responses across 7 countries).
- 6. Co-amoxiclav** (Amoxicillin/clavulanic acid) (67 responses across 10 countries).
- 7. Human Albumin** (68 responses across 12 countries).
- 8. Xylocaine/adrenaline** (68 responses across 9 countries).
- 9. Remifentanyl** (64 responses across 13 countries).
- 10. Enoxaparin** (58 responses across 7 countries).

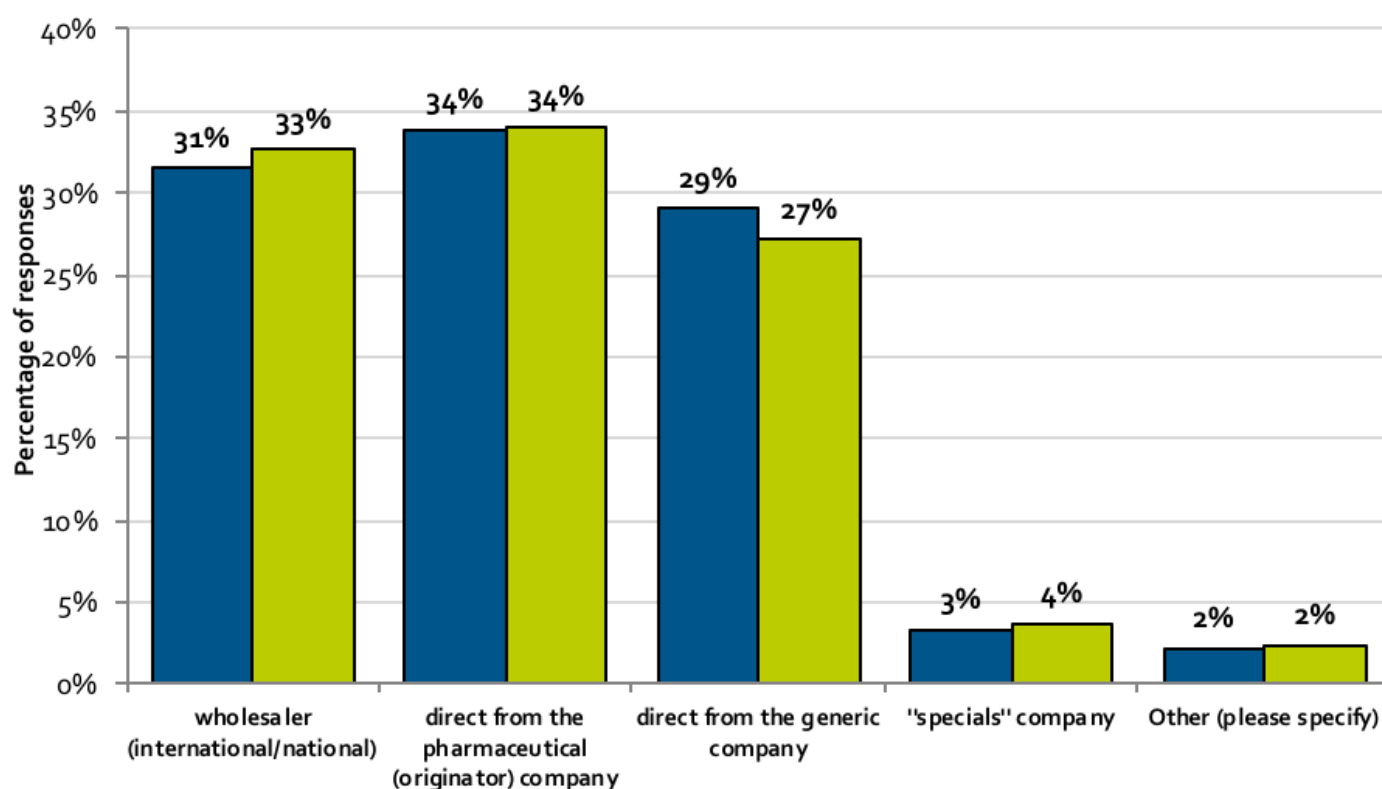
At the time of writing, there are seven medicines listed in the EMA Medicines Shortage Catalogue: Cerezyme (imiglucerase), DepoCyt (cytarabine), Maci (matrix applied characterised autologous cultured chondrocytes) implant, Nulojix (belatacept), Orgalutran (ganirelix), Trisenox (arsenic trioxide) and Tygacil (tigecycline). Only 3 of these appear in the responses, and only infrequently with 19 responses for DepoCyt (cytarabine), 5 for Trisenox (arsenic trioxide) and 1 for Nulojix (belatacept).

8. Sources of supply (Q7-8)

Q7. Which of the below categories best describes the main external source of supply of medicines to your hospital?

Q8. From which category of external supply does your hospital most frequently encounter problems with sourcing specific required medicines?

Data for questions 7 and 8 are shown together in **Figure 5**. From here it can be seen that the results of the two questions are extremely similar. In addition, after investigating the record level survey data it was observed that 63% of the 1,252 participants who answered both questions gave identical responses. This result implies that participants are saying that medication shortages are encountered among the various sources of supply to a similar degree.



■ 7. Which of the below categories best describes the main external source of supply of medicines to your hospital?

■ 8. From which category of external supply does your hospital most frequently encounter problems with sourcing specific required medicines?

Figure 5 Percentage of responses where this source of supply is identified in questions 7 and 8 of the survey. (Note that this was a tick all that apply question)

Comparing the sources of supply to the data from the 2014 survey is more difficult, as the 2014 survey only allowed participants to choose one option, whereas they could pick multiple options in 2018. For example, in 2014 only 12% of responses were for 'direct from the generic company', compared to 27% in 2018. We are unable to conclude that the source of supply from generic companies has greatly increased since 2014, since the more likely explanation is that respondents are choosing multiple options, and hence increasing the proportion of second/third line sources of supply compared to the 2014 data (53% of the 1,253 participants who answered this question in 2018 chose multiple options).

9. Duration of shortages (Q9-12)

Q9. In your experience, how long would you estimate the average or typical medicines shortage normally lasts for.

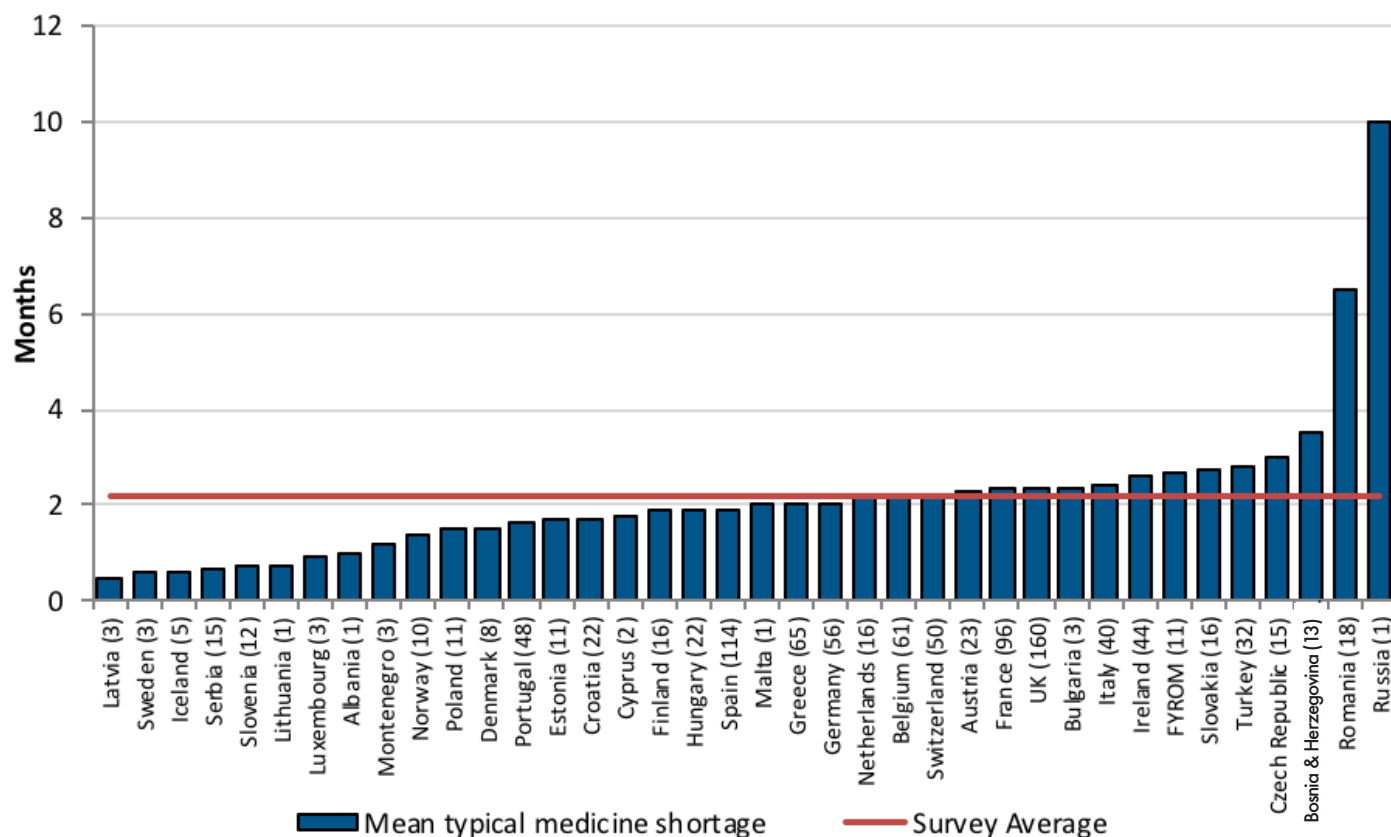


Figure 6 Mean duration (in months) of typical medicines shortage, grouped by country. Numbers in brackets represent number of responses from that country.

For this question, respondents gave a numeric value for the number of days/weeks/months that a typical shortage last for. Clearly erroneous data was removed, resulting in 1,031 useable responses which were all converted into number of months. The average duration of a typical medication shortage for the 2018 survey was 2.2 months, signifying the extent of the medication issue.

Figure 6 shows the data grouped by country, where it is observed that only 7 countries have an average typical shortage less than one month. Russia and Romania appear to be outliers with a mean shortage of 10 months and 6.5 months respectively but note that Romania's value is based on 18 responses which provides assurance that the result is valid.

Comparing data to the 2014 survey is difficult because the question was structured differently. Instead of requiring a numerical value for the number of days/weeks/months of a shortage duration the question was categorical with the choices for either a number of days/weeks/months. Of the 387 answering the question the most frequent response was a number of weeks (63%), followed by a number of months (30%) and a number of days (7%). Looking at **Figure 6**, most countries are measuring shortages in months rather than weeks, with over half of the countries (20 out of 38) displaying a mean shortage duration of over 2 months.

Q10. Please provide details about your personal experiences with typical shortage situations.

Response to this freetext question was quite varied, with some respondents focusing on the duration of typical shortages and others describing issues arising from shortages and the processes in handling them. One theme that emerged in the responses was the lack of reliable or timely information from manufacturers

and suppliers on the commencement or duration of shortages.

- *“Mostly there is no Information provided from the manufacturer. It should be as soon as possible, in detail and continuously.” – Austria*
- *“The worst is, that pharmaceutical companies do not communicate; the orders are not delivered and the information mostly is only achieved by asking the supplier.” – Germany*
- *“We are not informed about shortage, information from manufacturers is missing.” – Czech Republic*

There are some comments which suggest that the more advanced notice the hospital has on a shortage, they are able to manage the situation better, but sometimes notice of a shortage is not given and only found out about when products are not delivered.

- *“When there is sufficient or any notice they are easier to manage. Dealing with shortages when we get notice that the product is out of stock is much more challenging and reactive.” – Ireland*
- *“Not good. I found about shortage when wholesaler cannot deliver drugs when I order them.” – Croatia*
- *“Lack of information on availability from manufacturer and their wholesalers, lack of pre-warning of shortage resulting in panic buying, excess stock holding by some trusts. lots of time spent chasing orders, getting conflicting information, lots of time wasting trying to sort out what can be used as a replacement.” – UK*

Many respondents commented that information from companies about when stock will be back is very unreliable, and it has become normal to assume this date will be pushed back several times.

- *“Very often the companies announce a duration of the shortage which isn’t correct, so it goes longer and longer all the time. It would be better in this case to describe the duration as unknown.” – Switzerland*
- *“In most cases there is no data when the product will be delivered again (end of shortage). When a firm does have a delivery-date, you cannot always depend on it!” – Belgium*
- *“... Then there will be information on when the drug is expected to be delivered again - but this information is never to be trusted. That is in my opinion the biggest problem - because we never know how to advice the hospital.” – Norway*

Some responses highlighted the effect the shortages have. This can include possible shortages of alternative medicines, time spent dealing with shortages, additional expense or the effect on patients.

- *“Usually the shortages occur to classic medicines of first line treatments that are cheap and irreplaceable. Therefore we have to use second line treatments and the additional unexpected increase in the consumption of newer agents causes the domino effect of their shortage as well”. – Greece*
- *“A pharmacist of the team spend about 8 hours per week to solve the problems of drug shortage.” – France*
- *“The shortage of medicines in our hospital carries the following consequences: - an increase in extra work both at the care and administrative level - discomfort and nervousness on the part of all personnel, both health and non-health - Distrust towards the supplier laboratory - Increase in additional costs (loans between hospitals, importation of medicines) - Increase the chances of error in the dispensing of the substituted medication - Discontinuity in the treatment of the patient, so that the quality of care decreases.” – Spain*

Some hospitals have taken measures to deal with shortages, hiring staff dedicated to the issue or determining shortage durations based on previous data.

- *“We document every delivery shortage and can therefore determine the typical duration.” – Germany*

- *“... I have to create a ‘shortage memo’ for all relevant medical, nursing & pharmacy staff to inform them of the latest shortage (every time), proposed alternative, expected timeframe for shortage & any other important information (if alternative product is majorly different to original/needs manipulation etc).” – Ireland*
- *“For many issues we have sufficient stock to see us through to the end of the problem and we have to keep higher than desirable stock levels to mitigate against supply issues. Main problems are caused by single supplier products where there is no alternative often on critical lines. We have a full time post who spends all her time managing supply shortages and we are looking at needing to add addition resource to support this due to the growing issues.” – UK*

Q11. What is the longest duration that you can recall a medicine being in shortage for in the last 4 years?

This question was structured similarly to question 9, as respondents gave a numeric value for the number of days/months/years for the longest duration a medication has been in shortage. Again, clearly erroneous data was removed, resulting in 1031 useable responses which were then all converted into number of months.

Some of the answers raise the question of at what point should a product stop being considered in shortage and instead be considered to be discontinued. The average maximum medication shortage reported in the 2018 survey was 13.2 months.

When this question was asked in the 2014 survey, the response was entirely freetext. The data was investigated, and responses containing a specific duration were used to calculate an average maximum duration from the 2014 survey.

For example, a response specifying 3 months was used, but a response stating a few months was not. Based on the 250 responses which contained suitable data, the average maximum medication shortage duration reported in the 2014 survey was 9.3 months, providing more evidence that the magnitude of the medication shortages problem is increasing.

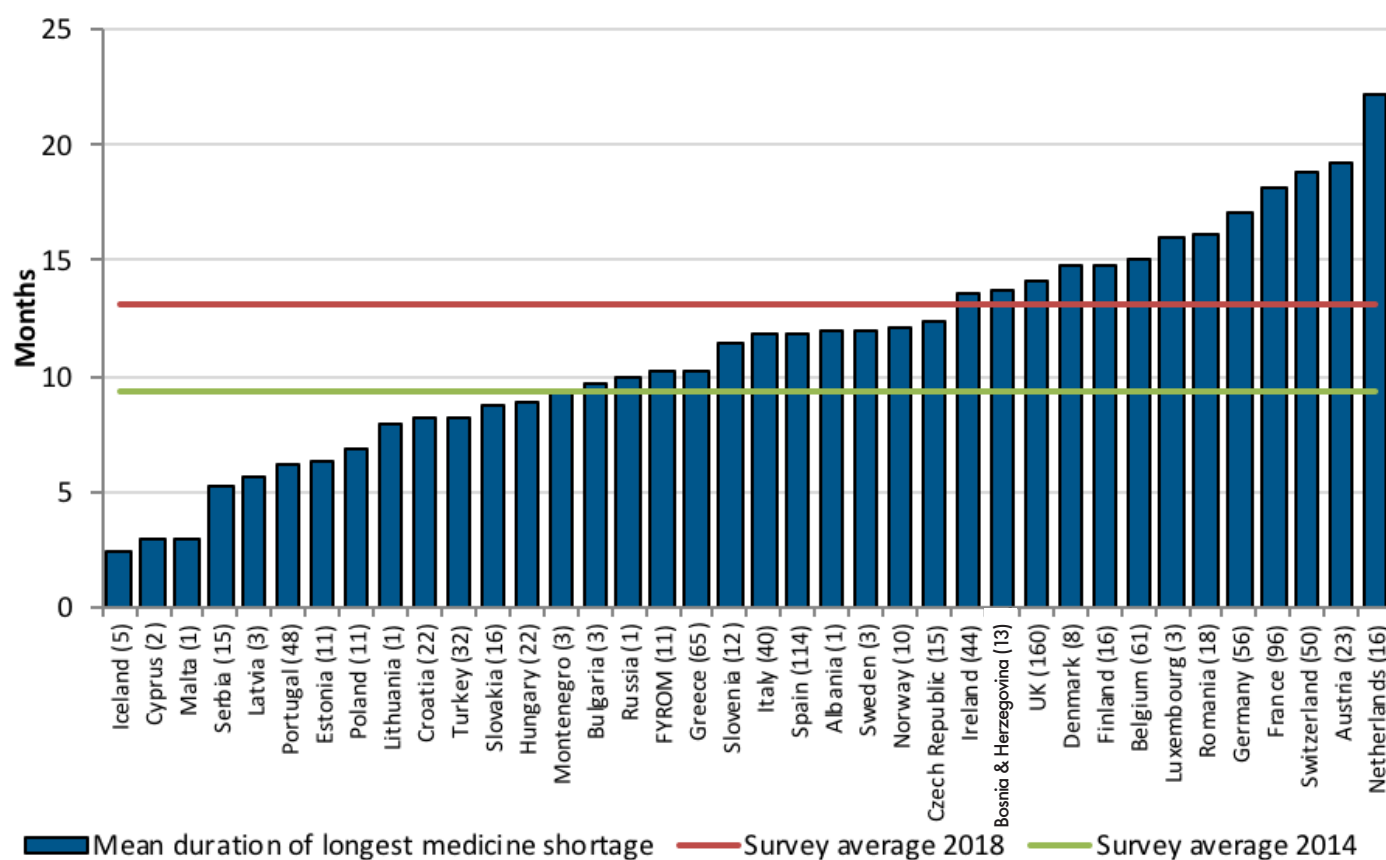


Figure 7 Mean duration (in months) of longest medicines shortage, grouped by country. Numbers in brackets represent number of responses from that country.

The 2018 survey data grouped by country is shown in **Figure 7**, alongside the average maximum medication shortage duration reported in both the 2014 and 2018 surveys for comparison.

Q12. Please provide details about the longest shortage you have personally experienced.

There were 503 freetext responses to this question. Freetext responses where both the product and shortage duration were specified were analysed and a list of examples was produced where the duration has been specified to be at least a year (duplicate mentions of a medicine were removed).

Approximately one year

- “Almost for one year we had a shortage of Lasix amp. which is unacceptable, since we are Institute for cardiovascular diseases and Lasix is one of our most used drugs. The shortage was in the whole country, and ministry of health did nothing to help.” – Serbia
- “That’s rather approximately 1 year. Piperacillin/Tazobactam - explosion in a factory.” – Norway
- “clonazepam (rivotril) injection - went short for approx one year. Consultant used midazolam instead during this period.” – Ireland

Up to two years

- “relistor (1,5 years and still on shortage)” – Austria
- “Guanethidin, novaban is still not available. Maniprex will not be available in the next 2 years.” – Belgium
- “alosplastine, colpotrophine (2 years shortage and then stop). The most difficult situation were shortage of enoxaparine.” – France

- *"2 years waiting for Ativan" – Ireland*
- *"Deanxit shortage lasted for 2 years approx." – Spain*
- *"The longest shortage was with Temesta (lorazepam im/iv) and it lasted approximately 2 years." – Slovenia*
- *"Depocyte > 1 year" – Ireland*
- *"Bleomycin has not been available on the market in Romania for almost 2 years now." – Romania*
- *"For MAGNEZII SULFAS 207,4 mg/ml, vials, the longest shortage I experienced was approx. 2 years." – Romania*
- *"There are no melfalan inj Product in Norway With a marketing authorisation and we depend on the "spotmarket" in Europe. For almost 2 years we had to ration the use of melfalan inj and there was a national consensus for which patients should receive treatment." – Norway*
- *"Ultiva got delivered only occasionally for about 2 years" – Germany*
- *"Phenindione - over a year." – United Kingdom*
- *"Fortum injection 500mg, 1g and 2g due to be out until January 2019 already short for over a year." – Ireland*
- *"Tobramycin inj. (Brulamycin) shortage lasted a year there was another brand that was imported and cost almost twice as more." – Hungary*
- *"Aztreonam has been on restricted supply for around 2 years now." – United Kingdom*
- *"Heparin-Natrium (Liquemin 5000 E/0.5 ml) is out of stock for 2 years now." – Switzerland*
- *"Tri-anal suppo's : 2 years, Augmentin : 6 months cefotaxim sandoz: 7 months." – Belgium*
- *"Gentamicin LEK inj sol 10x2ml/80mg - 8 months; eye drops Ophtalmo-septonex gtt oph - drops with antiseptic combination of drugs - 18 months." – Czech Republic*

Up to three years

- *"cefamandol = 3 years, still not available amox/acide clav = several months, still in contingency ropivacaine = several months, still in contingency." – France*
- *"Hyaluronidase (Hylase Riemsler), for our cytotoxic agents paravasation set and operating theatre of our clinic for ophthalmology, not available for over two years because of production problems." – Germany*
- *"The shortage of IMMUCYST BCG INMUNOTERAP 27MG 3 INJECTABLES INTRAVESICAL 1ML even meant the impossibility of treating new patients with bladder cancer and the substitution by other alternative drugs, other presentations and even other doses. The supply was not restored until two or three years later." – Spain*
- *"Co'trimoxazole IV has been in shortage for a few months at a time for last 3 years." – United Kingdom*
- *"Penadur, out of stock since 2015." – Belgium*

More than three years

- *"4 year (Antepsin - sucralfat oral) since 2014" – Finland*
- *"Shortage claventin (ticarcilline/ac clav) since 3-4 years" – France*
- *"more than 3 years (4-DMAP)" – Germany*
- *"Pentagastrin (used for the so called Pentagastrin test) has been out of stock since more than 5 years if I'm not mistaken." – Germany*
- *"gentamicin, longest shortage in Switzerland since Minimum 5 years" – Switzerland*

- *“Both UK Sucralfate (Antepsin) tablets and suspension have been unavailable for four years.”* – United Kingdom

Unspecified number of years

- *“Worldwide shortage of Adrenaline Minijets for emergency trolley for a number of years.”* – Ireland
- *“maxipime - cefepime. Was several years not available before was communicated, that it would not come again. Later it was brought by generic companies.”* – Switzerland
- *“Adrenaline 1:10,000 10ml Prefilled syringes. Critical resuscitation medicine. Intermittent supply problems for years but previously there was NO alternative on the market. Luckily now new supplier.”* – United Kingdom

10. Early reporting (Q13-15)

Q13. Does your country have a reporting system for shortages in place?

When asked if their country had a reporting system in place, 67% of respondents answered 'Yes' (N=1,029). However, when looking at the results broken down by country the response is much more varied, as seen in [Figure 8](#), where the results are ordered by the percentage of respondents in the country answering 'Yes'.

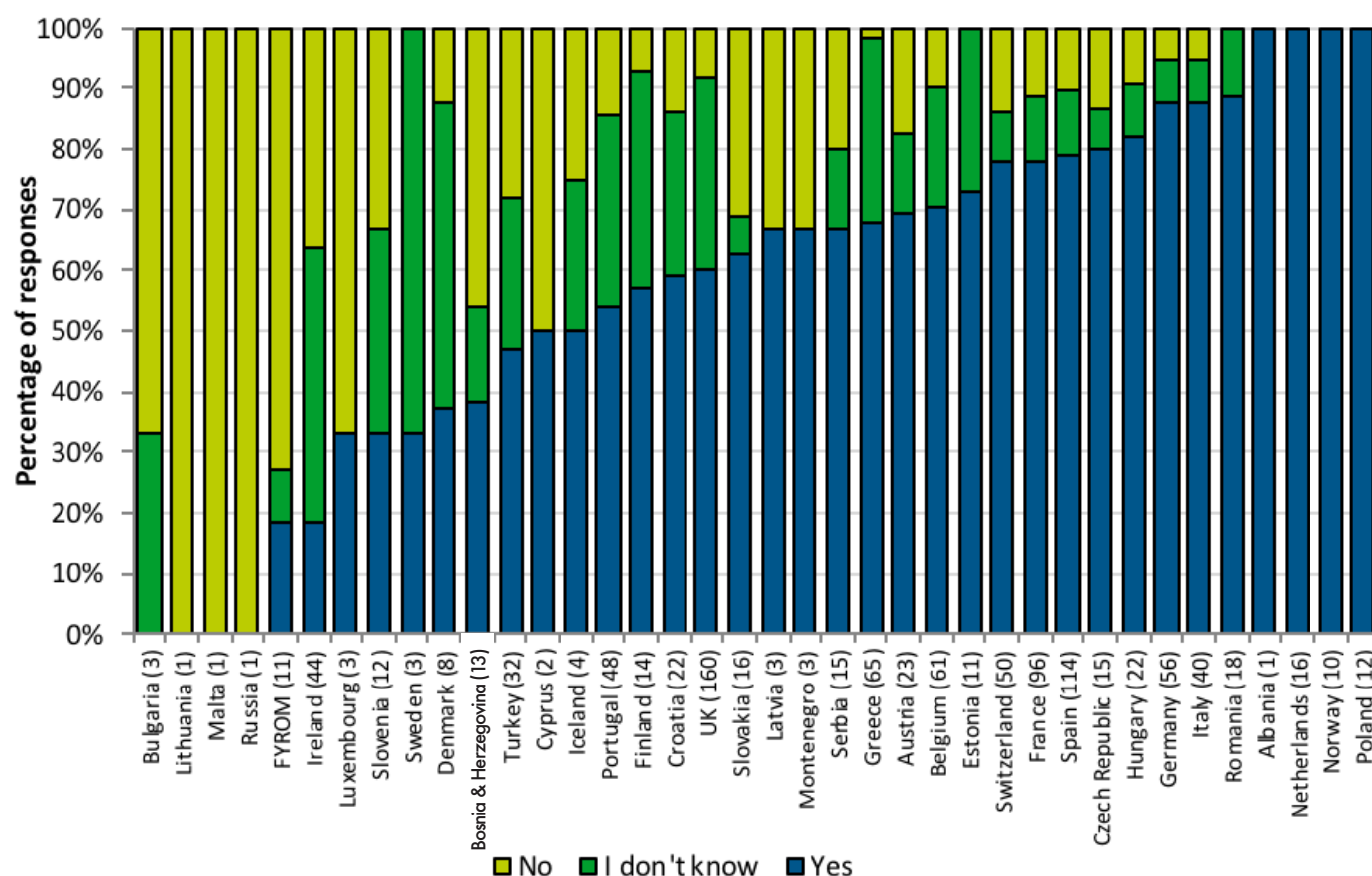


Figure 8 Percentage of responses for question 13 'Does your country have a reporting system for shortages in place?', grouped by country. (N=1,029). Numbers in brackets represent number of responses from that country.

Since this question is asking about a country level reporting system, it is surprising to see such a mixed response in individual countries. An explanation for this could be some of the respondents answering 'No' are not aware of the reporting system in place in their country, meaning work needs to be done in increasing awareness of such systems and the process in that country for reporting medicines shortages.

Q14. Please briefly explain how it works and include website if available.

In most countries the reporting system is part of a website, with data typically provided either by industry or hospitals. The completeness of the list of shortages and quality of other information provided varies by country. A list of website links and additional information based on the responses are provided in full in Appendix A. Some of the freetext responses have also been incorporated into the analysis of question 15.

Q15. Do you judge it as effective/working/functional?

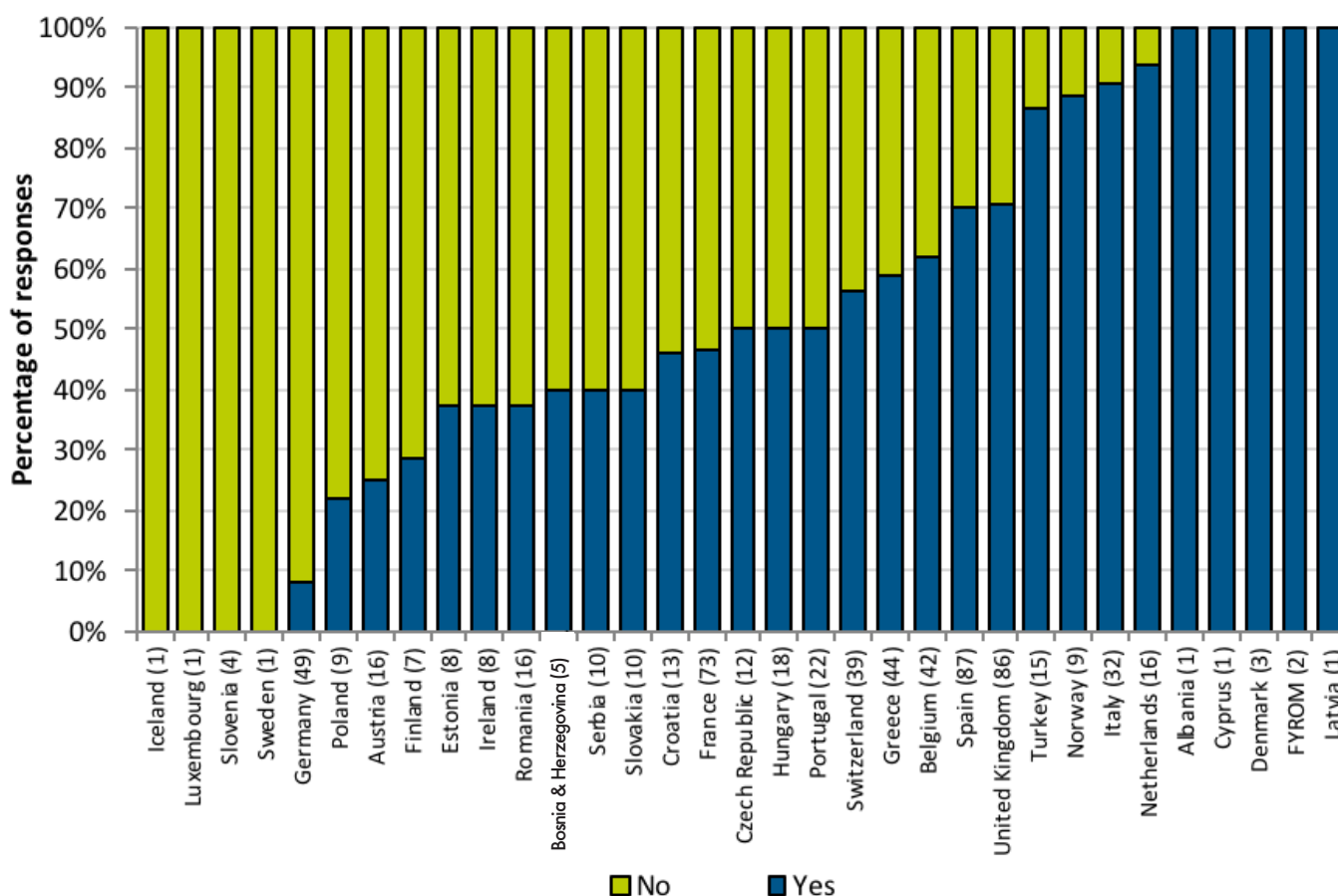


Figure 9 Percentage of responses for question 15 ‘Do you judge it as effective/working/functional?’, grouped by country. (N=663). Numbers in brackets represent number of responses from that country.

Only 56% of the 663 participants who answered this question judged their countries reporting system for shortages to be effective/working/functional. When grouping the results by country, there is a large range of responses, as seen in **Figure 9**. Participants were also asked to explain how their country’s reporting system works, which was used to further investigate the response from countries who gave very positive or negative opinions of their reporting systems.

In Poland, 22% of respondents (N=9) judged their system to be effective. A freetext response from Q14 provides some insight into this, as the self-reporting of shortages from pharmacies may be underreported, and the system is not user-friendly: “Chief Pharmaceutical Inspectorate collects data reported by pharmacies regarding drug shortages and produces a list of medicines at risk of being illegally exported. Pharmacists are obliged to report shortages online giving details of nature of shortage. Shortages are underreported due to pharmacy staff and time shortages. The reporting system is web based but considered by many not user friendly which may hinder the reporting system.” – Poland.

In Slovenia (0% positive, N=4) the main reported issue was that the output to pharmacists from the reporting system was not useful: “The main problem, as we see it is, that JAZMP (reporting system) does not inform pharmacies about received notifications, so we are usually notified about a drug shortage from a wholesaler when we’d like to purchase a drug and can’t get it. The information they put on their website is in form of a pdf file with over 600 pages and is certainly not user-friendly because it is hard to search for information.” – Slovenia.

From Germany (8% positive, N=49) there were several responses reporting that the main problem was that their system relies on companies to report shortages, but they are under no obligation to do so: *“The companies report shortages to different institutions which list them in the internet. The list is often not up to date, and not all shortages are listed here because it is not mandatory and there are different limitations (just shortages > 2 weeks etc.).”* – Germany.

In Cyprus 100% of respondents reported the system to be effective (N=1). The freetext response details a forum used by hospitals to share information on shortages which seems to be an effective and low cost solution, although it relies on people both knowing about it and utilising it: *“We have just created a forum in the common hospital purchasing database (SAP) where every hospital facing a drug shortage can notify other hospitals and seek for help.”* – Cyprus.

In Latvia (100% positive, N=1) a website is used where shortages can be reported by anyone, increasing the likelihood of a shortage being reported, addressing an issue observed in other systems. *“Anyone (hospital, pharmacy, patient) could use this website to make our medicines agency know about shortage.”* – Latvia.

In the Netherlands (94% positive, N=16) the shortage information is frequently updated, which based on some of the feedback seen in Q10, is important for helping pharmacists to manage shortages. *“The national society of pharmacist publicise the known shortages and alternatives on their website. It is updated on a daily basis.”* – Netherlands.

11. Impact of shortages (Q16-22)

Q16. Are causes for medicines shortages reported by suppliers/producers to health authorities/hospitals in your country?

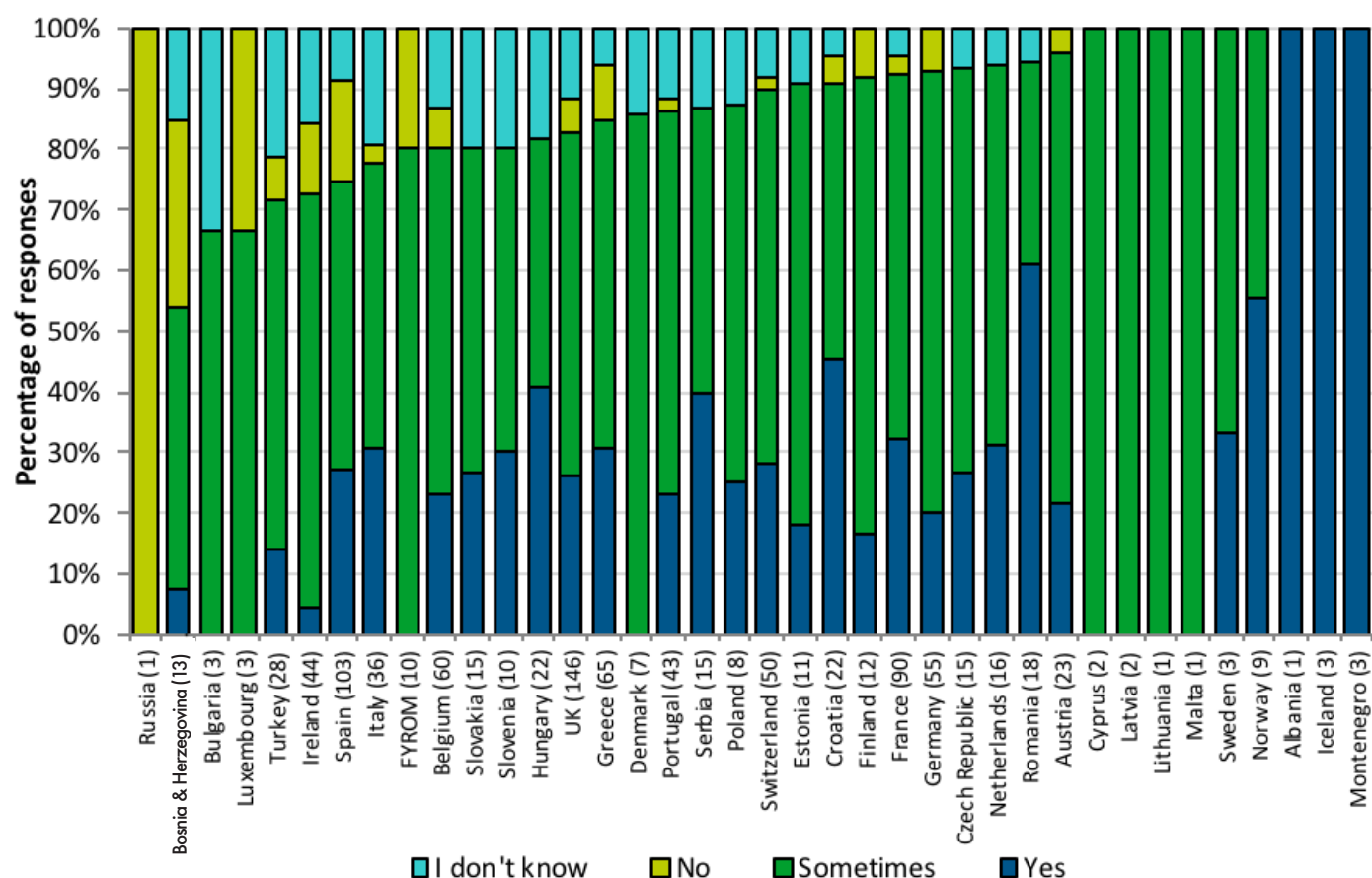


Figure 10 Percentage of responses for question 16 'Are causes for medicines shortages reported by suppliers/producers to health authorities/hospitals in your country?', grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

Of the 969 respondents who answered this question, the most common was 'Sometimes' with 57% of the responses, followed by 'Yes' with 27% of the responses. Responses for 'No' and 'I don't know' were much lower, at 7% and 9% respectively. The results broken down by country can be seen in **Figure 10** where it can be observed that in most countries the causes for medicines shortages are reported by suppliers/producers at least sometimes.

An intuitive assumption may be that countries where causes for shortages are frequently reported by suppliers may correlate with countries whose reporting system for shortages is deemed effective, as they may have up to date information from suppliers to share. However, several countries stand counter to that theory, for example, Iceland, Romania, Croatia, Sweden and Germany all have a comparatively high proportion of 'Yes' responses to causes for shortages being reported by suppliers, but all have less than 50% of respondents reporting the system to be effective.

Q17. In the case of a medicine in short supply, how often do you estimate your hospital is able to provide treatment to a patient by providing a therapeutic equivalent or near equivalent medicine, without major disruption to their treatment?

This question received 969 responses, with the most common response being 'most of the time' (69% of responses). 19% responded 'sometimes', and 9% responded 'all of the time'. There were few responses for 'rarely' and 'never', which received 2% and 0.3% of responses respectively.

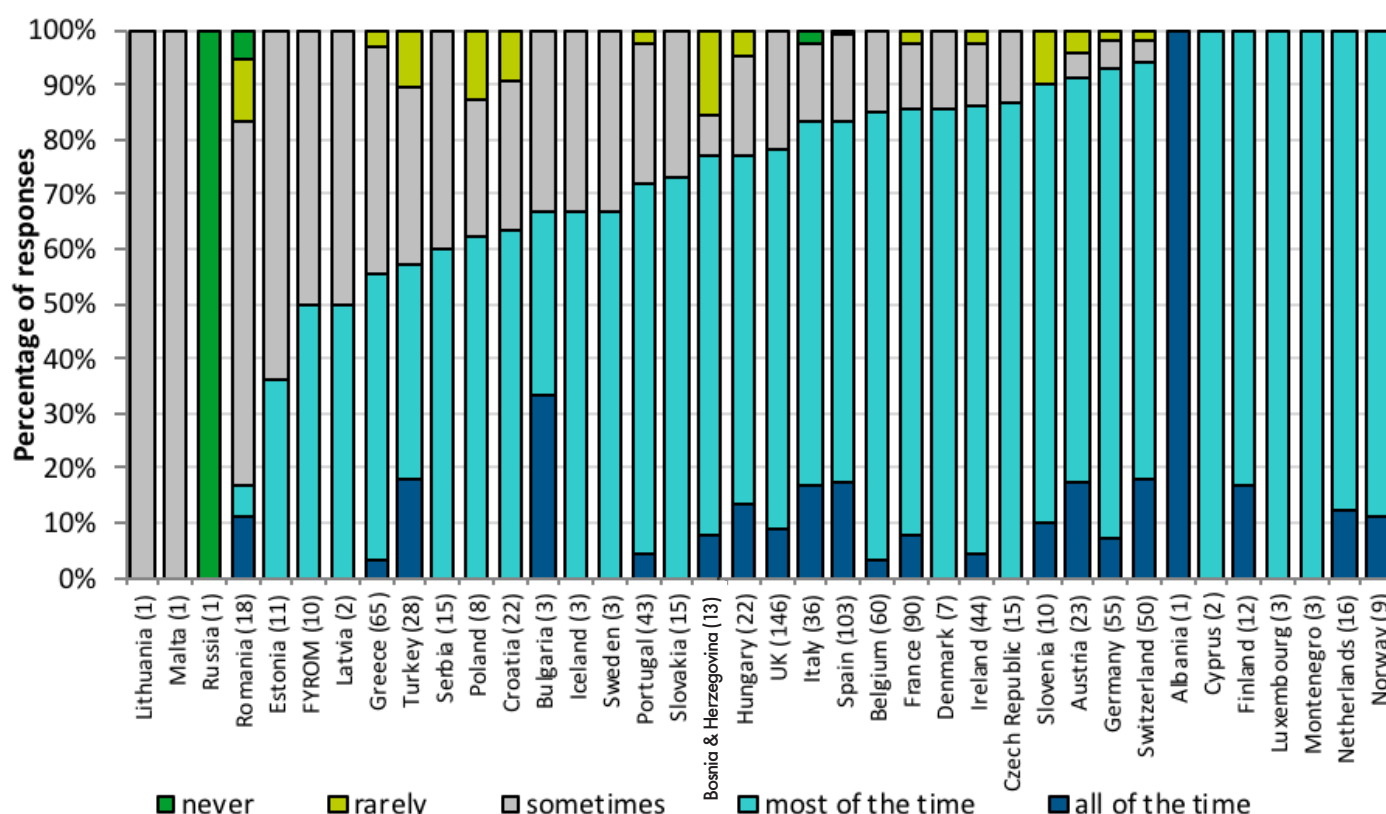


Figure 11 Percentage of responses for question 17 'In the case of a medicine in short supply, how often do you estimate your hospital is able to provide treatment to a patient by providing a therapeutic equivalent or near equivalent medicine, without major disruption to their treatment?', grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 11**, where they are sorted by the percentage of respondents reporting their hospital is able to treat a patient by providing alternative medication without major disruption at least most of the time (aka 'most of the time' responses + 'all of the time' responses). There are only 5 countries where less than half of respondents report not being able to provide alternate medication without disruption at least most of the time (Lithuania, Malta, Russia, Romania and Estonia).

These data were compared to results from the 2014 survey. The median percentage of respondents in a country reporting their hospital is able to provide treatment to a patient by providing alternative medication without major disruption at least most of the time decreased, from 80% in the 2014 survey to 78% in 2018 survey, although a sign test determined this decrease was not statistically significant ($Z = -1.540$, $p = 0.124$, $r = -0.296$).

Q18. In an average week in your hospital, how much time (staff working time) do you estimate is diverted because of medicines shortage problems?

The most frequently given responses to this question was 'up to five hours', with 46% of 969 respondents

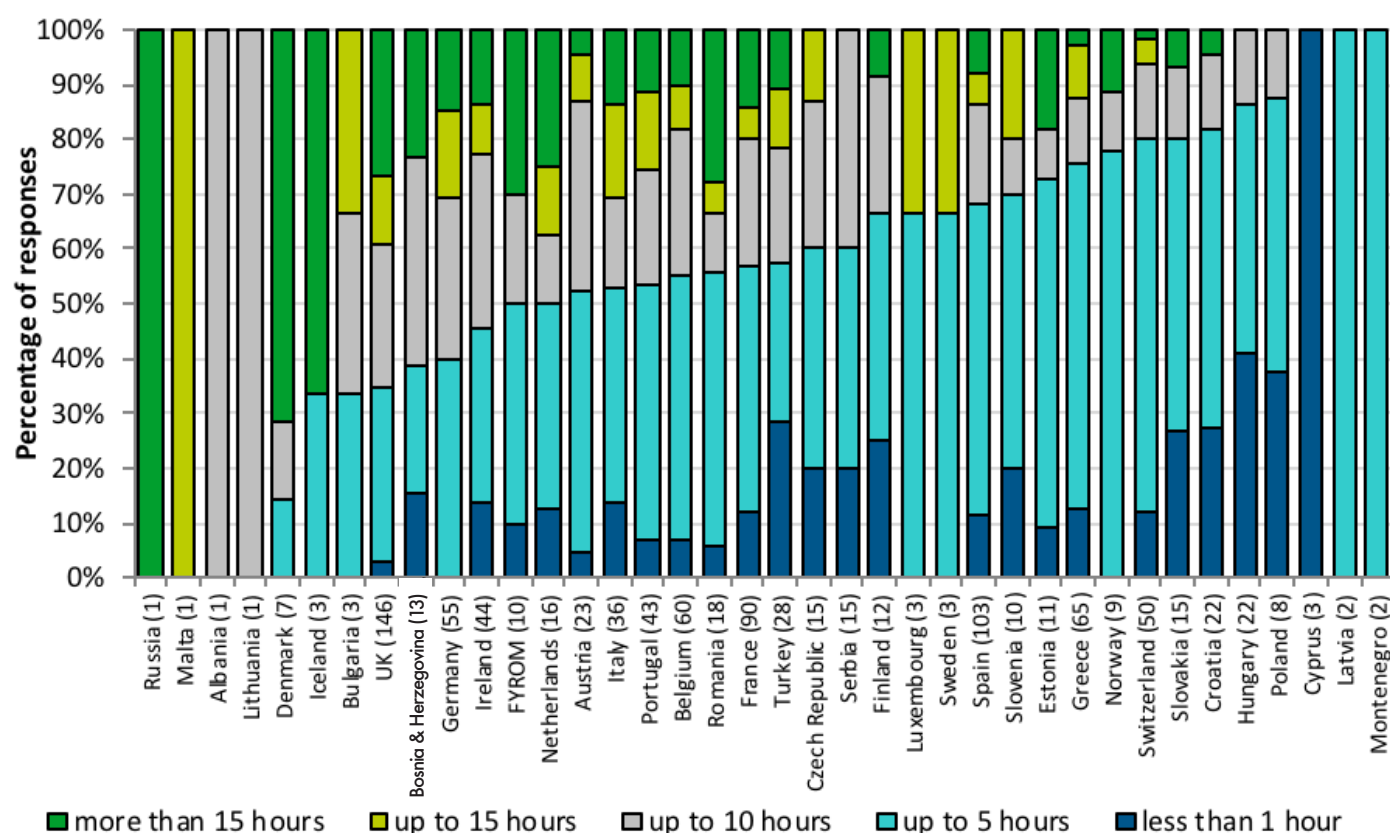


Figure 12 Percentage of responses for question 18 'In an average week in your hospital, how much time (staff working time) do you estimate is diverted because of medicines shortage problems?', grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

Figure 12 shows the responses grouped by country and sorted by percentage of respondents in a country reporting that more than 5 hours per week are spent dealing with medicines shortages (aka responses for 'up to 10 hours', 'up to 15 hours' and 'more than 15 hours'). Cyprus is the only country where the most frequent response was 'less than 1 hour', and Denmark, Iceland and Russia are the 3 countries where the most frequent response was 'more than 15 hours'.

This question was also asked in the 2014 survey, and the results were compared to see if the amount of time spent dealing with medicines shortages had changed. A paired samples t-test showed a statistically significant increase in the mean percentage of respondents in a country reporting that more than 5 hours per week are spent dealing with medicines shortages for the 2018 survey (M = 42.0%, SD = 18.7%) compared to the 2014 survey (M = 33.1%, SD = 25.9%), $t(26) = 2.275$, $p = 0.031$, $d = 0.438$.

Q19. Do you agree with the following statement? "Medicines shortages in my hospital are having a negative impact on patient care."

Of the 969 respondents who answered this question, there were very few who disagreed or strongly disagreed with the statement (8% of responses and 1% of responses respectively). The majority of respondents agreed or strongly agreed that medicines shortages in their hospital are having a negative impact on patient care (47% and 31% respectively), and 13% of respondents were unsure.

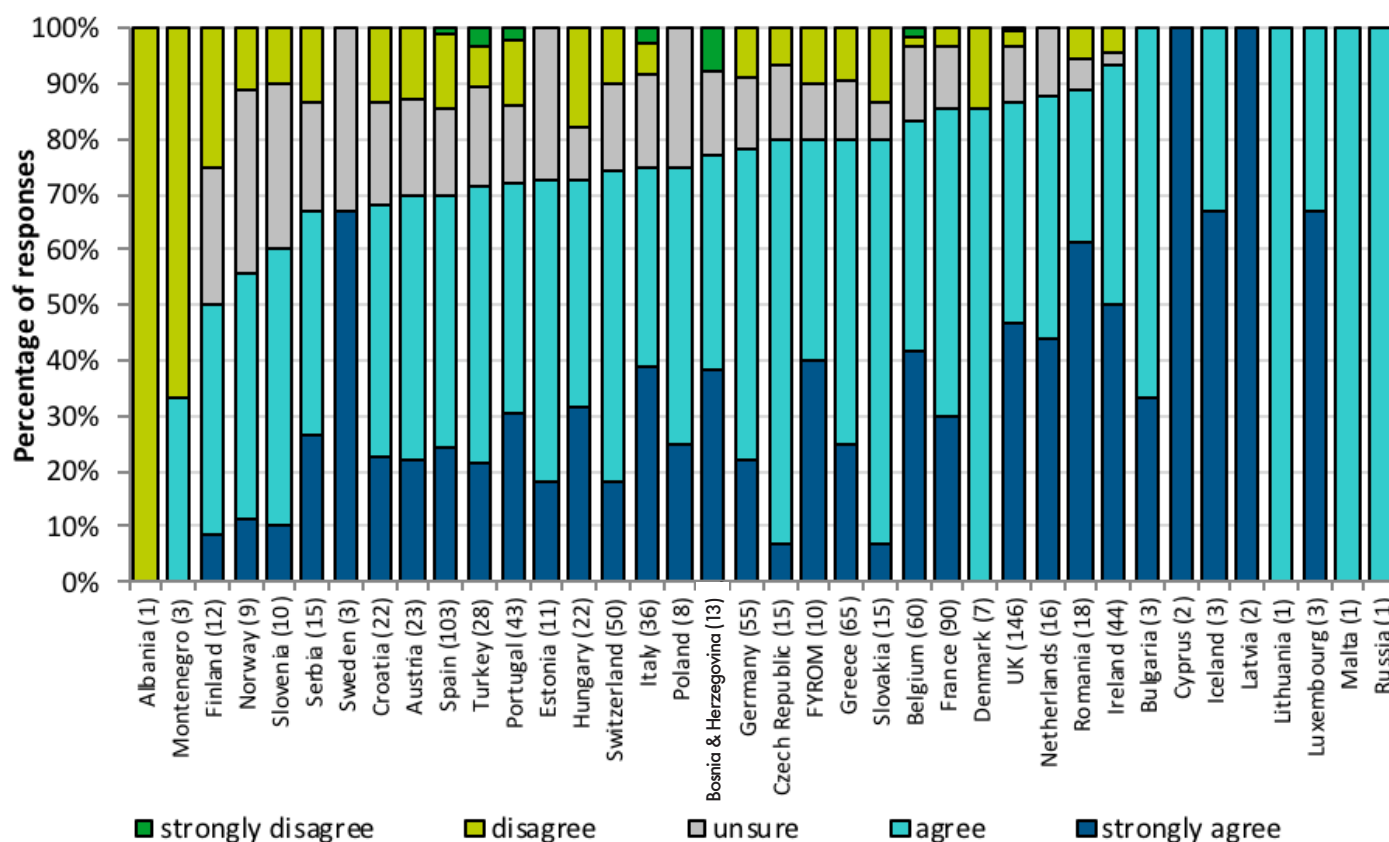


Figure 13 Percentage of responses for question 19 'Do you agree with the following statement? "Medicines shortages in my hospital are having a negative impact on patient care."', grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 13**, where they are sorted by the percentage of respondents who at least agree that medicines shortages are having a negative impact on patient care (aka 'agree' responses + 'strongly agree' responses).

Results from the 2018 survey were compared to results from the 2014 survey. The median percentage of respondents in a country reporting they agree or strongly agree that medicines shortages are having a negative impact on patient care decreased, from 79% in the 2014 survey to 77% in 2018 survey, although a Wilcoxon signed-rank test determined this decrease was not statistically significant ($Z = -.175$, $p = 0.861$, $r = -0.033$).

Q20. Do you agree with the following statement?" Medicines shortages in my hospital are having a negative impact on my overall budget."

Budgetary issues caused by medication shortages can be due to having to pay more to procure a drug from another supplier or paying more for an alternative drug (see Q21), having to devote more staff time to the issue (see Q10) or due to the impact on patients (such as potentially increased length of hospital stay, see Q22).

There were 969 responses to this question, with most choosing either 'agree' (43% of responses) or 'strongly agree' (38% of responses). The remaining choices were 'unsure' (13%), 'disagree' (5%) and 'strongly disagree' (1%).

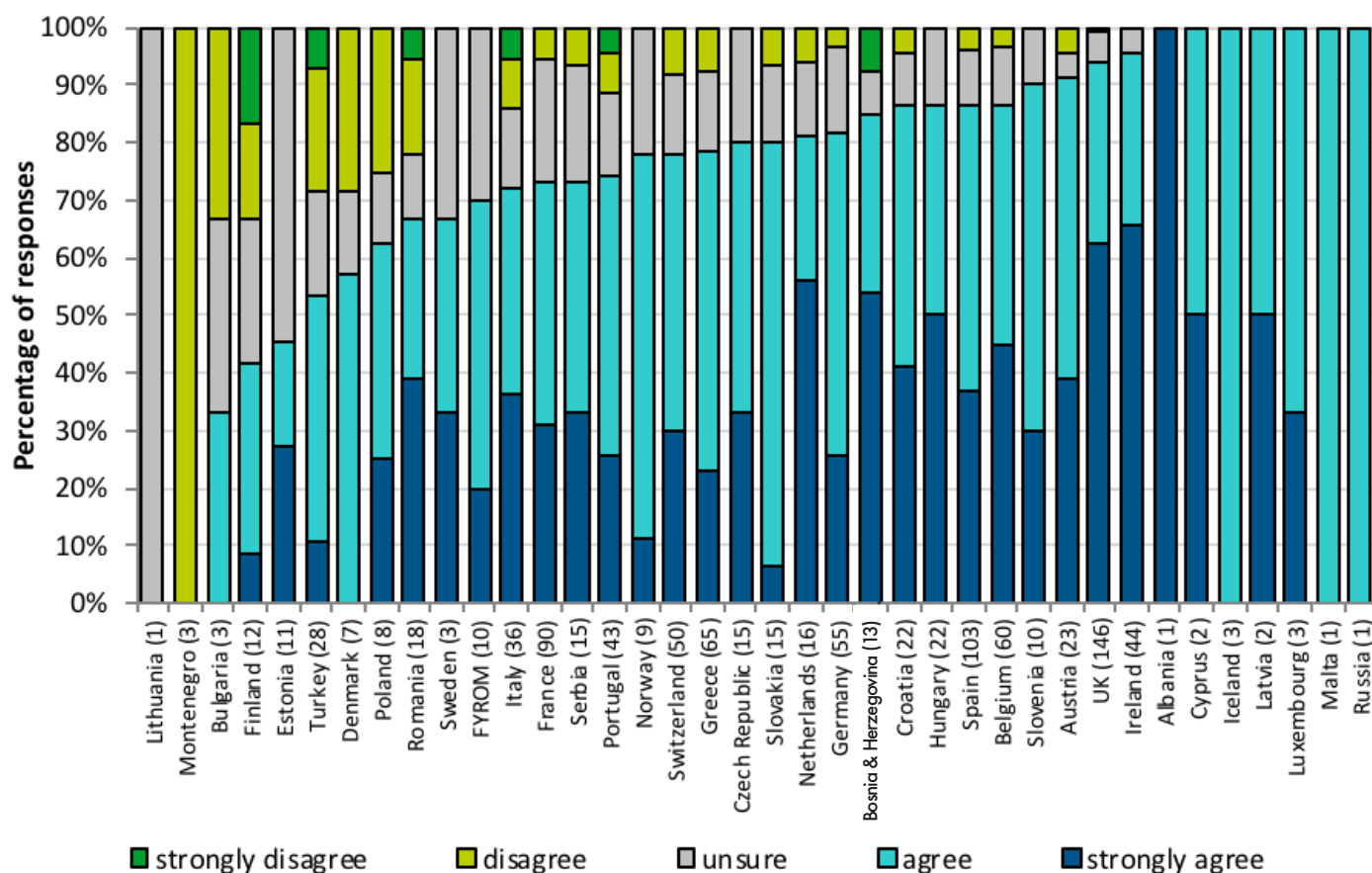


Figure 14 Percentage of responses for question 20 ‘Do you agree with the following statement?’ ‘Medicines shortages in my hospital are having a negative impact on my overall budget.’, grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

The responses grouped by country are shown in **Figure 14**, where they are sorted by the percentage of respondents who at least agree that medicines shortages are having a negative impact on their budget (aka ‘agree’ responses + ‘strongly agree’ responses).

Countries where over half of the respondents strongly agreed with the statement were Bosnia and Herzegovina, Netherlands, UK, Ireland and Albania. There were very few ‘strongly disagree’ responses overall, and countries which had more than 1 response of strongly disagree were Finland, Turkey, Italy and Portugal.

Q21. In case of shortage, how often do you have to pay a higher price to procure the drug from another supplier/hospital?

63% of responses for this question (N=969) report having to pay a higher price for drugs from alternate sources at least most of the time (46% most of the time, 17% all of the time), adding further evidence of the adverse effect on budgets due to medication shortages.

Only 6% of respondents rarely must pay a higher price for procurement from alternate sources, and 2% report never having to pay a higher price.

The results grouped by country can be seen in **Figure 15**, where the data has been sorted by the percentage of responses reporting at least most of the time. Interestingly, Cyprus, Lithuania and Montenegro only have responses for never or rarely.

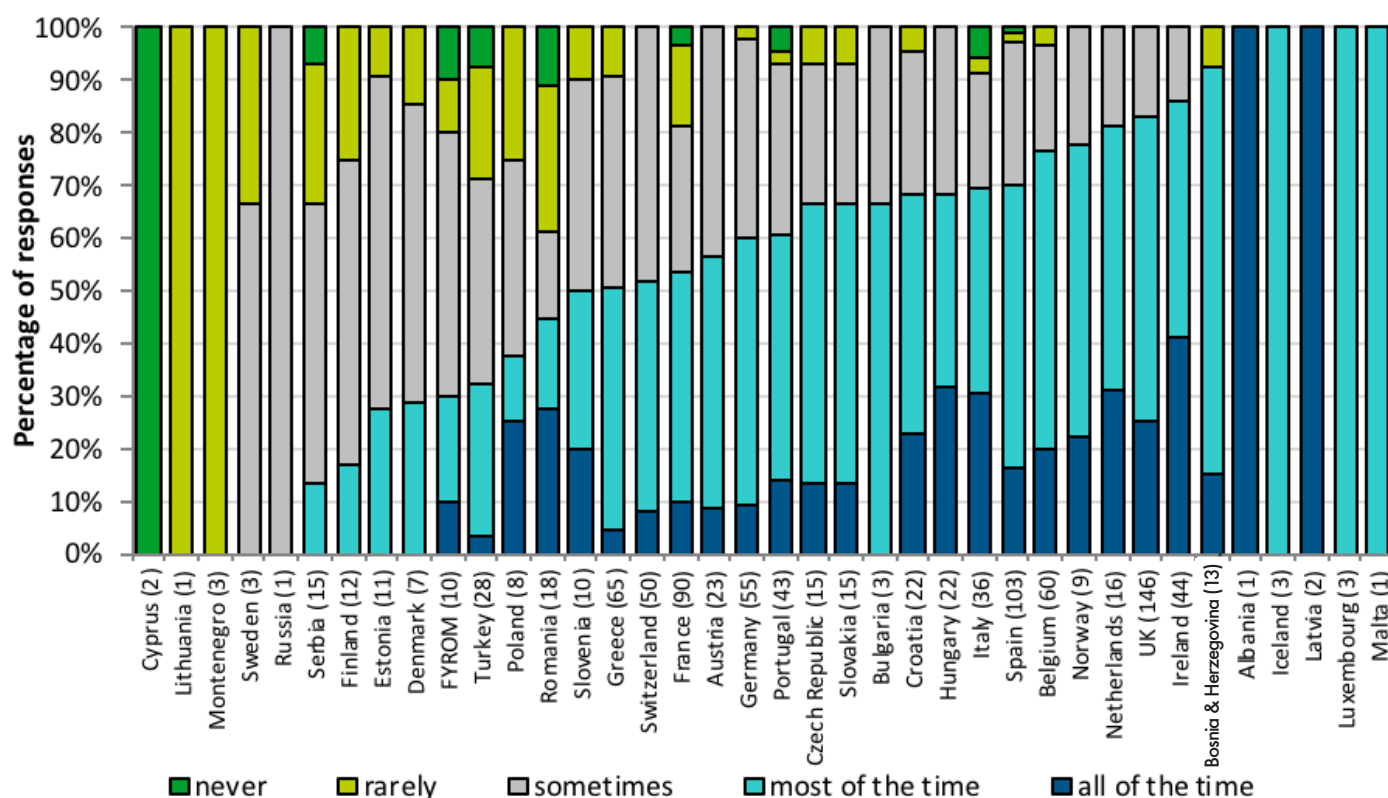


Figure 15 Percentage of responses for question 21 'In case of shortage, how often do you have to pay a higher price to procure the drug from another supplier/hospital?' grouped by country. (N=969). Numbers in brackets represent number of responses from that country.

Q22. Please provide any relevant examples from your hospital over the past year of the impact medicines shortages have had on patient safety/welfare. Tick all that apply.

The issues resulting from medication shortages in the last year are shown in **Figure 16**, which starkly shows the magnitude of this problem.

Over half of the 946 respondents to this question have seen care delayed as a consequence of medication shortages (59% of respondents), whilst the quality of care received by the patient is directly affected with cancellations of care (31% of respondents), medication errors (25% of respondents) and suboptimal treatment for patients (25% of respondents) also being frequently communicated. There were 12 reports of death being caused as a consequence of medication shortages (1% of respondents).

Reported events such as increased length of hospital stay (20% of respondents) and readmissions due to treatment failure (5% of respondents) add further strains to hospitals already struggling with capacity and budgetary issues.

Although not listed as specific option to the question, 19% of respondents chose none of the responses, presumably because they had not experienced any impact on patient care due to shortages or do not know. Responses to the 'Other' category were varied, with 5 responses saying there was no impact on patient care, and 4 responses restating the time burden of dealing with shortages and having less time to focus on patient care.

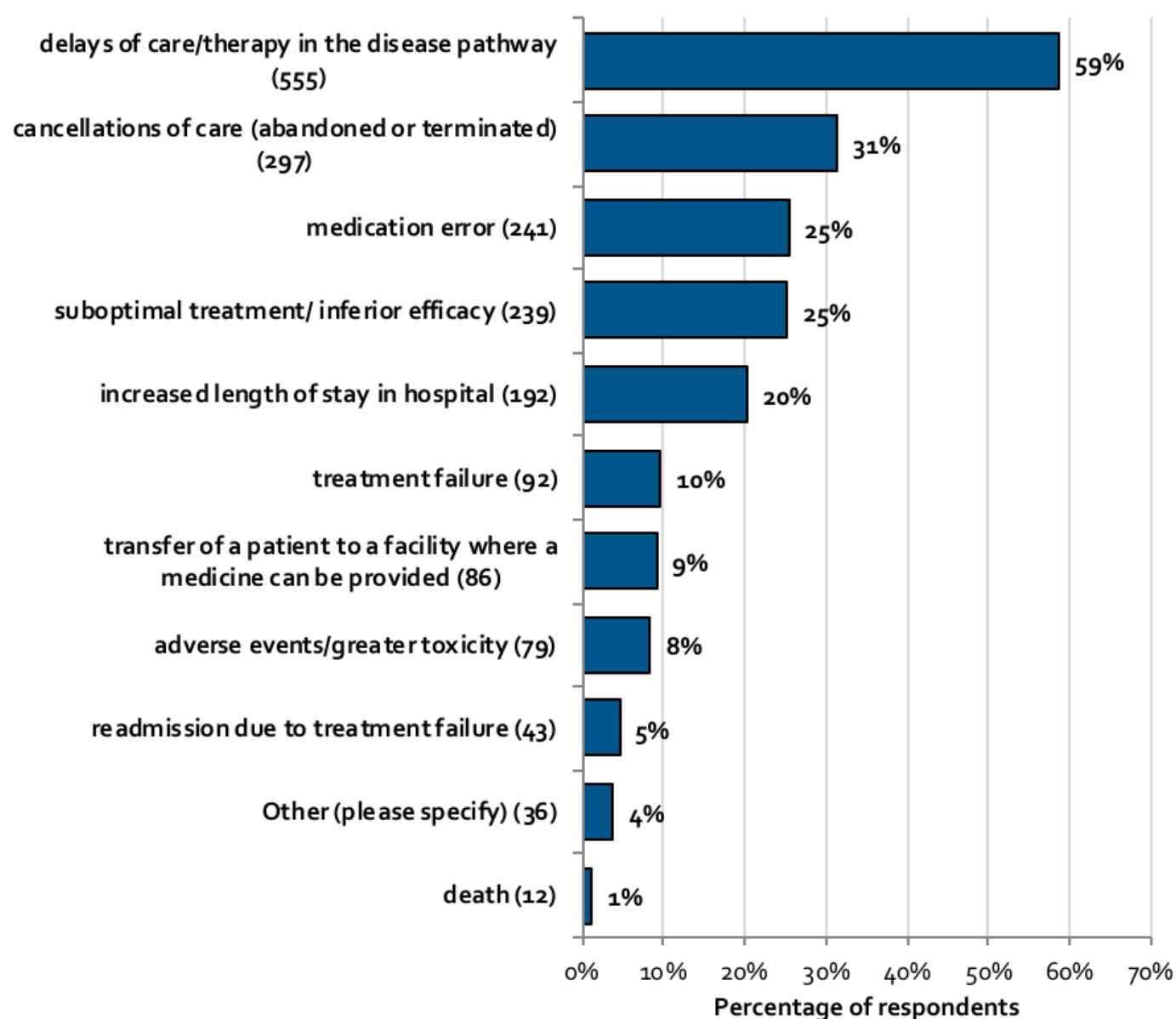


Figure 16 Percentage of participants in the survey who identified this category of impact on patient care due to medicines shortage. (N=946) (Note that this was a tick all that apply question)

12. Managing problems caused by shortages (Q23-26)

Q23. Please describe practically how a medicine in short supply is usually dealt with to minimise the impact on patient care. (Please tick all that apply)

The most frequently reported action in response to medicines shortages was to inform the prescriber and recommend an alternative (83% of 946 respondents). Over half of the respondents also reported attempting to source medicine from alternate sources, investigate when supply will be restored and to inform the prescriber with no recommendations (60%, 60% and 52% of respondents respectively).

45% of respondents selected both 'inform prescriber and recommend an alternative' and 'inform prescriber of the shortage'. This is explained by the most frequent theme from the freetext comments from the 'Other' category, which was how the course of action depends on the shortage. For example, *"prescribers are informed based on the nature of the drug. if it is a straight swap of generic manufacturer for the same drug it may not be necessary to contact the prescriber. prescribers are contacted in circumstances where there may be an effect on the patient, for example appearance is significantly different, bioavailability is different, change of formulation, different excipients, significant cost pressure, etc. this is not an exhaustive list, each drug is assessed on an individual basis and the best course of action decided."* – Germany.

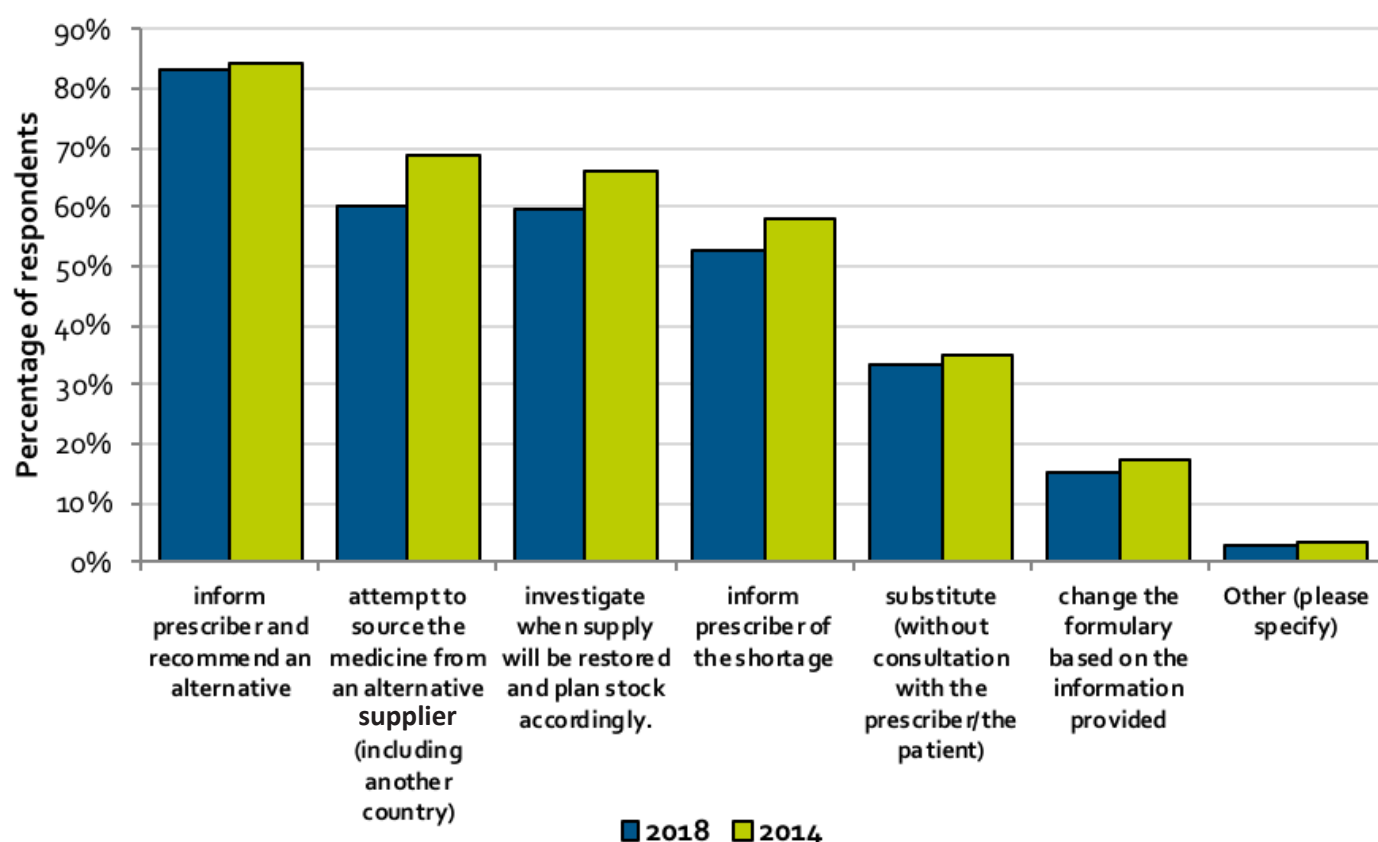


Figure 17 Percentage of participants in the 2018 and 2014 surveys who identified this action due to medicines shortage. (N2018=946, N2014=336) (Note that this was a tick all that apply question in both surveys)

Compared to the 2014 survey data, the percentage of respondents for each category is slightly lower, although the ranking of the options remains consistent, as seen in [Figure 17](#).

Q24. What changes (if any) in practice has your hospital needed to make in order to deal with the shortages problem? (Please tick all that apply)

Of the 946 respondents who answered this question, 62% report their hospital has created communication systems or tools to alert staff about shortages. Other common changes made include readjusting budget plans due to increased expenditure caused by shortages (29%) and reassigning staff's time to deal specifically with shortages (28%). 16% of respondents report that no changes have been required, up from 13% in 2014.

A common theme from the 'Other' freetext comments was that no changes had occurred but due to lack of resources and awareness of the problem (*"it is still a hidden problem but immense"* – Germany, *"No changes done but highly required. Burnout of the pharmacist"* – Spain).

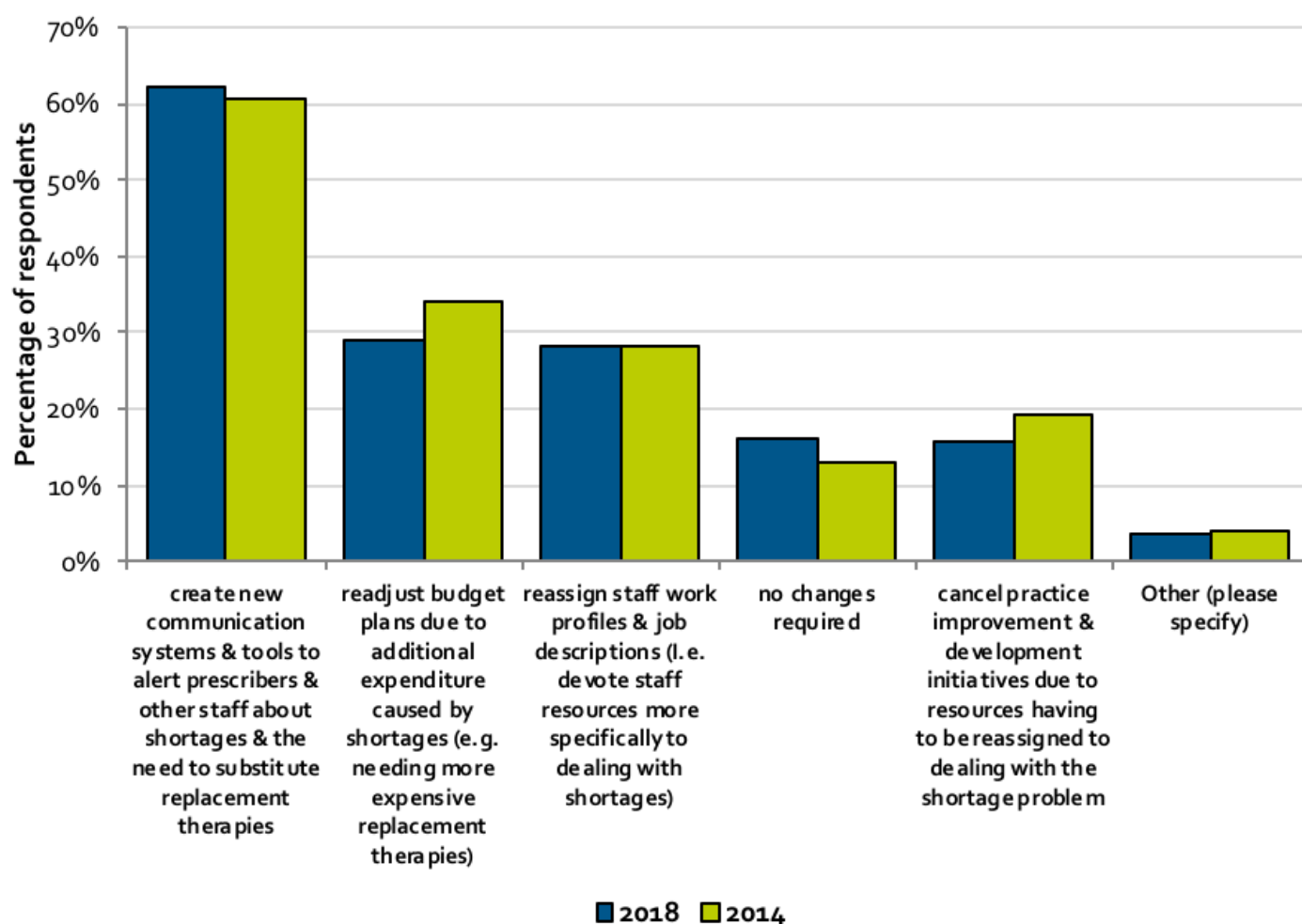


Figure 18 Percentage of participants in the 2018 and 2014 surveys who identified this change in practice due to medicines shortage. (N2018=946, N2014=331) (Note that this was a tick all that apply question in both surveys)

As with the previous question, the responses to this question are similar to the results from the 2014 survey.

Q25. Please provide any relevant anecdotal evidence from your hospital over the past year of the impact medicines shortages have had on patient safety and welfare.

Freetext responses to this question have been linked to the patient safety and welfare categories defined in question 22 to provide more insight into these issues.

Delays of care/therapy in the disease pathway

- *“Delay in care or being prescribed 2nd line antibiotics for an infection. Being forced to prescribe broader spectrum antibiotics because narrower spectrum was not available and increase risk for antimicrobial resistance.” – Ireland*
- *“Delay on the beginning of an antibiotic therapy because of an unknown shortage.” – Spain*

Readmission due to treatment failure

- *“Psychiatric patients stopped their therapy and it caused readmissions.” – Croatia*

Medication error

- *“We had alternative generic parallel of antibiotic which had a confusing name so nurse almost gave the wrong antibiotic to the patient (I have found out by accident -cases like this for sure can be found out more in practice at the ward).” – Croatia*
- *“Drug error due to the look alike sound alike drug 2. shortage of noradrenaline HCl - need to use tartrate and reconstitution with glucose solution.” – Estonia*

Adverse events/greater toxicity

- *“The shortage of amoxicillin IV has lead to treatment of patient with gentamicine/vancomycine with more toxicity!” – Netherlands*
- *“Suspicion of adverse events using some medicines without or insufficiently studies for children.” – Romania*

Increased length of stay in hospital

- *“Longer wake up times after OP, because of Remifentanyl shortage -> Impact on Duration of the stay in intensive care unit -> less beds to offer -> less surgery possible.” – Switzerland*
- *“Multiple antibiotic shortages have led to delayed doses, suboptimal alternative therapy, increased length of stay.” – UK*

Cancellations of care (abandoned or terminated)

- *“Patients on treatment with amiodarone couldn’t get the drug for about 3 months. Some stopped treatment, some where changed to new and more expensive drugs.” – Spain*
- *“Cancellation of cure for shortage of polyvalent immunoglobulins.” – France*

Suboptimal treatment/ inferior efficacy

- *“A patient with NARDELZINE treatment had to stop the treatment during a month and had to change her treatment but it was less adapted.” – France*
- *“Shortage of fractioned heparine caused us to use a therapeutic alternative that has a worse risk/benefit ratio.” – Bulgaria*

Transfer of a patient to a facility where a medicine can be provided

- *“Lack of IgG immunoglobulin and transfer of patient to another hospital where the drug was available.” – Greece*
- *“Shortages of same antibiotics and cytostatics causes sending patients to other facilities.” – Serbia*

There were also some responses where the respondents did not know of any impact because they do not interact with patients (e.g. *No access to this data as hospital pharmacists in Croatia are not included in clinical circle and have no access to hospital wards, no insight in patient files or contact with patients at all.* – Croatia). The role of the hospital pharmacist varies between countries. The EAHP European Statements of Hospital Pharmacy Survey revealed in some countries the role is entirely focused on procurement, whereas in others the role has more clinical focus and more patient facing ⁽⁵⁾.

Q26. In the country you work in, are there national level approaches in place to address the medicines shortage problem e.g. websites with information about current shortages and linked proposed solutions for therapy substitution? If so, please give a short description of these, including reference to both your country of practice, and the extent to which you consider the approach is working.

The responses to this question heavily overlapped with question 14, where respondents described the reporting system for shortages. In many cases, the website used for reporting shortages was the only national level approach to address the medication shortage problem. The amount of information provided (expected return date, reason for shortage, alternative suggestions) varies by country, as does the completeness of the list of shortages.

The list of website links and additional information are provided in full in Appendix A.

13. Regulation (Q27-29)

Q27. Are there any legal regulations in your country to ensure supply over a certain period of time?

Almost half (46%) of the 945 respondents who answered this question were not sure if there are legal regulations in their country ensuring supply over a certain time. The percentage of respondents answering 'Yes' and 'No' were similar (26% and 28% respectively). The high proportion of 'I don't know' responses suggests there is room for improvement on the knowledge of this topic, potentially incorporated into or redirected from a country's reporting system/website.

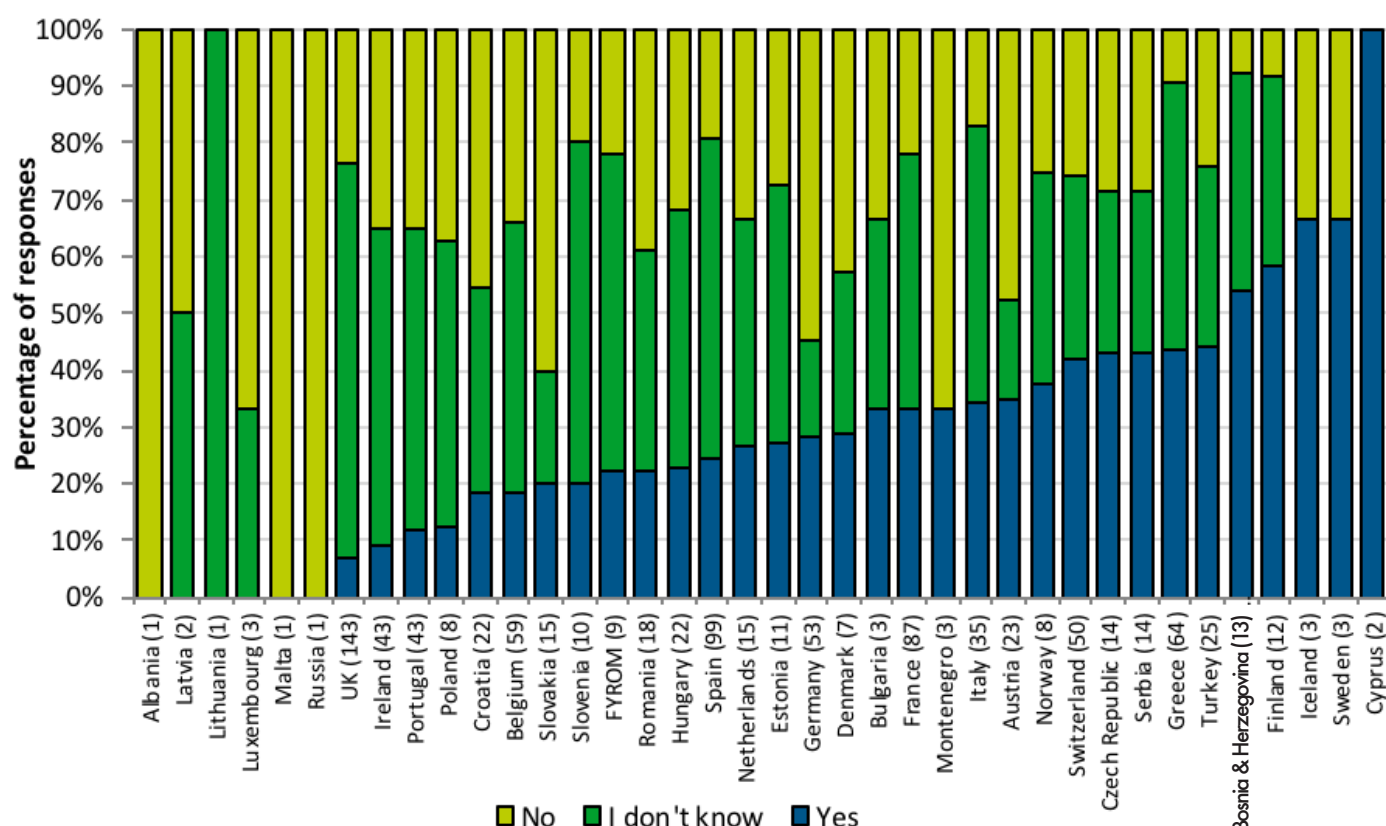


Figure 19 Percentage of responses for question 27 'Are there any legal regulations in your country to ensure supply over a certain period of time?', grouped by country. (N=945). Numbers in brackets represent number of responses from that country.

From looking at the data broken down by country in **Figure 19** it can be seen that there are only five countries where over 50% of the respondents answered 'Yes'.

Q28. For whom? (Are there any legal regulations in your country to ensure supply over a certain period of time?) (tick all that apply)

Following on from the previous question, respondents were asked for whom are there legal regulations (note that people responding 'No' to the previous question were not directed to this question). The most frequent response was the pharmaceutical industry (52% of 360 respondents reported this) closely followed by the hospital pharmacy (50% of respondents). Only 35% of respondents reported that wholesalers are subject to legal regulations to ensure supply.

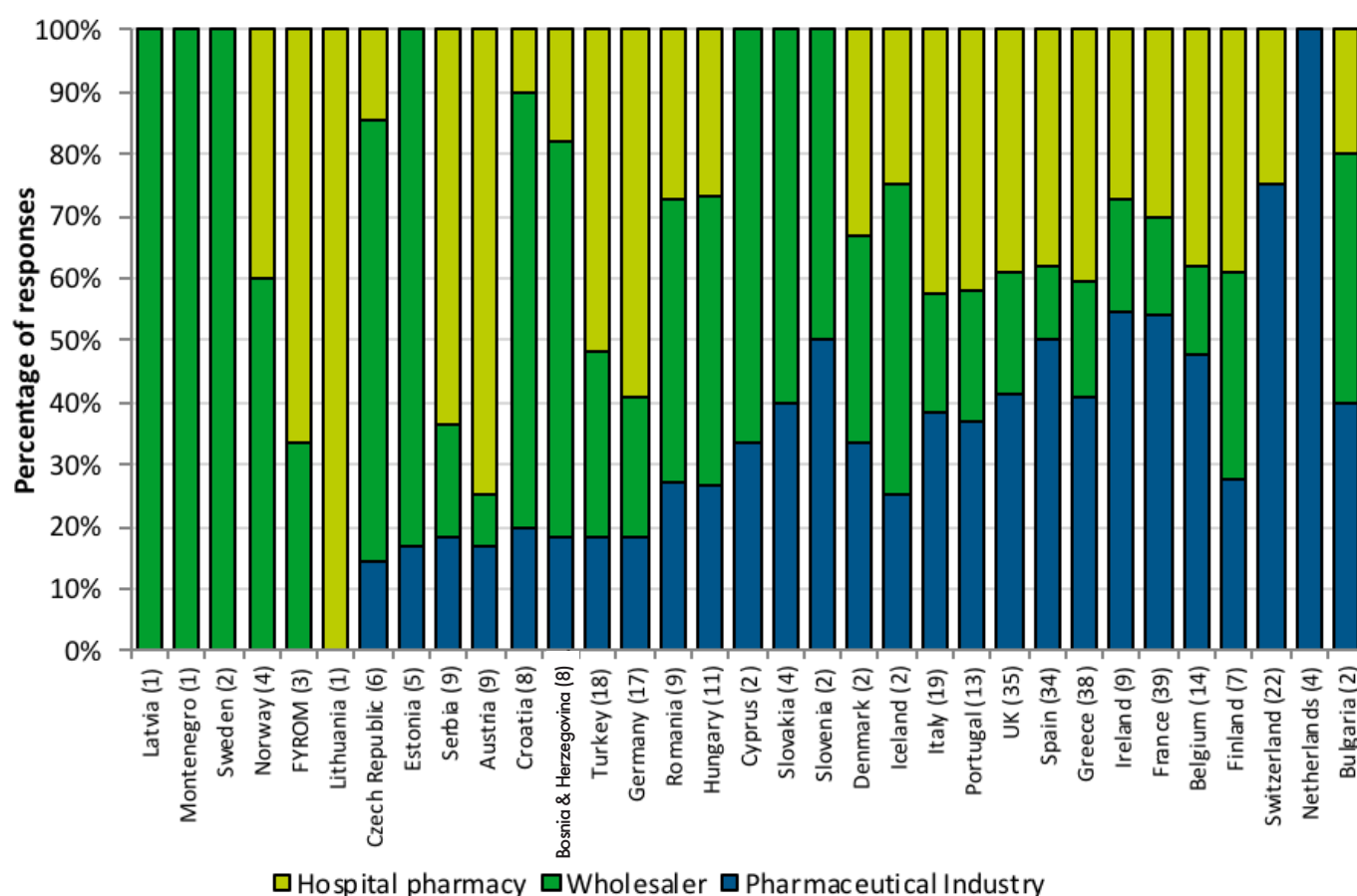


Figure 20 Percentage of responses for question 28 'For whom are there any legal regulations in your country to ensure supply over a certain period of time?', grouped by country. (N=360). Numbers in brackets represent number of responses from that country.

The results grouped by country are shown in **Figure 20**, where the reported subject of legal regulation varies greatly. 21 of 33 countries report all three options as being subject to legal regulations to ensure supply.

Q29. For how long? (Are there any legal regulations in your country to ensure supply over a certain period of time?)

This is the second follow up question regarding legal regulations for ensuring supply in a country. Of the 327 responses to this question 12% are for one week, 25% for two weeks and 23% for three weeks. The most frequent response was 'longer (please specify)' with 129 responses (39%).

Analysis of the associated freetext show 37 responses reporting they do not know, 30 responses reporting a duration of months, 14 responses reporting a duration of years and 17 responses saying as long as required. Data grouped by country is shown in **Figure 21**.

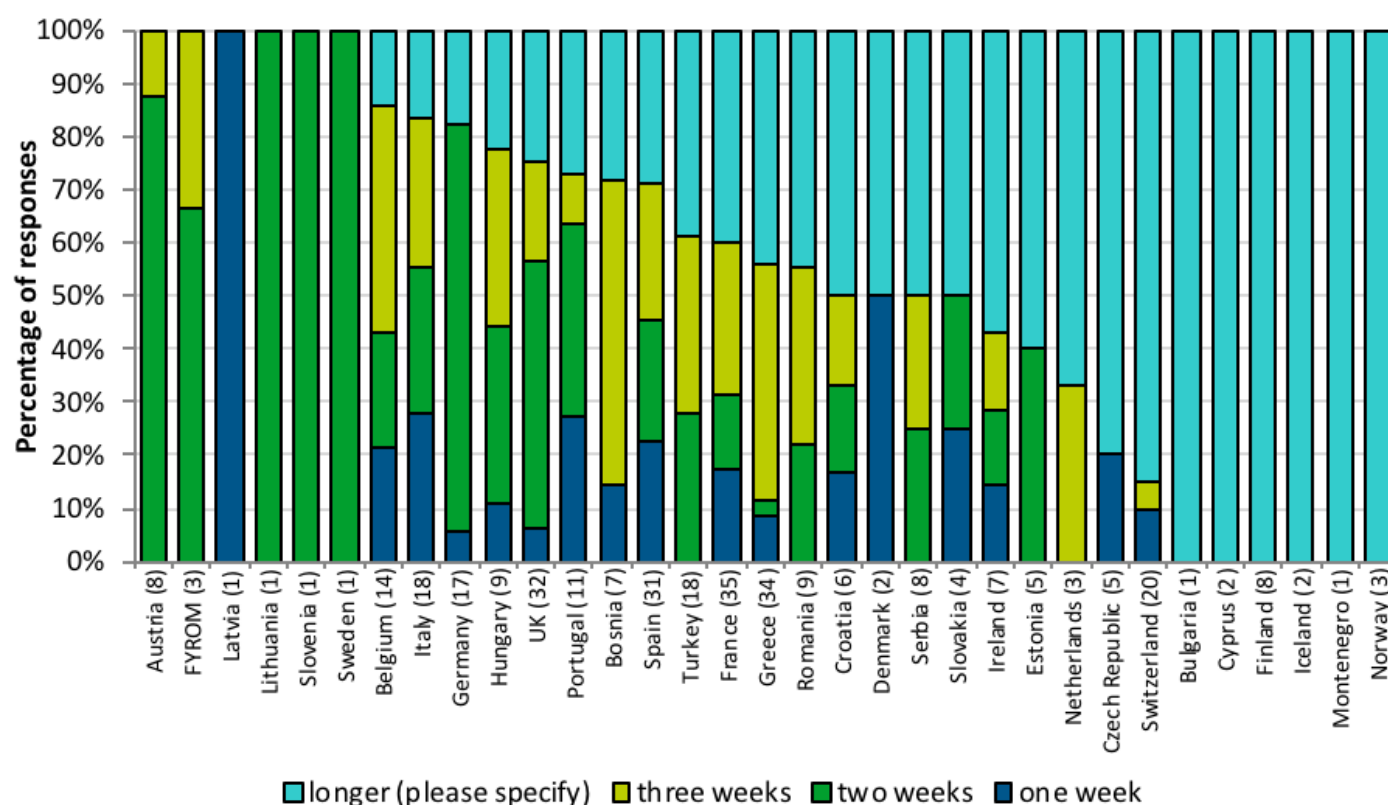


Figure 21 Percentage of responses for question 29 'For how long are there any legal regulations in your country to ensure supply over a certain period of time?', grouped by country. (N=327). Numbers in brackets represent number of responses from that country.

14. Policy solutions (Q30-31)

Q30. Which of the following proposed policy solutions on medicines shortages do you personally support? (tick all that apply)

The proposed policy solution with the most support was the medicines shortages catalogue of the EMA, with 43% of the 918 respondents answering this question choosing this option.

The second most frequent option was 'None of the above' from 42% of respondents, which may cover people who do not support any of the policies, but also people who are not aware of these policies and what they are. Although there was no freetext option in this question, there are freetext responses from subsequent questions saying people are not aware of what these policies are (e.g. "*not sure what these and I don't have time to read up on each option*").

The third and fourth most frequent choices were the Heads of Medicines Agency/EMA taskforce on availability of authorised medicines and the activities of COST Action 15105 - European Medicines Shortages Research Network with 35% and 28% of respondents supporting these policies respectively.

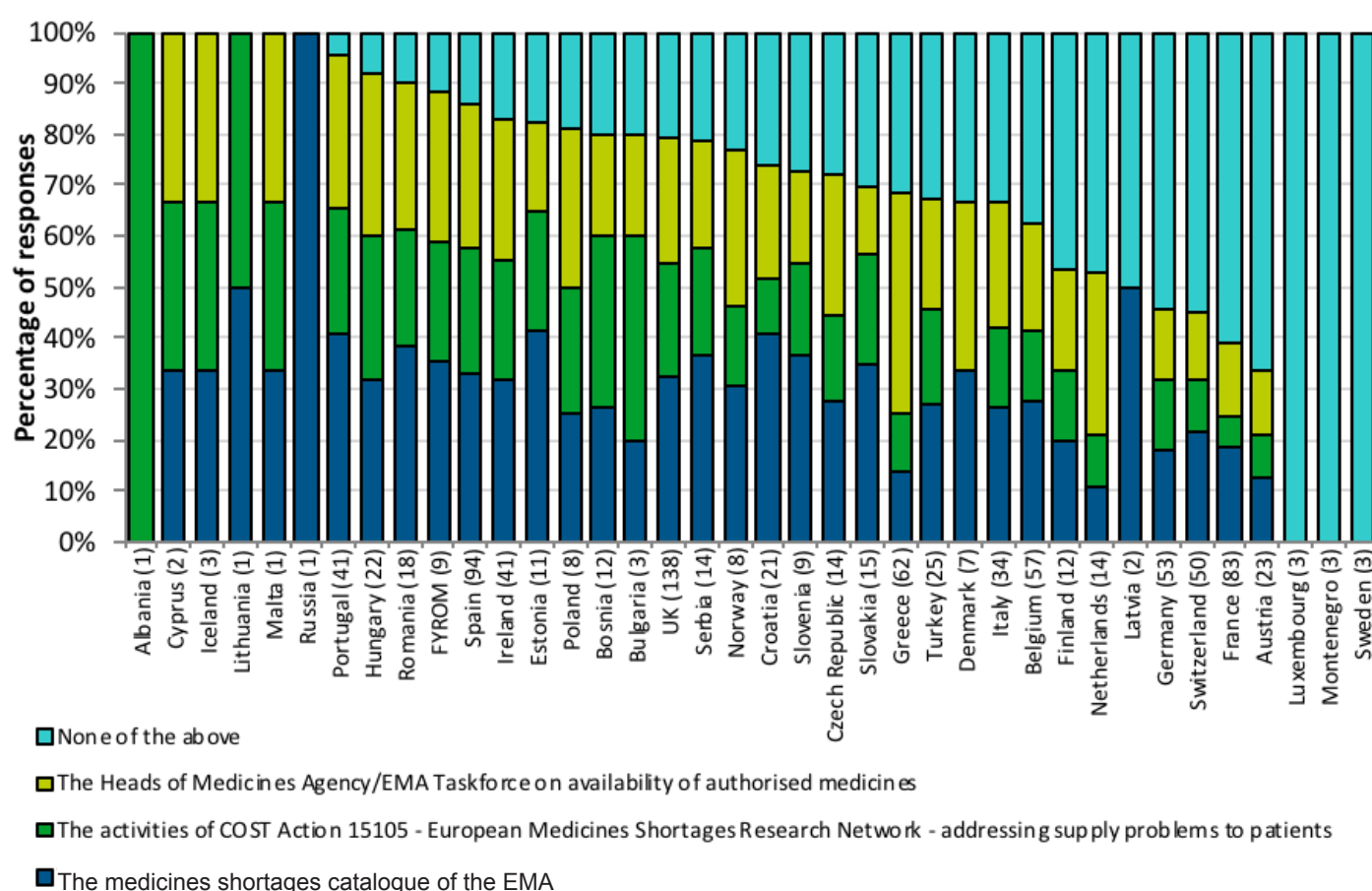


Figure 22 Percentage of responses for question 30 'Which of the following proposed policy solutions on medicines shortages do you personally support? (tick all that apply)', grouped by country. (N=918). Numbers in brackets represent number of responses from that country.

The responses grouped by country can be seen in **Figure 22**, where they are sorted by the proportion of responses answering 'None of the above' to see the variation of support across countries for the policy solutions.

Q31. Which of the following proposed policy solutions on medicines shortages would you personally support? (tick all that apply)

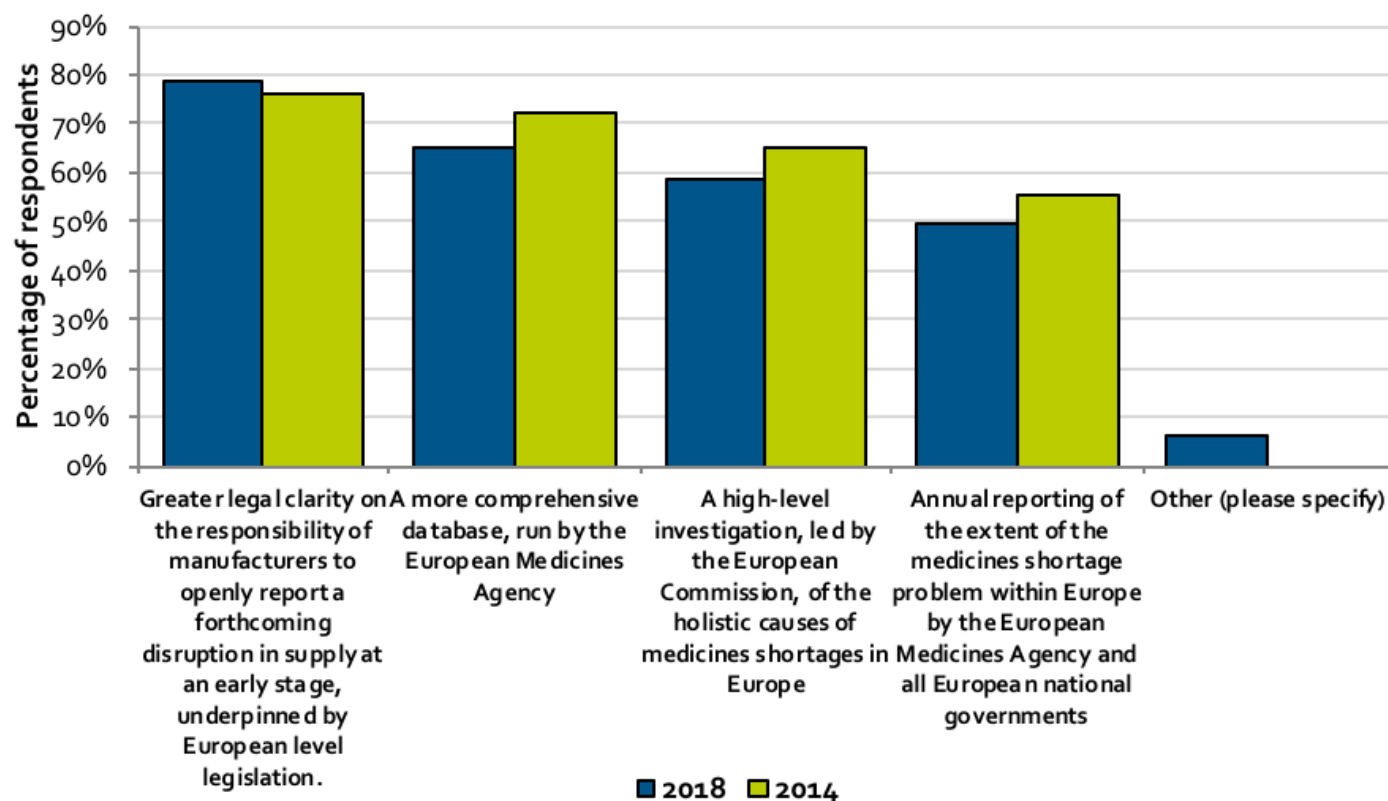


Figure 23 Percentage of participants in the 2018 and 2014 surveys who supported this proposed policy solution. (N2018=918, N2014=319) (Note that this was a tick all that apply question in both surveys)

It is not surprising to see that 79% of the 918 respondents to this question support greater legal clarity on the responsibility of manufacturers to report upcoming supply chain issues at an early stage; in question 10 many comments were observed regarding pharmacists not being aware of supply issues until a delivery did not show up and in question 14 it was observed that the reporting system for medication shortages was weakened by a lack of obligation for manufacturers to share information on supply issues.

A comprehensive database run by EMA was also a popular choice with 65% of respondents supporting the proposal, followed by a high level investigation on the causes for shortages and annual reporting on the extent of the problem with 58% and 50% respectively. This is the same order the proposals were ranked in the 2014 survey. The proportion of responses for 3 of the 4 proposed options is slightly lower in 2018 compared to 2014, but this may be partially due to the fact that respondents were given an 'Other' option in 2018 which was not available in the 2014 survey.

The most common theme from the 'Other' comments is for an increased legal clarity on manufacturers. This obligation should not just cover the reporting of potential shortages, but also help to ensure supply of medicines and maintain sufficient stock levels. Some examples of this are: *"clear responsibility for pharmaceutical companies in the continuity of medicines supply. Discontinuity should have legal and extensive financial consequences for registration holders"* – Netherlands, *"place obligations on manufacturers/ MA holder where they are the sole suppliers of that drug i.e. where there is not an alternative"* – Ireland and *"why not experience sanctions against pharmaceutical industry who cannot provide the medicine during a signed binding?"* – France.

15. Recommendations (Q32)

Q32. Please use the comment box below to make any further comments that might be helpful to EAHP's policy and advocacy activity on the topic of medicines shortages, including reflections on causation, reports of impacts, proposed solutions, and sources of evidence

There were 92 useable freetext responses to this question, which contains recommendations from respondents on how they would like to see the shortages issue managed. Some common themes which emerged from the responses are listed below:

Responses wanting more timely and accurate information from suppliers/manufacturers on shortages (10 responses)

- *"I beg for more effectiveness, more often in our countries, we have to deal with shortages far before authorities are aware of it."* – France
- *"Information on early state by manufacturer (to hospital, ministry of health) is most effective preventing measure."* – Poland
- *"I have ticked the box stating we would like clarity, as I don't think that the actual problem, and /or the replenishment date of the drug is truthful. I say this all the time to suppliers (please be honest) patient care hasn't been affected because of the massive resource we have put in place to manage these shortages."* – United Kingdom

Responses calling for suppliers/manufacturers to be legally obliged to maintain stock levels and ensure supply (8 responses)

- *"Policy resp. the government's should have more legal handle to obligate companies to increase their Stock in the countries of delivering. I miss the serious care of the governments about this problem."* – Germany
- *"More responsibility of producers to assure the presence of their medicines in commerce, even if they have other countries where they commerce these medicines, perhaps where they gain more."* – Italy
- *"Greater legal clarity on the responsibility of manufacturers to organize their own sufficient stock keeping."* – Austria

Responses calling for increased communication/collaboration, either nationally between hospitals, or internationally across Europe (7 responses)

- *"A better information network should be initiated so that information about shortages and availability of medicines among European countries."* – Bulgaria
- *"Better national connection, information exchange and drug distribution between hospitals."* – Croatia
- *"Collaboration between countries is very useful."* – Iceland

Responses calling for a central lead/agency to work on the problem to reduce duplication of efforts (at European, EU, or national level) (8 responses)

- *"A common framework in European level (SOP) could be useful."* – Greece
- *"A record at European level"* – Romania
- *"Every hospital in the UK has pharmacists dealing with the same problem. Valuable loss of time. If one person did it & the rest comply/tweak would be time effective."* – United Kingdom
- *"At the moment we seem to have no National System in Ireland and we rely on information that is drip-fed from Pharmaceutical Reps. The EU needs to lead on this. Also I have serious concerns on how the EU Falsified Medicines Directive will impact on Ireland, as a peripheral EU English Speaking country in the context of Brexit."* – Ireland

Responses relating to importing medicines from other countries and comments on price difference for the same product (11 responses, 4 specifically referring parallel trade)

- *"I don't understand that one product in a country is not available but we can buy the same product in a foreign country in that case the firm should be obligated to import it itself out of the foreign country instead of we have to buy it in the foreign country."* – Belgium
- *"It would be useful if there could be regulation to prevent companies charging significantly higher prices for a very similar medicine imported unlicensed from UK. This can be very costly in regularly prescribed items and must be profitable for these companies."* – Ireland
- *"The cause of medicines shortages is often re-exports from countries where the drug is cheaper- restrictions on the re- export of drugs."* – Czech Republic

Responses with specific mentions of parallel trade (4 responses)

- *"We need an initiative by the European Commission: API must produced in Europe. The production of medicines must be hold in Europe and not in far East. Parallel Imports have to be forbidden."* – Austria
- *"I think EU could ask for a report from every Ministry of Health in EU member countries about this topic (to be compulsory and maybe verifiable, being known that some countries like Romania tend to make fake reports in order to not give explanations about shortages). And parallel export policies with harsh consequences if the regulations are not respected."* – Romania
- *"More actions to control parallel trade."* – Spain

Responses related to identifying the specific causes of shortages (10 responses)

- *"More needs to be done to investigate the root cause of these shortages. I believe the medicines are available, they are just being funnelled to where the manufacturer can make most profit rather than keeping up supply with their regular customers."* – Ireland
- *"I think it would be useful to get information about why are there shortages in general, and about the specific cause in every shortage."* – Spain
- *"A more holistic review needs to be undertaken to understand why shortages occur and try and prevent them. Currently most shortages are managed reactively instead of proactively."* – United Kingdom

Responses with suggestions specifically for the EAHP (3 responses)

- *"The EAHP activity must be more connect with reality of European member states."* – Italy
- *"The same evidence of this problem, for all the hospitals in Europe. I suppose that EAHP can do it."* – Romania
- *"There needs to be a more joined up approach to medicines shortages e.g. FIP, COST, EAHP, EMA. Also needs to be open information on the number of API manufacturers globally."* – United Kingdom

16. References

1. **EAHP**. *Medicines Shortages in European Hospitals - The evidence and case for action*. [Online] October 2014. [Cited: 31 July 2018.] http://www.eahp.eu/sites/default/files/shortages_report05online.pdf.
2. EAHP. *European Statements Survey 2017, focusing on sections 2 (Selection, Procurement and Distribution), 5 (Patient Safety and Quality Assurance) and 6 (Education and Research)*. **Horák P, Underhill J, et al.** 2018, *Eur J Hosp Pharm* Epub ahead of print.
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4. **Field, Andy and Hole, Graham**. *How to Design and Report Experiments*. s.l. : SAGE Publications Ltd, 2003. 9780761973829.
5. EAHP. *European Statements baseline survey 2015: results*. **Horák P, Peppard J, Sýkora J, et al.** 69-75, s.l.: *Eur J Hosp Pharm*, 2016, Vol. 23.

Appendix A: Reporting system for shortages & national approaches in place (Q14/ Q26)

The table below gives a summary of each country's reporting system and other national approaches to the shortages problem. All text are direct quotes from respondent's free text responses. Also included are data from Q13 and Q15 (% respondents in country saying there is a reporting system / % respondents in country judging it to be effective). (These quotes have not been altered)

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/working/functional? (%yes)	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Albania	100%	100%	-	-	-
Austria	70%	25%	www.basg.gv.at	BASG (Bundesamt für Sicherheit im Gesundheitswesen): voluntary list provided by pharmaceutical companies regarding shortages of their products, managed by the public health institution.	AAHP Mailing list of Austrian Hospital Pharmacists: E-Mail discussion Forum concerning drug shortages and strategies to cope with.
Belgium	70%	62%	www.afmps.be	Also FAGG and BCFI publish an overview of out of stock medication.	Working group with the authorities in which the pharmacists are involved. New laws are being drawn to help with solutions on a national level. Industries have to report by law any shortage that will last for 2 weeks. This is under change, a working group has started and it will be changed to 3 days. There will also be an evaluation for each drug shortage, to look for alternatives more quickly and give nationwide advice when a shortage occurs.
Bosnia & Herzegovina	38%	40%	http://www.almbih.gov.ba/	Manufacturers or wholesalers inform medicine agency which provides information on their website.	There is no national level for the medicines shortage problem.
Bulgaria	0%	-	-	-	-
Croatia	59%	46%	www.halmed.hr	There is a list available for download at HALMED (Agency for Medicinal Products and Medical Devices of Croatia). There are no proposed solutions for therapy substitution. Not sure how often is list being updated.	

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/ working/ functional? (%yes)	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Cyprus	50%	100%	Created a forum in the common hospital purchasing database (SAP) .	We have just created a forum in the common hospital purchasing database (SAP) where every hospital facing a drug shortage can notify other hospitals and seek for help.	-
Czech Republic	80%	50%	www.sukl.cz	There are information about shortages and (if available) possible reimbursement. Additionally, www.epin.phoenix.cz - wholesaler - information about current shortages and sometimes solutions for therapy substitution.	-
Denmark	38%	100%	Amgros (the national Danish buyer for medicines for public hospitals) has a database "Amro".	The Danish medicines Agency has a reporting system, besides that Amgros has at internal self reporting system together with til Danish Hospital Pharmacy.	Initiatives for at national taskforce Group to handle medicines shortage problems, there is a person at Amgros who is dedicated to shortage situations.
Estonia	73%	38%	http://www.ravimiamet.ee/en/node/1403	Republic of Estonian Agency of medicines have lists for shortages of medicines. It changes with new information every day.	We also consult with Agency of Medicines about our problems and how to solve it.
Finland	57%	29%	http://www.fimea.fi/tietoa_fimeasta/ajankohtaista/saatavuushairiotiedotteet	FIMEA (Finnish medicine agency) has websites where medicine company can inform about common shortages and proposed solutions, and where pharmacy can get the information.	We also get information from "pharmacists unions" and medicine companies e-mail.
France	78%	47%	www.ansm.fr	In France there is just ANSM that lists medicine shortages and sometimes by what replace the drug. But not really efficient because shortage information is not given early enough (sometimes several weeks without news) and advice are not always direct equivalent.	Some clinical societies give guidelines to switch medicin in shortage (Oxacilin, Amoxicilin/Ac clavulanic, Normal immunoglobulin human).
FYROM	18%	100%	malmed.gov.mk	In my country we address problems to MalMed healthcare services LTD.	-
Germany	88%	8%	www.bfarm.de	The companies report shortages to different institutions which list them in the internet. The list is often not up to date, and not all shortages are listed here because it is not mandatory and there are different limitations (just shortages > 2 weeks etc.).	Also, The drug shortage list for the vaccines is a lot better: https://www.pei.de/DE/arzneimittel/impfstoff-impfstoffe-fuer-den-menschen/lieferengpaesse/informationen-lieferengpaesse-impfstoffe-node.html . recommendation by the German Society of Hospital Pharmacists, disseminated via email.

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/working/functional?	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Greece	68%	59%	www.eof.gr	There is an on-line reporting system for medicine shortages in the website of the National Organization for Medicines (EOF). The tool is supervised by EOF and hospital pharmacists can report any relevant problem. We get quick response by e-mail or phone call from EOF that informs us about the level of information that the National Organization for Medicines already has about the specific shortage problem we reported.	Proposed alternatives are rarely listed in this website.
Hungary	82%	50%	Ogyei.gov.hu	There is a list that's being updated frequently, it's run by the governing body and it's based by the manufacturer's notice. We have a national website where they propose solution for substitutions.	-
Iceland	50%	0%	Medicinal Agency - report	-	-
Ireland	18%	38%	www.HPRA.ie	There is very little that I am aware of in Ireland. On occasion we have contacted the Health Product Regulatory Authority only to find out that they were not aware of the shortage.	Currently there aren't any but I believe the HPRA are setting some centralised procedure, however, no concrete evidence of its existence yet.
Italy	88%	91%	www.aifa.it	AIFA detailed all shortages of medicines in the website after the declaration of the companies, specially if they are brand companies. Information about therapy substitutions are lacking.	-
Latvia	67%	100%	https://www.zva.gov	Anyone (hospital, pharmacy, patient) could use this website to make our medicines agency know about shortage. But there is a lot of cases when drug isn't mentioned there, because no one applied this issue.	-
Lithuania	0%	-		-	-
Luxembourg	33%	0%	The authorities inform us of some shortages via email.	-	Not of my knowledge.

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/ working/ functional?	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Malta	0%	-	-	-	-
Montenegro	67%	100%	-	-	-
Netherlands	100%	94%	https://farmanco.knmp.nl	Run by the Royal Dutch Society of Pharmacy. Manufacturers and wholesalers can report shortages to this website.	There is a new regulation in place (since January 1st) allowing to import medication from other EU countries in case of shortage that could help (but has to be tested first).
Norway	100%	89%	www.legemiddelverket.no	Both NOMA and the national centre of shortage of drugs in hospital (https://oslo-universitetssykehus.no/fag-og-forskning/nasjonale-og-regionale-tjenester/nasjonalt-senter-for-legemiddelmangel-og-legemiddelberedskap-i-spesialisthelsetjenesten) has webpages open to everyone.	There are websites, newsletters, a national centre for hospitals which gives recommendations for handling shortages, recommends alternative therapy and has the right to give priority to patients when there are shortages.
Poland	100%	22%	http://wif.waw.pl/zglaszanie-brakow-produktow-leczniczych/	Chef Pharmaceutical Inspectorate collects data reported by pharmacies regarding drug shortages and produces a list of medicines at risk of being illegally exported. Pharmacists are obliged to report shortages online giving details of nature of shortage. Shortages are underreported due to pharmacy staff and time shortages. The reporting system is web based but considered by many not user friendly which may hinder the reporting system.	There is a plan to introduce by October 2018 a national system that will require all pharmacies (community and hospital), wholesalers and manufacturers to report all stock movements daily to the central database. There are several technical difficulties in introducing a complex reporting system. At this stage it is not clear how the uploaded data will be analysed and what actions will be taken to prevent shortages.
Portugal	54%	50%	www.infarmed.pt	-	INFARMED Sometimes proposes solutions for therapy substitution.
Romania	89%	38%		Health professionals and patients can use this site to report medicine shortages. This site is correlated with a daily stock reporting system for pharmacies and medical wholesalers. Unfortunately, medicines reported missing are inexplicably found in daily stock reports, but they are not actually available for patients, but rather meant for parallel export. However, this makes government officials say there are no medicine shortages.	ANMDM (https://www.anm.ro/) offers us information about current shortages without linked proposed solutions for therapy substitution.
Russia	0%	-	-	-	-

Country	Is there a reporting system for shortages in place? (%yes)	Do you judge it as effective/ working/ functional? (%yes)	Website link or system name	Description of system (Q14)	Other national level approaches (Q26)
Serbia	67%	40%	www.rfzo.rs	National insurance fund runs website where pharmacists can report shortage. But we cannot see data base with all reported shortages from other institutions.	-
Slovakia	63%	40%	sukl.sk	website with information is available but with no solutions, manufacturers often don't want to inform about the length of shortage of the drug with is not in the list from the website.	-
Slovenia	33%	0%	http://www.jazmp.si	System exists, but manufacturers don't report consistently to the system.	-
Spain	79%	70%	https://cima.aemps.es/cima/publico/home.html	provides information via e-mail and website, and there is a webpage in which it is possible for hospital to get medicines from abroad.	When we have the option to import the medicine, we have the information at: https://mse.aemps.es/mse/documentoSearch.do?metodo=buscarDocumentos . It is here where we create the order to import the drug.
Sweden	33%	0%	www.mpa.se	-	-
Switzerland	78%	56%	https://www.bwl.admin.ch/bwl/de/home.html	Information System is too dull/slow. most of time we already run out of stock when the official Information reaches us. . Additionally, a hospital pharmacist launched the site http://www.drugshortage.ch/index.php to provide the manufacturer a place to voluntarily report shortages. Other health care professionals can also report shortages.	For certain essential groups of drug like f.e. vaccines or antibiotics... there is a federal office taking care of the situation and managing the situation together with the pharmacy. companies.
Turkey	47%	87%	http://www.titck.gov	-	The Ministry of Health set up a whatsapp group with all pharmacist - officer for medical depot stock control -and we share our problems in there.
UK	60%	72%	Commercial Medicines Unit run by DoH. (email responses)	CMU sends out shortage list on monthly basis. PMSG also provide shortage list.	Trusts get together and share / Info via national and regional networks.

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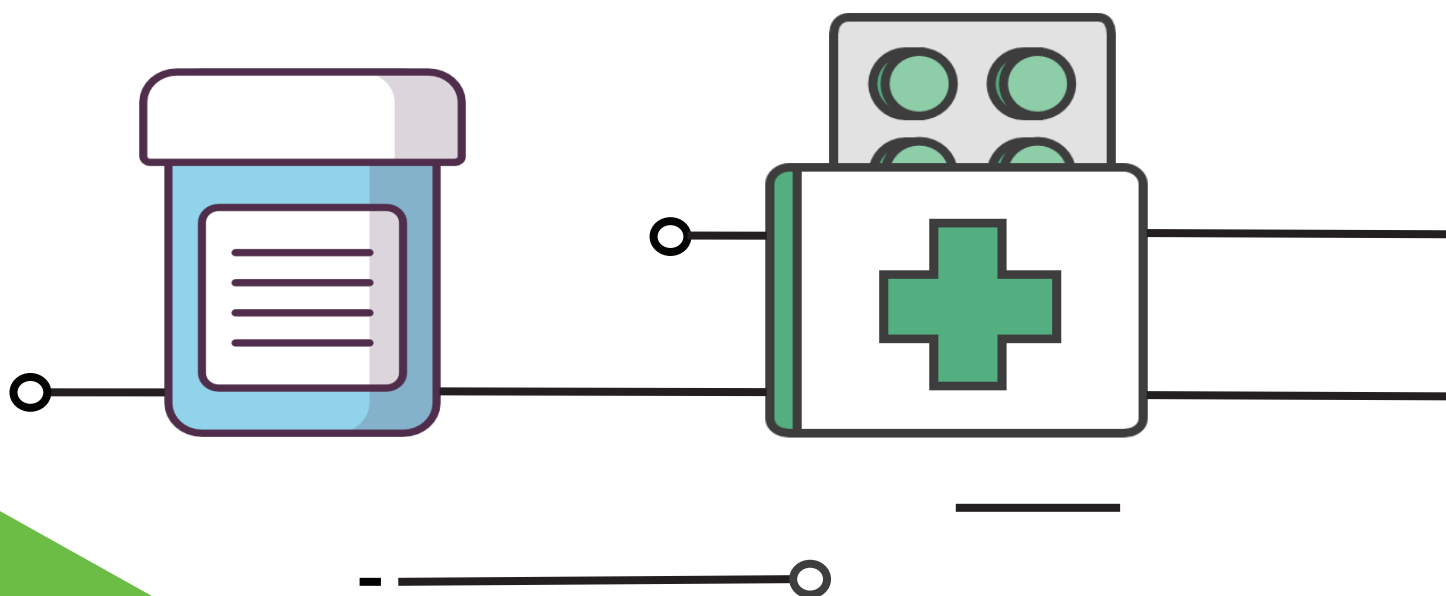
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Branche kompakt | Indien | Arzneimittel, Diagnostika

15.07.2019

Branche kompakt: Indien ist die Generika-Apotheke der Welt

Export treibt das Branchenwachstum an / Von Heena Nazir (Juni 2019)

Mumbai (GTAI) - Die indische Pharmaindustrie hat gute Aussichten auf Wachstum. Allerdings sind die Kunden sehr preissensibel und immer mehr Medikamente unterliegen staatlichen Preisobergrenzen.

Marktentwicklungen und -trends

Pharmaindustrie ist eine der exportstärksten Branchen Indiens

Die indische Arzneimittelindustrie ist nach der Japans und der VR Chinas die drittgrößte Asiens und hat sich in den vergangenen Jahren zu einer der exportstärksten Branchen Indiens entwickelt. Insbesondere bei Generika (wirkstoffgleiche Imitate von Originalmedikamenten) liegt das Land weltweit im Spitzenbereich. Das Rechercheinstitut Business Monitor International (BMI) schätzt den Gesamtumsatz der Pharmabranche für das Jahr 2018 auf rund 20,9 Milliarden US-Dollar (US\$). Bis 2022 soll der Gesamtumsatz mit einer durchschnittlichen Wachstumsrate von 8,6 Prozent auf 28,9 Milliarden US\$ steigen.

Entwicklung des Pharmamarktes in Indien (in Milliarden US\$, Veränderung in Prozent) *)

	2017	2018	Veränderung 2018/17
Gesamtumsatz von Pharmaunternehmen	19,2	20,9	8,9
Exporte	14,1	15,4	9,2
Importe	1,7	1,8	5,9
Gesundheitsausgaben (GA)	131,8	147,9	12,2
Anteil der Regierung an GA in %	30,4	31,8	4,6

*Schätzungen

Quelle: Business Monitor International, Pressemitteilung, Juni 2019

Gleichwohl dürfte das Wachstum hinter den zweistelligen Raten der Vergangenheit zurückbleiben. Die Konkurrenz unter den Generikaherstellern ist größer geworden, auch durch chinesische Produzenten. In Punkto Sicherheit und Qualitätskontrolle belasteten Zulassungsverbote von diversen Medikamenten die Branche. Insgesamt sollen im Jahr 2018 circa 174 Medikamente von der US-Behörde FDA überprüft worden sein. Die USA ist der größte Abnehmer indischer Pharmazie, ein Drittel aller Exporte sind für Nordamerika bestimmt.

Inlandsabsatz soll steigen

Mehrere Faktoren deuten auch auf einen steigenden Bedarf am indischen Binnenmarkt hin. Neben altersbedingten Krankheiten nehmen Zivilisationskrankheiten stark zu. Zudem geben immer mehr Inder einen wachsenden Teil ihres Einkommens für eine bessere medizinische Versorgung aus. Das wichtigste Absatzsegment im Inland sind Heilmittel für akute Erkrankungen. Chronische

Krankheiten sind jedoch auf dem Vormarsch. Am schnellsten wächst der Bedarf an Mitteln gegen Diabetes sowie Magen- und Darmgeschwüre.

Dem wachsenden Bedarf steht allerdings entgegen, dass die Mehrheit der Bevölkerung nur schlechten Zugang zur Gesundheitsversorgung hat. Dazu kommt die geringe Verbreitung von Krankenversicherungen und ein schwaches regulatorisches Umfeld. Reformen sind schlecht konzipiert und werden oft nicht ordnungsgemäß umgesetzt, beklagen mehrere Geschäftsführer in Gesprächen mit Germany Trade & Invest. Kurzfristig dürfte das Geschäft deutscher Pharmalieferanten schwierig sein, da die Kunden insbesondere bei hochwertigen verschreibungspflichtigen Produkten sehr preissensibel sind. Immer mehr Medikamente unterliegen staatlichen Preisobergrenzen, wobei das Preisniveau ohnehin sehr tief ist. Eine einwöchige Antibiotikatherapie kostet nicht selten weniger als einen Euro, Schmerzmittel meist nur wenige Cents.

Segment verschreibungspflichtiger Arzneimittel dominiert den Markt

Der Verkauf von verschreibungspflichtigen Medikamenten in Indien wird in den kommenden Jahren von robusten Wachstumstreibern profitieren. Im Jahr 2018 entfielen circa 85,7 Prozent des Gesamtumsatzes auf verschreibungspflichtige Medikamente. Trotz der Bemühungen der Regierung, die Gesundheitskosten zu senken, werden die stark wachsende Bevölkerung und die zunehmende Belastung durch chronische Krankheiten dafür sorgen, dass verschreibungspflichtige Medikamente das dominierende Marktsegment bleiben.

Entwicklung des Umsatz der Pharmaindustrie (in Milliarden US\$; Veränderung in Prozent)

	2017	2018	Veränderung 2018/17
Verschreibungspflichtige Medikamente	16,4	17,9	9,1
Over-the-Counter-Medikamente (OTC)	2,8	3,0	7,1
Gesamtumsatz Medikamente	19,2	20,9	8,9

*Schätzungen

Quelle: Business Monitor International, Juni 2019

Der indische Markt für nicht verschreibungspflichtige Arzneimittel, sogenannte Over-the-Counter-Medikamente (OTC), wird immer attraktiver für einen großen Teil der Bevölkerung. Vor allem Inder, die in ländlichen Gebieten leben und kaum Zugang zu medizinischer Versorgung haben, bleibt oft keine andere Wahl, als auf OTC-Präparate zurückzugreifen. Sie können sich kaum Arztbesuche oder die höheren Gebühren für verschreibungspflichtige Medikamente leisten. Vor diesem Hintergrund investieren einige der größten Arzneimittelhersteller wie Sun Pharmaceuticals, Dr. Reddy's und Glenmark in ein Portfolio von OTC-Produkten in Indien.

Indien ist der weltweit größte Generika-Produzent

Patentierte Arzneimittel spielen eine geringe Rolle im indischen Gesamtmarkt und erwirtschafteten umgerechnet ungefähr 2,1 Milliarden US\$ im Jahr 2018. Mehr als 80 Prozent der verkauften Medikamente sind Generika. Das südasiatische Land ist weltweit der größte Hersteller von medizinischen Nachahmerprodukten. Der Umsatz der Generikabranche betrug 2018 etwa 15,8 Milliarden US\$. Marktforscher von BMI prognostizieren einen Anstieg auf 21,7 Milliarden US\$ bis 2022. Die Wachstumsaussichten bleiben positiv: Um den Zugang zu Medikamenten für die eigene Bevölkerung zu steigern, muss Indien stärker Kosten senken und auf Generika setzen. Das drückt das Umsatzwachstum von patentierten Medikamenten.

Großteil von Medikamenten wird über Apotheken vertrieben

Zuständig für Beschaffungen für das öffentliche Gesundheitssystem sind das Gesundheitsministerium und fünf staatliche Unternehmen, die sogenannten Central Public Sector Enterprises (CPSEs). Für deutsche Hersteller ist der staatliche Markt nur bedingt von Interesse, da die staatlichen Unternehmen sehr preissensibel sind und in circa 98 Prozent der Fälle Generika aus der indischen

Eigenproduktion kaufen. Weitere Informationen enthält die Internetseite des Ministeriums <http://pharmaceuticals.gov.in/cpses>.



Der Großteil von Medikamenten, circa 90 Prozent, wird über Apotheken vertrieben. Die Gesundheitsinfrastruktur ist stark auf städtische Gebiete ausgerichtet. Fast 75 Prozent der Apotheken, 60 Prozent der Krankenhäuser und 80 Prozent der Ärzte befinden sich in städtischen Zentren. Der Verkauf von Medikamenten konzentriert sich auf die Ballungszentren. Die vier größten Städte Mumbai, Neu Delhi, Kolkata und Channai vereinen etwa ein Viertel des Branchenumsatzes auf sich. Entsprechend bietet sich für deutsche Unternehmen in urbanen Regionen höheres Absatzpotenzial.

Anteil gefälschter Arzneimittel nimmt zu

Die Weltgesundheitsorganisation (WHO) geht davon aus, dass 10 Prozent aller weltweit gehandelten Medikamente Fälschungen sind und meistens aus der VR China oder Indien stammen. In Indien werden Medikamente gefälscht, die dringend benötigt werden, aber sehr teuer sind, beispielsweise Antibiotika, Arzneimittel für Chemotherapie, Malaria, Tuberkulose und AIDS. Der Bedarf ist hoch und die Arzneimittel lassen sich einfach über das Internet weltweit verkaufen.

Geschäftspraxis

Zulassung für Arzneimittel unterliegt verschiedenen Regulierungsbehörden

Der indische Pharmamarkt unterliegt einer umfassenden staatlichen Kontrolle. Es gibt unterschiedliche Regulierungsbehörden, die für die Zulassung von Arzneimitteln verantwortlich sind. Branchenkenner zufolge ist der Zulassungsprozess oft intransparent, ineffizient und zeitaufwendig.

Die Hauptregulierungsbehörde in Indien ist die Central Drug Standard Control Organization (CDSCO). Sie arbeitet unter der Aufsicht und Anleitung des indischen Gesundheitsministeriums und der Drug Controller General of India (DCGI). Neben dem DCGI, CDSCO und dem Ministerium für Gesundheit kann die Abteilung für Biotechnologie, das Ministerium für Wissenschaft und Technologie sowie das Ministerium für Umwelt bei dem Zulassungsprozess involviert sein.

In Indien ist die Herstellung, Qualität und Vermarktung von Arzneimitteln in Übereinstimmung mit dem Drugs and Cosmetics Act von 1945 geregelt. Andere Rechtsakte umfassen den Pharmacy Act von 1948, den Drugs and Magic Remedies Act von 1954 und die Drug Price Control Order (DPCO) von 1995 sowie verschiedene andere Richtlinien der Abteilung für Chemikalien und Petrochemie. An den meisten Rechtsvorlagen wurden in den letzten Jahren mehrere Änderungen vorgenommen. Weitere Informationen erhalten Sie unter: <http://pharmaceuticals.gov.in/act>.

Krankenversicherungen sind wenig verbreitet

In Indien gilt die öffentliche Gesundheitsversorgung als mangelhaft, es fehlt an medizinischem Personal und Krankenhäusern. Wer es sich leisten kann, lässt sich privat behandeln. Für die ärmsten Bevölkerungsschichten sind solche Behandlungen aber nicht erschwinglich.

Von den im Jahr 2017 geschätzt ausgegebenen 147,9 Milliarden US\$ für die Gesundheitsversorgung entfallen gerade einmal 31,8 Prozent auf staatliche Ausgaben. Die Patienten tragen den Großteil (68,2 Prozent) der Kosten selbst. Circa 7 Prozent aller Inder werden jedes Jahr aufgrund von Krankheitskosten in die Armut getrieben. Nur circa 5 bis 10 Prozent der Bevölkerung soll versichert sein.

Die Regierung unter Premierminister Narendra Modi will das ändern und kündigte das größte staatlich finanzierte Gesundheitsfürsorgeprogramm der Welt an. Für circa 500 Millionen hilfsbedürftige Inder sollen Gesundheitskosten von bis zu umgerechnet 7.600 Euro pro Jahr für Krankenhausbesuche übernommen werden. Bisher wurden 27 Millionen Menschen im Rahmen des Programms registriert, berichtet die Regierungsbehörde National Health Authority, die für die Implementierung von "Modicare" zuständig ist. Allerdings werden Sekundärgesundheitsdienste wie frei verkäufliche Arzneimittel nicht abgedeckt. Die Kosten für eine ambulante Versorgung und wichtige Arzneimittel müssen weiterhin selbst getragen werden.

Die Mittel- und Oberschicht hingegen ist entweder bei einer betrieblichen oder privaten Krankenkasse versichert oder bezahlt die Medikamente im Bedarfsfall aus eigener Tasche. Versicherungsunternehmen wie Apollo Munich Easy Health und Religare Health Insurance bieten Versicherungen für Familien und Firmenbelegschaften an. Durch sie hat der Versicherungsnehmer Zugang zu be-

stimmten, vergleichsweise gut ausgestatteten privaten Krankenhäusern in Indien. Üblicherweise zahlen die Versicherungen Medikamente nur im Falle einer stationären, nicht bei einer ambulanten Behandlung. Offiziell gibt es, neben Preisobergrenzen, keine Vorschriften oder Mechanismen bei Zuzahlung und Erstattung von Arzneimittelkosten.

Preisobergrenzen bremsen Absatz von Pharmaunternehmen

Die National Pharmaceutical Pricing Authority (NPPA, <http://www.nppaindia.nic.in/en>) hat die Aufgabe, die Preise für Medikamente festzusetzen. Die "Essentiality of Drugs" gehört zu den wichtigsten Prinzipien des Landes. Hierbei geht es um die Bereitstellung von lebenswichtigen Medikamenten, in ausreichender Menge und zu "angemessenen Preisen". Mehreren Zeitungsartikeln zufolge wurden bis 2018 mehr als 800 Preisobergrenzen für Präparate, darunter Wirkstoffe wie Insulin, Aspirin und Penicillin, festgelegt. In der letzten veröffentlichten offiziellen Liste der NPPA von 2015 unterliegen circa 376 Präparate der staatlichen Preisaufsicht.

Für Medikamente, die nicht unter Preiskontrolle stehen, können Unternehmen einen Mindestverkaufspreis festlegen. Der NPPA greift nur in Fällen ein, in denen Arzneimittel einen erheblichen Umsatz erzielen und/oder der jährliche Preis um 10 Prozent steigt. Die vom NPPA beschlossenen Preiskontrollen führten zu einer Verlangsamung von Wachstumsraten von Unternehmen.

Reformprogramm soll Investitionen locken

Die indische Regierung hat am 20.6.16 angekündigt, die Bestimmung für ausländische Direktinvestitionen für Brownfield-Projekte in der Pharmaindustrie zu lockern. In der Vergangenheit brauchte man ab einer Beteiligung von 49 Prozent die Zustimmung der Regierung. Nun ist deren Genehmigung bei einer Beteiligung von bis zu 74 Prozent nicht mehr nötig. Für Greenfield-Investitionen erlaubt Neu Delhi bereits eine 100-prozentige Beteiligung. Dies sollte auf lange Sicht Investitionen in der Branche weiter antreiben.

Patentschutz ist und bleibt ein Problem in der indischen Pharmaindustrie

Der Schutz des geistigen Eigentums ist bei den Verhandlungen um ein Freihandelsabkommen zwischen der EU und Indien ein besonders heikles Thema. Indien verweigert sich bisher einem Ausbau des Patentschutzes. Letzte Änderungen gab es im Jahr 2005, damals wurden die rechtlichen Rahmenbedingungen für die Herstellung von Generika in Indien erschwert. Allerdings blieb den Behörden ein gewisser Spielraum. Nach der Regelung können drei Jahre nach Erteilung eines Patents unter bestimmten Kriterien Zwangslizenzen erteilt werden, um ein Pharmazeutikum kopieren zu können. Weiterhin konnten Unternehmen preiswerte Alternativen zu innovativen Medikamenten auf den Markt bringen, solange der Herstellungsprozess sich unterschied.

Ausführliche Informationen zum Wirtschafts- und Steuerrecht stehen unter <http://www.gtai.de/recht> sowie zu Einfuhrregelungen, Zöllen und nichttarifären Handelshemmnissen unter <http://www.gtai.de/zoll> zur Verfügung.

Kontaktadressen

Bezeichnung	Internetadresse	Anmerkungen
Germany Trade & Invest	http://www.gtai.de/Indien	Außenhandelsinformationen für die deutsche Exportwirtschaft
Exportinitiative Gesundheitswirtschaft	http://www.exportinitiative-gesundheitswirtschaft.de	Portal der Exportinitiative des Bundesministeriums für Wirtschaft und Energie
AHK Indien	https://indien.ahk.de	Anlaufstelle für deutsche Unternehmen
Department of Pharmaceuticals	http://pharmaceuticals.gov.in/act	Informationen zu Ministerien und Behörden
ASSOCHAM	http://assochem.net	Nationaler Branchenverband
CPhI India	https://www.cphi.com/india/india-pharma-week	Größte Fachmesse Indiens findet vom 26 - 28.11.19 in Neu Delhi statt

Die Reihe "Branche kompakt" liefert Analysen zu wichtigen Schlüsselbranchen der deutschen Exportwirtschaft. Weitere Länderberichte zum Pharmasektor und zu weiteren Branchen sind unter <http://www.gtai.de/branche-kompakt> zu finden.

Ansprechpartnerin für die Pharmaindustrie: Beate Voell; E-Mail: beate.voell@gtai.de 

Dieser Inhalt ist relevant für:

Indien
Arzneimittel, Diagnostika
Branchen

Kontakt

Wilma Knipp

Wirtschaftsexpertin



+49 228 24 993 259



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Europe 'panicking' over India's pharmaceutical export curbs: industry group

Neha Dasgupta, Ludwig Burger

4 Minuten

NEW DELHI/FRANKFURT (Reuters) - India's top pharmaceuticals export group said a government curb on some drug exports as the coronavirus outbreak spreads has caused panic in Europe and will "severely impact" businesses in the sector.

A pharmacist checks weight of Paracetamol, a common pain reliever also sold as acetaminophen, tablets inside a lab of a pharmaceutical company on the outskirts of Ahmedabad, India, March 4, 2020. REUTERS/Amit Dave

The world's main supplier of generic drugs has restricted the export of 26 active pharmaceutical ingredients (APIs) and the medicines made from them, in a move seen as aimed at tackling possible domestic shortages of medicine during the outbreak.

On Wednesday, Dinesh Dua, chairman of the Pharmaceuticals Export Promotion Council of India (Pharmexcil), told Reuters that some of the restricted APIs and medicines were widely exported to Europe and the United States.

"I am getting a huge number of calls from Europe because it is

very sizeably dependent on Indian formulations and we control almost 26% of the European formulations in the generic space. So they are panicking,” Dua said.

Indian drugmakers rely on China, the source of the virus outbreak, for almost 70% of the APIs for their medicines.

The list of restricted medicines accounts for 10% of India’s total pharmaceutical exports and includes several antibiotics, as well as Paracetamol, a common pain reliever also sold as acetaminophen.

“We are very alarmed that other countries would pursue other, more narrow strategies, which won’t solve the issue,” said Adrian van den Hoven, director general of the Medicines for Europe association of the region’s generic and biosimilar drugmakers.

He added that the restrictions did not seem to affect large export volumes to Europe and stockpiles would last a few months.

The European Union’s drugs regulator, the European Medicines Agency, did not immediately reply to a request for comment.

The Food and Drug Administration in the United States, where Indian imports accounted for 24% of medicines in 2018, said on Tuesday it was working to determine how the restrictions will affect U.S. supplies.

The restrictions could hurt India’s image as a pharmacy to the world and would effect shipments already lined up for export at warehouses and ports, Pharmexcil argued in a letter to India’s Directorate General of Foreign Trade (DGFT), which was seen by Reuters.

The DGFT did not respond to a request for comment.

“The exporters not only suffer the monetary losses but also their

credibility and reputation in the international market is at stake,” said the letter, which urged the government to allow exports of drugs manufactured before the restrictions kicked in.

Dua told Reuters there were \$10 million worth of drugs currently at Indian ports or close to being readied for export.

Pharmexcil counts dozens of pharmaceutical firms such as Pfizer Ltd [PFIZ.NS](#) and Abbott [ABOT.NS](#) among its members. The council falls under the federal commerce ministry.

Novartis AG [NOVN.S](#) said on Wednesday it would adapt measures as the Indian export situation evolves, although it does not currently anticipate supply chain disruption.

India - which has so far confirmed 28 cases of the coronavirus, including 16 Italians - has urged calm and said there were enough stocks to manufacture formulations for two to three months.

Additional reporting by Ludwig Burger in Frankfurt; Editing by Aditya Kalra, Kim Coghill, Kirsten Donovan

TESTIMONY

Safeguarding Pharmaceutical Supply Chains in a Global Economy

OCTOBER 30, 2019

 **Testimony of**

Testimonies (/news-events/congressional-testimony)

Janet Woodcock, M.D.

Director - Center for Drug
Evaluation and Research**Before the**House Committee on Energy and
Commerce, Subcommittee on
Health

(https://energycommerce.house.gov/subcommittees/health-116th-congress)

Introduction

Madam Chairwoman, Ranking Member Burgess, and Members of the Subcommittee, I am Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS).

The United States, through its investment in biomedical research, has become a world leader in drug discovery and development, but is no longer in the forefront of drug manufacturing. Historically, the production of medicines for the U.S. population has been domestically based. However, in recent decades, drug manufacturing has gradually moved out of the United States. This is particularly true for manufacturers of active pharmaceutical ingredients (APIs), the actual drugs that are then formulated into tablets, capsules, injections, etc. As of August 2019, only 28 percent of the manufacturing facilities making APIs to supply the U.S. market were in our country. By contrast, the remaining 72 percent of the API manufacturers supplying the U.S. market were overseas, and 13 percent are in China. **(See Figure 1)** FDA's data show that the number of registered facilities making APIs in China more than doubled between 2010 and 2019.

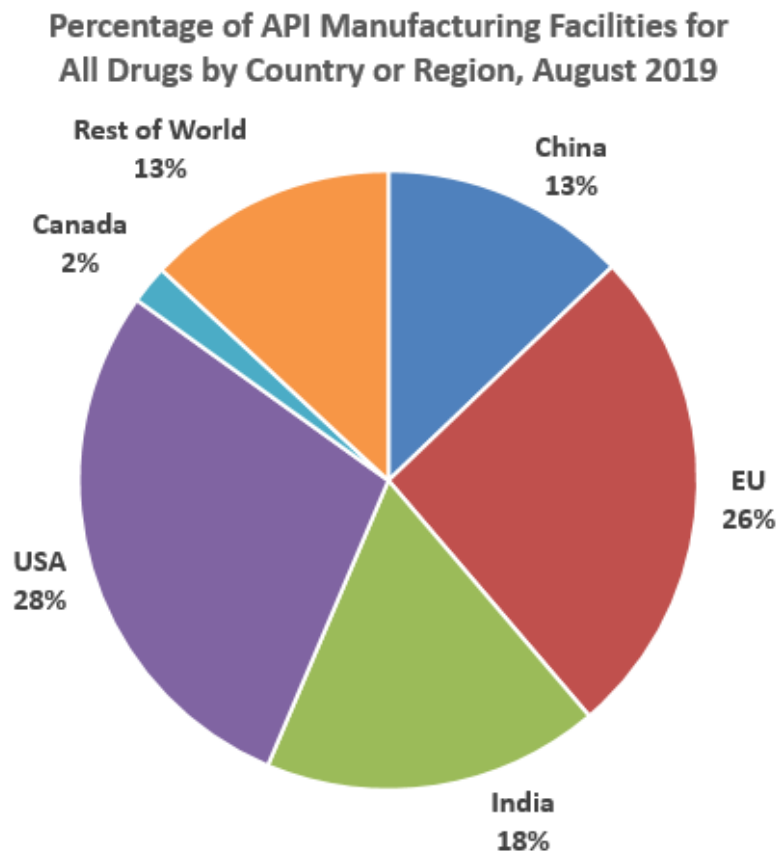


Figure 1: Manufacturing Sites of APIs for U.S. Market by Country or Region, August 2019

While there are many reasons for this shift, underlying factors that are often cited include the fact that most traditional drug production processes require a large factory site, often have environmental liabilities, and can utilize a low-cost labor force. A 2009 paper by the World Bank, “Exploratory Study on Active Pharmaceutical Ingredient Manufacturing for Essential Medicines,” stated that if a typical Western API company has an average wage index of 100, this index is as low as 8 for a Chinese company and 10 for an Indian company.[1] China has lower electricity, coal, and water costs. Chinese firms are also embedded in a network of raw materials and intermediary suppliers, and so have lower shipping and transaction costs for raw materials. They also face fewer environmental regulations regarding buying, handling, and disposing of toxic chemicals, leading to lower direct costs for these firms. FDA’s 2011 report, “Pathway to Global Product Safety and Quality,” noted that

both China and India enjoy a labor cost advantage and that API manufacturing in India can reduce costs for U.S. and European companies by an estimated 30 percent to 40 percent.[2]

Using traditional pharmaceutical manufacturing technology, a U.S.-based company could never offset the labor and other cost advantages that China enjoys simply by achieving higher productivity. However, FDA believes that advanced manufacturing technologies could enable U.S.-based pharmaceutical manufacturing to regain its competitiveness with China and other foreign countries, and potentially ensure a stable supply of drugs critical to the health of U.S. patients. Advanced manufacturing is a collective term for new medical product manufacturing technologies that can improve drug quality, address shortages of medicines, and speed time-to-market. Every field has a different set of production techniques that are considered advanced. Examples of some cross-cutting advanced manufacturing technologies include continuous manufacturing and 3D printing. Advanced manufacturing technology, which FDA supports through its Emerging Technology Program (ETP), has a smaller facility footprint, lower environmental impact, and more efficient use of human resources than traditional technology, as will be explained later in this testimony.

The pharmaceutical sector relies heavily on foreign sourcing for critical components, materials, and finished products, as identified in the U.S. Department of Commerce's Office of Technology Evaluation's 2011 report, "Reliance on Foreign Sourcing in the Healthcare and Public Health (HPH) Sector: Pharmaceuticals, Medical Devices and Surgical Equipment." [3] However, use of foreign-sourced materials creates vulnerabilities in the U.S. drug supply. For example, in August 2018 FDA issued an alert that a Chinese API manufacturer, Sichuan Friendly Pharmaceutical Co. Limited, was recalling certain lots of porcine thyroid API due to inconsistent quality of the API.[4] This thyroid API comes from porcine (pig) thyroid glands and is used to make a medicine to treat hypothyroidism (underactive thyroid). FDA laboratory testing confirmed that the Sichuan Friendly API had inconsistent levels of active ingredients and should not be used

to manufacture or compound drugs for patient use. Risks associated with over- or undertreatment of hypothyroidism could result in permanent or life-threatening adverse health consequences.

In December 2015, FDA alerted drug compounders that certain lots of baclofen API manufactured by Chinese manufacturer Taizhou Xinyou Pharmaceutical & Chemical Co., Limited might be at risk for contamination with particulates and should not be used to compound sterile injectable drugs. Taizhou manufactures APIs for repackagers and distributors, some of which sell these products to compounding facilities in the United States.[5]

FDA contacted Taizhou and the company confirmed that, due to the level of controls in the manufacturing process, the baclofen API it manufactures was not suitable for use in injectable drugs. FDA recommended that no baclofen API from Taizhou be used to manufacture or compound any injectable drugs. The affected API potentially could have posed serious safety risks for U.S. patients who used or received injectable drug products compounded with the affected baclofen, especially when administered directly into the spine (intrathecally). There was also a potential risk that the baclofen API might have been contaminated by endotoxin or microorganisms.

Today, I would like to share CDER's information about the location of API manufacturing facilities in China, the United States, and the rest of the world; discuss the implications for national security; and explain how advanced manufacturing can increase the security and reliability of the U.S. drug supply.

Explanation of CDER's Data and its Limitations

From a national security perspective, it is useful to look at the locations of facilities for three sets of drugs:

- All drugs on the U.S. market, including brand and generic drugs under approved applications, over-the-counter

(OTC) drugs, and compounded medications.

- Drugs on the World Health Organization (WHO) Essential Medicines List that are marketed in the United States.
- Drugs on the medical countermeasures (MCM) lists. These include drugs we would use to counter biological, chemical, nuclear, or radiation threats and influenza.

CDER maintains a Site Catalog (“Catalog”) of all manufacturing facilities making drugs for the U.S. market, either through an approved application or that have registered and listed to supply drugs for the U.S market. This includes suppliers for API, finished dosage forms (FDF), or both. The APIs manufactured in these facilities may be used in prescription drugs (brand or generic), OTC drugs, and compounded drugs.

Data available to CDER have several limitations, including the following:

- Facilities listed in the Catalog may or may not be producing APIs. Including a facility in an application or the registration and listing process does not require a facility to produce API. Producing an API at the facility, or not producing it, is a business decision made by the company.
- Manufacturers are not required to report to FDA whether they are actually producing an API at a facility, and if they are, the volume they are producing.
- APIs made in listed facilities may be used in drugs for both the U.S. and other markets, and some APIs distributed in the United States are subsequently formulated into FDF that are then exported.
- Some FDF applications list more than one API supplier in the application. FDA has no visibility into which API supplier an FDF manufacturer uses at any given time.
- CDER has limited information about API suppliers for products that do not need an approved application from FDA to be marketed, such as compounded and OTC

monograph drugs. API suppliers for such products may not register their facility with FDA if they are sending material to a drug product manufacturer outside the United States to make the FDF, which is then sold in the United States.

- Information in the Catalog is continually being updated. The analysis presented below is based on August 2019 listings and represents a snapshot at a point in time.

These limitations mean that, although CDER can describe the locations of API manufacturing facilities, we cannot determine with any precision the volume of API that China is actually producing, or the volume of APIs manufactured in China that is entering the U.S. market, either directly or indirectly by incorporation into finished dosages manufactured in China or other parts of the world.

API Manufacturing Facilities for All Regulated Drug Products

CDER's analysis shows that overall, China has only a modest percentage of the facilities able to produce APIs for the U.S. market. For all regulated drugs, China has 230 (13 percent) of the API manufacturing facilities, while the United States has 510 (28 percent), and the rest of the world has 1048 (59 percent). "All regulated drugs" includes prescription (brand and generic), OTC, and compounded drugs. **(See Figure 2)** However, the percentages of APIs produced at these facilities may differ, and as mentioned above, cannot be determined from the data available to FDA.

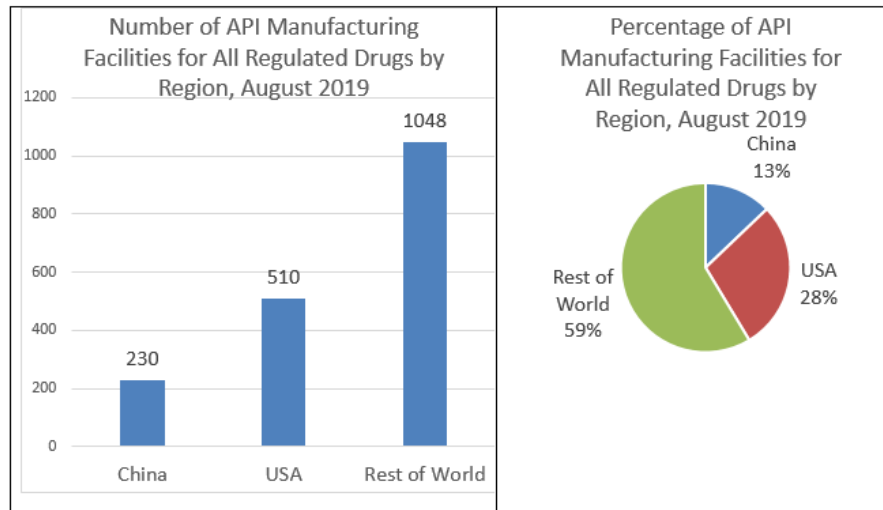


Figure 2: Number and Percentage of API Manufacturing Facilities for All Drugs by Region, August 2019

API Manufacturing Facilities for WHO Essential Medicines on the U.S. Market

The 2019 WHO Essential Medicines List comprises 461 drugs that have been selected by the WHO Expert Committee to meet the most important needs in a health system. This list includes application and non-application products across a wide range of therapeutic categories such as anesthetic, antibacterial, antidepressant, antiviral, cardiovascular, anti-diabetic, and gastrointestinal agents.

FDA matched 370 of the drugs on the WHO Essential Medicines List with products listed for the U.S. market and determined the location of the facilities used to make their APIs.[6] FDA data show that there is a total of 1,079 API facilities worldwide that make the 370 drugs on the WHO list that are marketed in the U.S. Of these, 166 (15%) are in China, 221 (21%) are in the United States, and 687 (64%) are in the rest of the world. **(See Figure 3)**

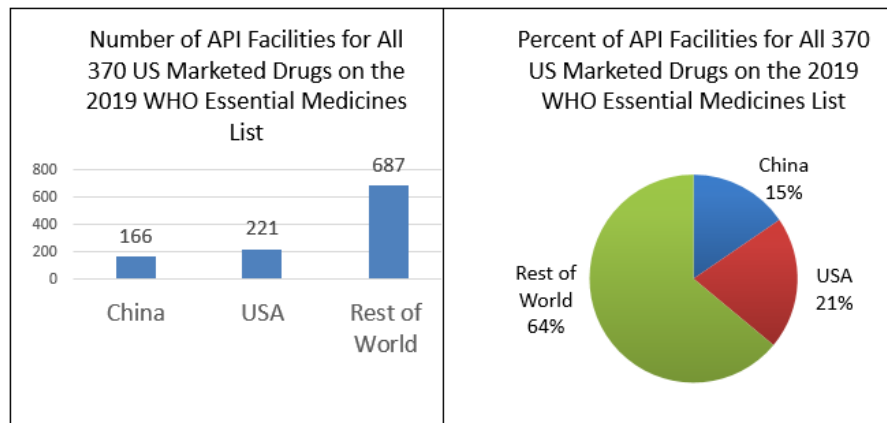


Figure 3: Number and Percentage of API Facilities for the 370 U.S. Marketed Drugs on the 2019 WHO Essential Medicines List

FDA determined that there are three WHO Essential Medicines whose API manufacturers are based only in China. The three medicines are: capreomycin and streptomycin, both indicated to treat *Mycobacterium tuberculosis*; and sulfadiazine, used to treat chancroid and trachoma.

The distribution of API facilities worldwide varies from drug to drug and may differ from the patterns for all drugs or WHO Essential Medicines List Drugs.

API Manufacturing Facilities for Medical Countermeasures

FDA maintains a list of drugs that are used as medical countermeasures (MCMs) against threats in four categories: biological threats, chemical threats, influenza, and radiation threats. Many of these drugs are contained in strategic drug stockpiles, including the Nation's Strategic National Stockpile, the Nation's largest supply of potentially life-saving pharmaceuticals and medical supplies for use in a public health emergency severe enough to cause local supplies to run out.

For APIs for 14 drugs in the biological threat category, China has 37 facilities, the United States has 19, and the rest of the world has 117. China has just six of the facilities producing APIs for the 10 drugs in the chemical threat category, versus 24 in the United States and 52 in the rest of the world. **(See Table 1)**

MCM Type (# products)	U.S. API Sites # (%)	China API Sites # (%)	Other Foreign API Sites # (%)
Biological (14)	19 (11%)	37 921%	117 (68%)
Chemical (10)	24 (29%)	6 (7%)	52 (64%)
Influenza (3)	2 (11%)	0 (0%)	16 (89%)
Radiation (7)	13 (46%)	0 (0%)	15 (54%)

Table 1: Number and Percent of API Manufacturing Sites for MCM Drugs for Use Against Biological, Chemical, and Radiation Threats, and Influenza, August 2019

China has none of the facilities making APIs for medicines to prevent or treat influenza versus two in the United States and 16 in the rest of the world. China also has none of the facilities producing APIs for radiation threats. The United States has 13 of these facilities versus 15 in the rest of the world.

Ciprofloxacin and doxycycline are two drugs considered critical as MCMs and used to treat anthrax and plague. As shown in Table 2 below, the United States has one facility for ciprofloxacin, versus three in China and 21 in other foreign countries. The United States has fewer facilities than China or other foreign countries for doxycycline. **(See Table 2)**

MCM	# (%) U.S. API Sites	# (%) China API Sites	# (%) Other Foreign API Sites
Ciprofloxacin	1 (4%)	3 (12%)	21 (84%)
Doxycycline	2 (18%)	3 (27%)	6 (55%)

Table 2: Number and Percent of API Manufacturing Sites for Ciprofloxacin and Doxycycline by Region, August 2019

Implications for National Security

The security of the nation's drug supply rests on three main factors: freedom from dependence on foreign sources of API, the resilience of our domestic manufacturing base, and the reliability of the facilities that make products for the U.S. market.

Dependence: How dependent are we on China, India, or other countries for the APIs used in drugs produced for patients in the United States? How has this dependence changed over time?

The number of Chinese facilities producing APIs for the U.S. market has increased over the past decade, as part of a massive movement of pharmaceutical production offshore. This movement is being driven by the pharmaceutical industry's desire for cost savings and less stringent environmental regulations. Absent any intervention, FDA believes that this trend is likely to continue.

However, data available to FDA do not enable us to calculate the volume of APIs being used for U.S.-marketed drugs from China or India, and what percentage of U.S. drug consumption this represents. As mentioned above, we do not know whether Chinese facilities are actually producing APIs, how much they are producing, or where the APIs they are producing are being distributed worldwide, including in the United States.

Resilience: How resilient is the U.S. manufacturing base? How quickly could U.S.-based manufacturers increase their production of APIs to meet domestic demand if China or India, or another country, ceased supplying the United States, particularly for drugs on the WHO Essential Medicines list or a subset that is widely used by the U.S. population?

To answer this question, FDA would need to know:

- how much unused capacity exists in the U.S. manufacturing base for APIs;
- how much additional API this capacity could supply within a given time period;
- how far this capacity would go in filling the gap between U.S. patients' needs and the amount available if China or

India, or another country, were to reduce or stop the supply to the U.S. market; and

- how long would it take to increase production enough to meet patients' needs, and whether the financial investment would be sustainable for the pharmaceutical industry.

Since we do not currently know whether API manufacturing facilities are actually producing the drug, or in what volume, or what portion of U.S. drug consumption is dependent on APIs from China or India, or another country, we cannot perform a reliable gap analysis.

Even if we could estimate the potential API shortfall and available production capacity, pharmaceutical companies make business decisions about whether to produce a drug product, including an API, and FDA does not have the power to tell them to make a drug. This provides additional uncertainty in assessing the potential responsiveness of the U.S. manufacturing base to a crisis triggered by another country's withdrawal.

Reliability: How reliable is the manufacturing base that produces APIs for the U.S. market?

FDA recently analyzed 163 drugs that went into shortage during the five-year period from 2013 to 2017 and found that quality problems were responsible for the shortages 62 percent of the time.[7] These shortages can worsen patients' health outcomes by causing delays in treatment or changes in treatment regimens, such as substituting less-effective or well-tolerated medicines when a drug of choice is not available. In looking for ways to ensure Americans' access to a supply of safe and effective drugs, we need to consider all three dimensions of the problem.

Summary of National Security Findings

FDA's information shows that overall, the number of China's API facilities is somewhat smaller than the United States, but comparable in size and growing. However, because of the limitations of available data, we cannot assess the extent of

U.S. dependence on China. For instance, we do not have information about the volume of API being produced in China or even in the United States, or how much of China's API output reaches the U.S. market through other countries.

Similarly, we do not have information that would enable us to assess the resilience of the U.S. manufacturing base, should it be tested by China's withdrawal from supplying the U.S. market. We do know that the U.S. drug supply is being compromised by drug shortages, in most cases triggered by manufacturing quality problems by U.S.-based as well as foreign producers.

Advanced Manufacturing Offers a Multi-dimensional Solution

Advanced manufacturing is the use of innovative technology to improve products and processes. Although widely used in some other industries, such as automotive, aerospace, and semiconductors, advanced manufacturing is now just beginning to be used by pharmaceutical companies. For API and/or FDF manufacturing, new technologies include "continuous manufacturing" (CM), wherein the finished drug product is produced as a continuous stream, as opposed to traditional batch manufacturing where breaks or stops exist between different processing steps. In some examples of advanced pharmaceutical manufacturing, production can be continuous from chemical synthesis of the active ingredient through production of the tablets or other dosage forms.

Advanced manufacturing offers many advantages over traditional pharmaceutical manufacturing, and if the United States invests in this technology, it can be used to reduce the Nation's dependence on foreign sources of APIs, increase the resilience of our domestic manufacturing base, and reduce quality issues that trigger drug shortages or recalls. For example:

- Product quality can be precisely controlled with modern automation and control systems and can be closely monitored during production by using high-resolution

analytics.

- High technology, computer-controlled production facilities are better able to rapidly respond to changes in demand because they typically do not have the equipment scale-up issues associated with traditional methods and can be capable of seamlessly producing a variety of dosages and even dosage forms.
- Advanced manufacturing platforms also have a much smaller footprint than traditional manufacturing platforms, and the equipment can be made portable so that it can be moved closer to markets, reducing the need for transcontinental shipping of components.
- Medicines can be produced at lower cost than by traditional methods.
- Environmental impact of manufacturing is significantly reduced.

By supporting the growth of advanced manufacturing in the United States, we can reduce our dependence on China and other overseas manufacturers for APIs as well as improve the resilience and responsiveness of our manufacturing base and reduce drug shortages.

FDA's advanced manufacturing initiative is fostering this growth in several ways.

Emerging Technology Program (ETP)

The ETP, launched in late 2014, encourages and supports the adoption of innovative technology to modernize pharmaceutical development and manufacturing through close collaboration with industry and other relevant stakeholders starting from early technology development.

To reduce barriers to entry for advanced manufacturing, the Emerging Technology Team (ETT) provides a gateway for the early (pre-submission) discussion of innovative technologies and approaches, even before a candidate drug is identified.

The ETT supports the entry, assessment, and lifecycle management of advanced manufacturing at CDER. It provides

subject matter experts and fosters coordination within CDER and FDA's Office of Regulatory Affairs (ORA) for precedent-setting issues regarding quality and good manufacturing practices. ETT serves as a hub for identification of application-driven regulatory and research needs and provides strategic input for supporting advanced manufacturing innovation.

Based on ETT efforts in continuous manufacturing, CDER's Office of Pharmaceutical Quality (OPQ) published a draft guidance, "Quality Considerations for Continuous Manufacturing" of solid oral dosage forms in early 2019.[8]

Under this program, CDER has approved five drug applications utilizing continuous manufacturing for FDF manufacturing, and the first application utilizing 3-D printing technologies. Currently, these drugs are being made in the United States, and one drug is being made both in the United States and in the United Kingdom.

Regulatory and Policy Initiatives

The adoption of advanced manufacturing technologies may pose a challenge to the current regulatory framework, because most regulations were developed based on traditional batch manufacturing methods under a unified pharmaceutical quality system. As a result, FDA has launched an effort to identify and implement needed changes in the regulatory structure. For example, new policy and regulatory topics related to emerging technologies include the management of data-rich environments, the evolving concepts of process validation for advanced manufacturing systems, and the regulatory oversight of post-approval changes for such systems. Furthermore, CDER, in collaboration with the Biomedical Advanced Research and Development Authority (BARDA), is working on a strategy and new regulatory framework to develop and implement miniature, mobile manufacturing platforms ("Pharmacy on Demand") for manufacture of essential drugs near or at the point of care.

FDA actively engages with stakeholders in industry, academia, and other regulatory agencies to identify and address regulatory hurdles to adoption of advanced manufacturing.

For example, CDER, in partnership with FDA's Center for Biologics Evaluation and Research (CBER), is leading the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) effort to develop the Q13 guideline on continuous manufacturing of drug substances and drug products for both small-molecule and biological products, which will help to achieve global regulatory harmonization.

Intramural and Extramural Research

Laboratories in CDER's OPQ actively conduct advanced manufacturing research and invest in equipment, facilities, and personnel with expertise to investigate these topics. OPQ has established the Center of Excellence for Manufacturing Science and Innovation to coordinate internal advances in manufacturing research for both small molecules and biologics. OPQ publishes and leads research on continuous manufacturing, advanced analytics for process controls, and modeling and simulation. OPQ also provides training for assessment and inspection personnel.

Extramurally, OPQ awards research grants and contracts for advanced manufacturing and emerging technologies. OPQ also participates in consortia with academia and industry to identify new areas for research in advanced manufacturing. Participation in these intramural and extramural research efforts occurs with strong alignment and coordination between assessment, policy, and surveillance offices. This ensures that resources are allocated to projects that provide practical approaches to regulating innovative technologies.

On behalf of FDA, I would like to thank Congress for having the foresight to provide resources to support our efforts to assist the pharmaceutical industry as it makes a transition from traditional manufacturing methods to the use of advanced technologies. These new tools and methods have the potential to reinvigorate our pharmaceutical manufacturing base and repatriate it from overseas. This will help to ensure that Americans have a secure and reliable supply of medicines in the future, as well as contribute to our economy.

Promoting Domestic Manufacturing

In FY19, Congress approved appropriations to promote domestic manufacturing with the intent that FDA advance modern drug and biological product technologies. The spending plan for these additional resources builds on the CDER strategic goals to improve overall staff understanding and expertise in advanced manufacturing by expanding support of these innovative technologies in assessment, policy, surveillance, and research, as well as by making programmatic improvements. In addition, this funding is used to reinforce extramural outreach with stakeholders via planned technology forecasting activities with the National Academies of Sciences, Engineering, and Medicine and other forums.

Conclusion

The increasing number of API manufacturing sites in China and other countries suggests that the United States' reliance on Chinese and other foreign sources of API is growing. FDA has been working diligently in collaboration with industry and other federal agencies to ensure our reliance of foreign manufacturing does not pose a national security risk. While FDA cannot tell industry where they can and cannot manufacture APIs, we can work with industry to utilize new technologies and new manufacturing methods to further incentivize domestic production of drugs and APIs. These new ways of making drugs could, with the proper strategies, revitalize pharmaceutical manufacturing in the United States.

Footnotes

1. Bumpas, Janet; Betsch, Ekkehard. *Exploratory study on active pharmaceutical ingredient manufacturing for essential medicines (English)*. Health, Nutrition and Population (HNP) discussion paper. Washington, DC: World Bank. *Exploratory study on active pharmaceutical ingredient manufacturing for essential medicines* (<http://documents.worldbank.org/curated/en/848191468149087035/Exploratory-study-on-active-pharmaceutical-ingredient-manufacturing->

for-essential-medicines) [↗](http://www.fda.gov/about-fda/website-policies/website-disclaimer) (<http://www.fda.gov/about-fda/website-policies/website-disclaimer>). Accessed September 30, 2019.

2. U.S. Food and Drug Administration, “Pathway to Global Product Safety and Quality (<https://www.hsdl.org/?view&did=4123>) [↗](http://www.fda.gov/about-fda/website-policies/website-disclaimer) (<http://www.fda.gov/about-fda/website-policies/website-disclaimer>),” A Special Report, p. 20. Accessed October 4, 2019.

3. See Reliance on Foreign Sourcing in the Healthcare and Public Health (HPH) Sector: Pharmaceuticals, Medical Devices, and Surgical Equipment (<https://www.bis.doc.gov/index.php/documents/other-areas/642-department-of-homeland-security-dhs-assessment-impact-of-foreign-sourcing-on-health-related-infra/file>), accessed October 15, 2019.

4. See FDA alerts drug makers of a recall of porcine thyroid API from Sichuan Friendly Pharmaceutical Co., Limited, China (</drugs/drug-safety-and-availability/fda-alerts-drug-makers-recall-porcine-thyroid-api-sichuan-friendly-pharmaceutical-co-limited-china>), accessed October 6, 2019.

5. See FDA Warns of potential contamination of baclofen active pharmaceutical ingredient from Taizhou Xinyou Pharmaceutical & Chemical Co., Limited, China (</drugs/drug-safety-and-availability/fda-warns-potential-contamination-baclofen-active-pharmaceutical-ingredient-taizhou-xinyou>), accessed October 7, 2019.

6. Some of the 461 drugs on the 2019 WHO Essential Medicines List were excluded from the analysis because they are not regulated by CDER. The List includes products regulated by the Center for Biologics Evaluation and Research (CBER), such as cholera vaccine and anti-rabies immunoglobulin, and products regulated by the Center for Devices and Radiological Health (CDRH), such as diaphragms and condoms.

7. U.S. Food and Drug Administration, “Drug Shortages: Root Causes and Potential Solutions,” October 2019.

8. Quality Considerations for Continuous Manufacturing, Draft Guidance for Industry (/regulatory-information/search-fda-guidance-documents/quality-considerations-continuous-manufacturing), accessed October 15, 2019.

WOHER KOMMEN UNSERE WIRKSTOFFE? EINE WELTKARTE DER API PRODUKTION

Finaler Report



Berlin, September 2020

GLOSSAR

API	Active Pharmaceutical Ingredient; aktiver Wirkstoff eines Arzneimittels
ATC Klassen	Anatomisch-Therapeutisch-Chemische (ATC) Klassifikation; amtliche Klassifikation für pharmakologische Wirkstoffe anhand anatomischer, therapeutischer oder chemisch/struktureller Merkmale
CEP	Certificate of Suitability of Monographs of the European Pharmacopoeia; Nachweis zur Wirkstoffqualität, wird für Zulassungen von Arzneimitteln verwendet
DDD	Defined daily dose; statistische Messgröße zur Bestimmung der verordneten Arzneimittelmenge, definiert von der World Health Organization (WHO), gibt die angenommene, durchschnittliche Erhaltungsdosis eines Arzneimittels in seiner Hauptindikation für einen Erwachsenen an
ROA	Rest of Asia; Sammelkategorie in den Auswertungen, fasst alle Länder Asiens außer Indien und China zusammen
ROW	Rest of World; Sammelkategorie in den Auswertungen, fasst alle Länder, die nicht explizit in der Abbildung erwähnt werden, zu einer Kategorie zusammen

ZUSAMMENFASSUNG

- **Europas Versorgung** mit pharmazeutischen Wirkstoffen ist **verschiedenen Risiken ausgesetzt**
 - **2/3 der heutigen CEP-Zulassungen für APIs** liegen bei **asiatischen Herstellern**
 - **Indische und chinesische Standorte** konzentrieren sich auf **wenige Provinzen**
 - **Für 1/6 der untersuchten APIs** gibt es **keine europäische Produktion**; für mehr als **die Hälfte der APIs** gibt es mit **ein bis fünf CEPs** nur **wenige Hersteller weltweit**
- **Europa** hat seine **starke Position als API Hersteller verloren**, bei der **Anzahl der Neuzulassungen** von CEPs zwischen **2000 bis 2020 übertraf Asien Europa signifikant**: **Asiatische Hersteller** erhöhten die Anzahl ihrer **CEPs** von **183 auf 2.369**, **europäische** von **348 auf 1.260**
- Neben **ungleichen regulatorischen Rahmenbedingungen** gilt der **Kostendruck** als einer der **Hauptgründe**; **Profiteure** der Entwicklung sind **Indien und China**
- **Europa** ist heute **fokussiert auf spezielle APIs** (z.B. niedrige Produktionsvolumen, komplexe Herstellungsweise); **technisches Know How** und **Kapazitäten für eine Erhöhung der europäischen Produktion** sind aber (noch) **vorhanden**

DIE KONZENTRATION DER API PRODUKTION KANN DIE VERSORGUNGSSICHERHEIT IN EUROPA BEEINTRÄCHTIGEN

- 1 Nur 33% der CEPs für in Europa benötigte APIs werden von europäischen Standorten gehalten. Über 50% der CEPs liegen in Indien und China; Asien gesamt erreicht über 60% der CEPs
- 2 Die starke Konzentration der Hersteller innerhalb Indiens und Chinas kann sich bei Störereignissen negativ auf die Versorgungssicherheit auswirken
- 3 Für 93 der in Europa benötigten APIs gibt es keine CEPs in Europa
- 4 Für mehr als die Hälfte der APIs gibt es mit ein bis fünf CEPs nur wenige Hersteller

EUROPA STARTETE AUS EINER STARKEN POSITION, ABER DANN KONTINUIERLICHER ZUWACHS DER API PRODUKTION UND DEREN HERSTELLER IN ASIEN

- 5 **Europa ist aus einer dominanten Position gestartet** – aber der **starke Zuwachs** von **neuen CEPs** in **Asien**, **hauptsächlich** in **Indien** und **China**, **hat zu einer Verlagerung** nach **Asien** geführt
- 6 Als **Gründe** für die **Abwanderung** sind **Preisdruck** und **regulatorische Rahmenbedingungen** in **Europa** hervorzuheben
- 7 **Viele** der **Trends** waren in den Jahren **um 2000 am stärksten** und haben sich **inzwischen abgeschwächt**. **Europa** ist nun **hauptsächlich** Produzent **komplexer APIs** mit **kleineren Volumina**
- 8 Bei den **Herstellern von APIs** ergibt sich ein **ähnliches Bild**. Die **steigende Anzahl asiatischer Hersteller** führt bei **gleichzeitiger Stagnation** der **europäischen Hersteller** zu einer **klaren Verschiebung Richtung Asien**
- 9 Die **Entwicklungen** in **China** und **Indien** **verlaufen** zwar **ähnlich**, weisen aber **dennoch deutliche Unterschiede** auf, was **Zunahme** von **CEPs** und **Anzahl Hersteller** betrifft

EUROPÄISCHE HERSTELLER HABEN TENDENZIELL GRÖßERES PORTFOLIO BEI KLEINEREN VOLUMINA; BEI ASIATISCHEN HERSTELLERN IST ES UMGEKEHRT

10

Viele Hersteller in Indien und China bieten ein recht **kleines Portfolio** an, dass sie **aber stetig erweitern**

11

Produktportfolios der Hersteller unterscheiden sich in Indien und China. Indische Hersteller sind **tendenziell größer** und **fokussieren** sich mehr auf **großvolumige APIs**

AUS DEN CEP-DATEN LÄSST SICH AB 2000 EINE ZUNEHMENDE AKTIVITÄT IN ASIEN ABLEITEN

12

Die **API Hersteller** in **Asien** waren **seit 2000 wesentlich aktiver als europäische Hersteller** – insbesondere **Indien** und **China** zeigen eine **starke Dynamik**

13

Die **Wachstumstreiber** waren in **Europa** und **Asien** **ähnlich**. Der **Zuwachs** an **CEPs** wurde **durch Patentausläufe** und die damit **einhergehende Zunahme** der **generischen APIs**, andererseits **durch neu hinzugekommene Hersteller** vorangetrieben. **Beiden Trends** wird in **Zukunft weniger Dynamik** unterstellt

14

Je später ein **API** in das **CEP-Verfahren** eintritt, **desto kleiner** ist von Anfang an der **Anteil europäischer Hersteller**. Während **ältere APIs** nach **Patentablauf hauptsächlich in Europa** hergestellt wurden und **asiatische Hersteller** nur **langsam** in den **jeweiligen Markt** eintraten, sind **asiatische Hersteller** bei **neueren APIs** von **Anfang an dominierend**

ANALYSEN AUF EBENE DER ATC-KLASSEN BESTÄTIGEN DIESE ERGEBNISSE

15

Die **Untersuchung** anhand von **ATC Klassen bestätigt** alle **Ergebnisse**, wobei **innerhalb** der **ATC Klassen beträchtliche Unterschiede** auftreten

16

Ausgewählte APIs wurden **detailliert untersucht**, die **Ergebnisse bestätigen** die **Erkenntnisse** für das **Gesamtportfolio**

- Mit **Zunahme** des **Volumens** der einzelnen **Produkte** treten **verstärkt asiatische - insbesondere indische - Hersteller** in den Vordergrund
- Die **Analysen** realer **Produktionsvolumina** für den **europäischen Bedarf decken** sich im **Mittel** sehr **gut** mit den auf **Anzahl** der **CEPs basierenden Auswertungen**. Im **Einzelfall** kann es zu **Abweichungen** kommen
- **Es scheint**, dass die **Treiber** für eine **Standortwahl** recht **stark** wirken: So werden die **APIs** hauptsächlich **entweder** in **Europa** oder in **Asien hergestellt**, bei **wenigen APIs** gibt es ein **ausgeglichenes** Europa zu Asien **Verhältnis**
- **Ältere APIs** sind **historisch** in **Europa stark** und zeigen nur **langsame Abwanderung** nach **Asien**, während **jüngere APIs** bereits **beim Eintritt** ins **CEP-Verfahren hohen Anteil asiatischer Hersteller** aufweisen und/ **oder** eine **Abwanderung schneller** erfolgt

EUROPA HEUTE FOKUSSIERT AUF „NISCHENPRODUKTE“, ABER POTENTIAL UND KAPAZITÄTEN SIND NOCH VORHANDEN

17

Europa ist heute fokussiert auf **APIs** mit **niedrigem Produktionsvolumen**, **technisch komplexer Herstellungsweise** und **Produkte mit besonderen Qualitätsansprüchen**

Studienteilnehmer unterbreiten verschiedene **Verbesserungsvorschläge**.

18

Neben einer **Verbesserung** der **Datenlage** als Basis für **Entscheidungen** werden **Änderungen** auf verschiedenen **Stufen** der **Wertschöpfungskette** vorgeschlagen. **Besonders stark** ist der **Wunsch** nach **Veränderungen** sowohl **arzneimittelrechtlicher** als auch **erstattungsrechtlicher Regulierungen**

19

Konkrete Maßnahmen zeigen Möglichkeiten auf, um die **Abhängigkeit** von **Asien** zu **reduzieren**

UNTERSUCHUNGSUMFANG, METHODIK UND DATENQUELLEN

Untersuchungs- umfang

- Generische APIs, die mit mind. einem CEP in der Datenbank des European Directorate for the Quality of Medicines & HealthCare (EDQM) vertreten sind (gesamt: 565 APIs)
- Exemplarische Auswahl von 21 APIs aus obiger Gruppe für eine detaillierte Untersuchung
- Fokussierung auf API, keine Berücksichtigung der Rohstoffe und Vorprodukte

Methodik

- Erstellung einer bereinigten CEP Datenbank – angereichert mit weiteren Herstellerinformationen
- Detaillierte Auswertung obiger Datenbank nach verschiedenen Kriterien
- Desk Research für weitergehende Betrachtungen
- Interviews mit API Herstellern und Stakeholdern
 - Zur quantitativen Abschätzung der Deckung des europäischen Bedarfs für ausgewählte APIs
 - Zur Validierung der Ergebnisse und Bestätigung von Trends und Ursachen

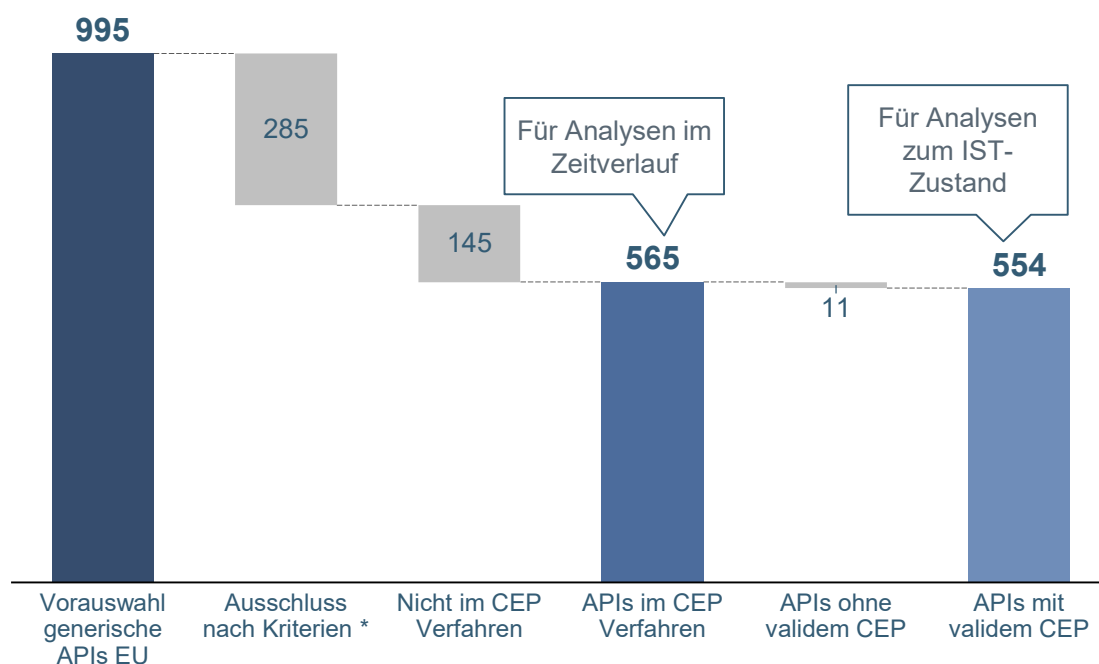
Datenquellen

- CEPs: Aus der Datenbank des European Directorate for the Quality of Medicines & HealthCare: https://extranet.edqm.eu/publications/recherches_CEP.shtml
- Import- und Exportdaten: QYOBO Market Platform
- Europäische Verbrauchsdaten: IQVIA
- Herstellerinformationen: Unternehmens-Webseiten, Pharmaoffer, CPhI, Pressemitteilungen, andere Webseiten
- Trends- und Volumenabschätzungen: Interviews mit API Herstellern und Stakeholdern

565 WIRKSTOFFE IN DIE ANALYSEN DER REGIONALEN VERTEILUNG DER API-HERSTELLUNG EINGESCHLOSSEN

ÜBERBLICK API-AUSWAHL FÜR DIE GESAMT- UND EINZELAUSWERTUNG

API-Auswahl für die Gesamtauswertung



Exemplarische API-Auswahl für Einzelauswertung

APIs wurden anhand folgender Kriterien bewertet und **21 Kandidaten exemplarisch** für die **Detailbetrachtung** priorisiert:

- Wichtiger Vertreter aus der ATC-Klasse
- Hoher Bedarf in Europa
- Kritisch in der Versorgung lebensbedrohlicher Erkrankungen
- Lieferengpässe in der Vergangenheit
- Volkswirtschaftlich relevant

*) APIs mit folgenden Eigenschaften wurden ausgeschlossen: nicht generisch, pflanzlich, Biosimilar, Vitamin/ Supplement sowie API der ATC-Gruppen: A1 Stomatologika, A11 Vitamine, A12 Mineralstoffe, A16 Andere Mittel für das alimentäre System und den Stoffwechsel, D2 Emolienta und Hautschutzmittel, V3 Alle übrigen therapeutischen Mittel, Excipients

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

DATENGRUNDLAGE DER ANALYSEN BILDET DIE CEP DATENBANK¹ ALS REPRÄSENTATIVE QUELLE FÜR DIE VERTEILUNG DER API-HERSTELLER

ÜBERSICHT ZUM CEP-VERFAHREN

Informationen zum CEP-Verfahren

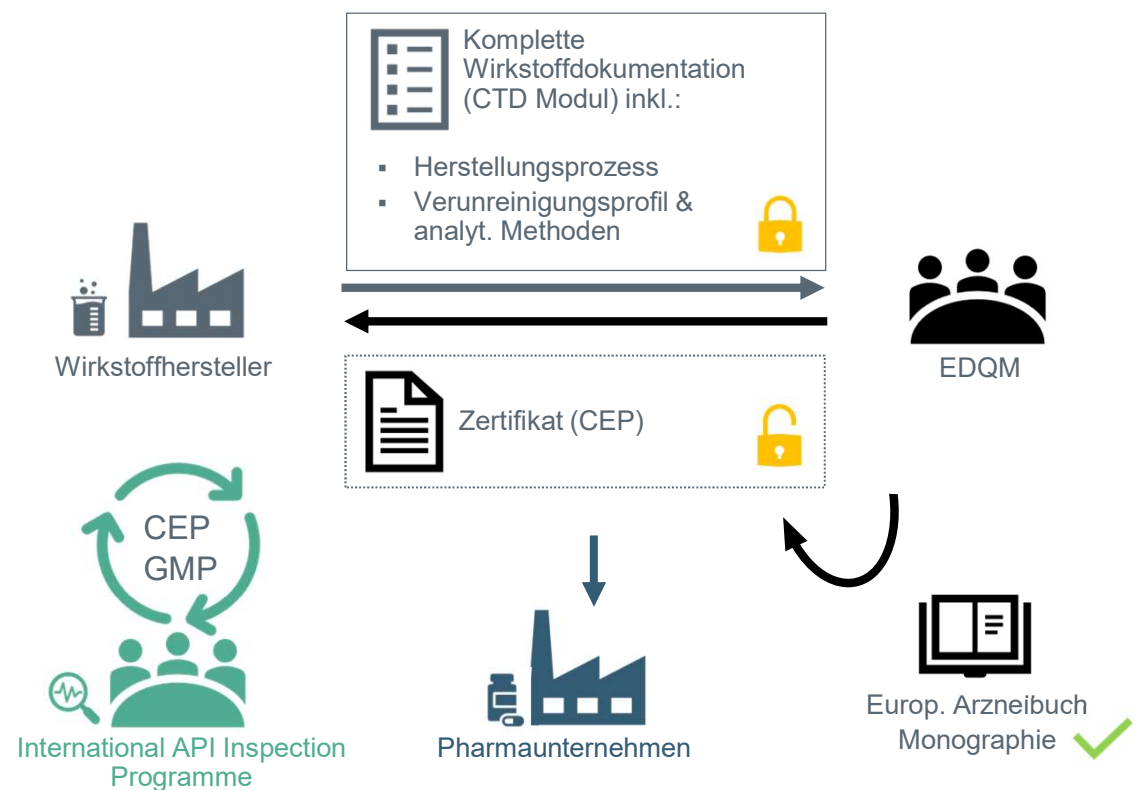
Allgemein

- 1994 eingeführt
- Anerkannt in Europa und Australien, Kanada, Neuseeland, Saudi Arabien, Südafrika, Taiwan
- Einmalige Erneuerung nach 5 Jahren

Qualitätsmanagement

- Inspektionsprogramm für Produktionsstätten von CEP-Inhabern
- Inspektionsvorschlag durch nationale Arzneimittelbehörden
- Bestätigung der CEP-Compliance & Ausstellung eines GMP-Zertifikats bei erfolgreicher Prüfung
- Ausstellung eines Non-Compliance-Reports bei nicht-erfolgreicher Prüfung

Schematische Darstellung des CEP-Verfahrens



¹⁾ Zertifikate anderer Zulassungsverfahren, wie beispielsweise die Ausstellung eines DMF, werden in der repräsentativen Analyse nicht eingeschlossen
Quelle: Dr. Helga Blasius, 02.08.2018, Das Valsartan-CEP, <https://www.deutsche-apotheker-zeitung.de/daz-az/2018/daz-31-2018/das-valsartan-cep>

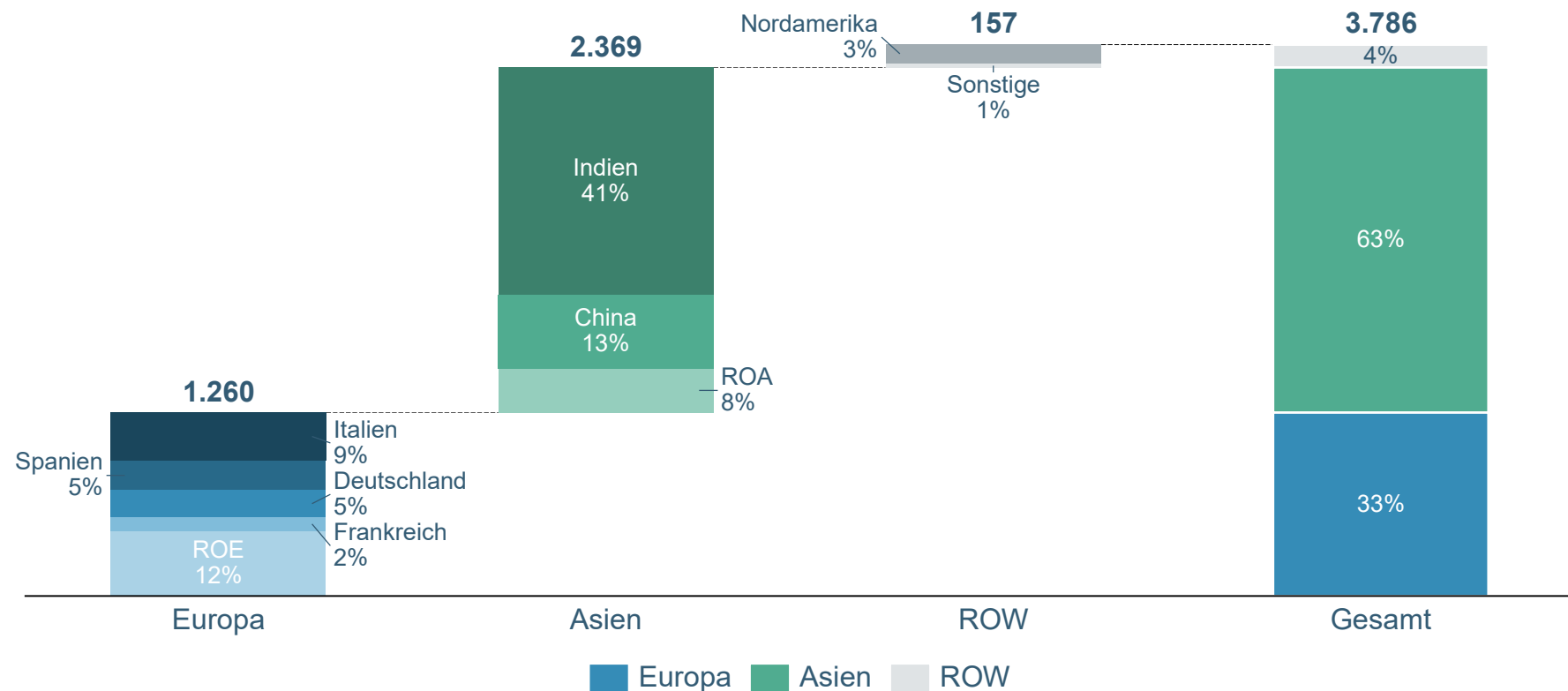
DIE KONZENTRATION DER API PRODUKTION KANN DIE VERSORGUNGSSICHERHEIT IN EUROPA BEEINTRÄCHTIGEN

- 1 Nur 33% der CEPs für in Europa benötigte APIs werden von europäischen Standorten gehalten. Über 50% der CEPs liegen in Indien und China; Asien gesamt erreicht über 60% der CEPs
- 2 Die starke Konzentration der Hersteller innerhalb Indiens und Chinas kann sich bei Störereignissen negativ auf die Versorgungssicherheit auswirken
- 3 Für 93 der in Europa benötigten APIs gibt es keine CEPs in Europa
- 4 Für mehr als die Hälfte der APIs gibt es mit ein bis fünf CEPs nur wenige Hersteller

ASIEN HÄLT AKTUELL FAST DOPPELT SO VIELE CEPS WIE EUROPA, ANDERE REGIONEN SPIELEN EINE UNTERGEORDNETE ROLLE

ÜBERBLICK: VERTEILUNG DER AKTUELL VALIDEN ZERTIFIKATE (STAND 2020*)¹

Anzahl CEPs



*) Stichtag der Datenerhebung ist der 30.04.2020, gilt für alle folgenden Analysen

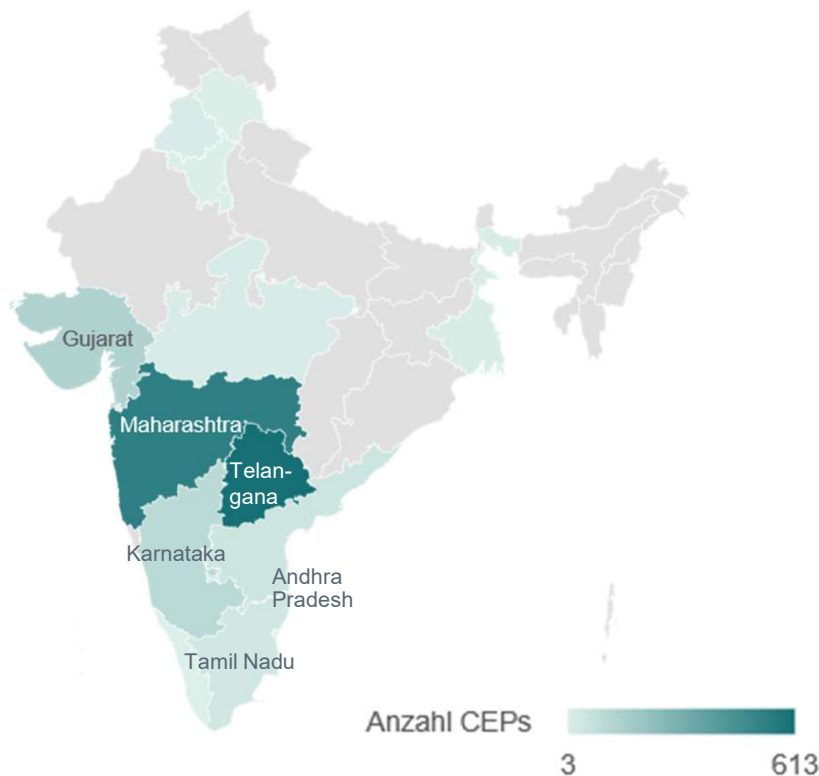
¹) Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

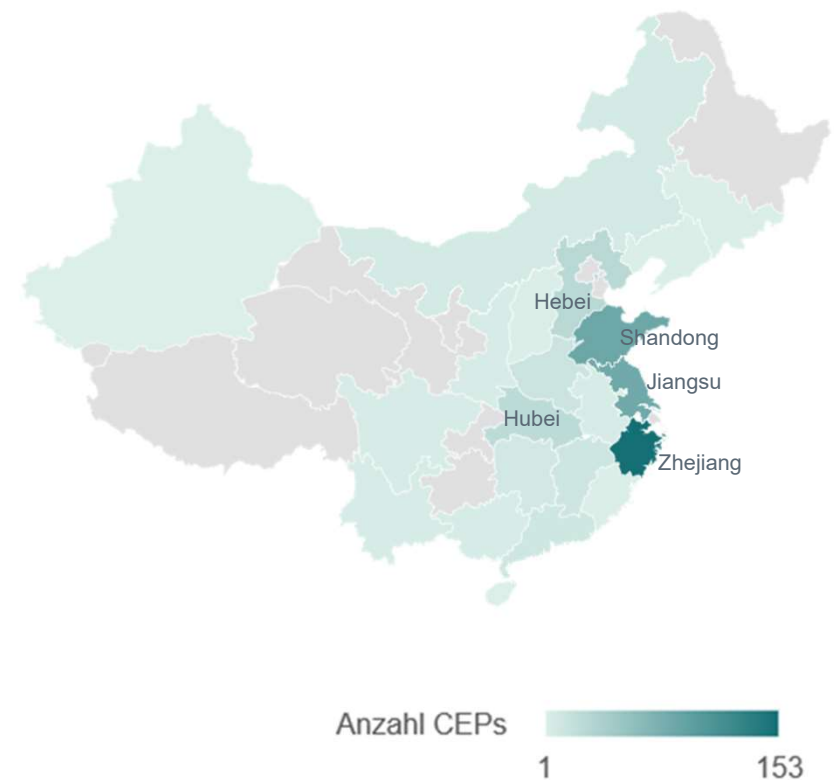
INNERHALB INDIENS UND CHINAS KONZENTRIEREN SICH DIE HERSTELLER STARK IN BESTIMMTEN PROVINZEN

GEOGRAPHISCHE VERTEILUNG ASIATISCHER CEPS (STAND 2020)¹

Indien: Verteilung CEPs nach Provinzen



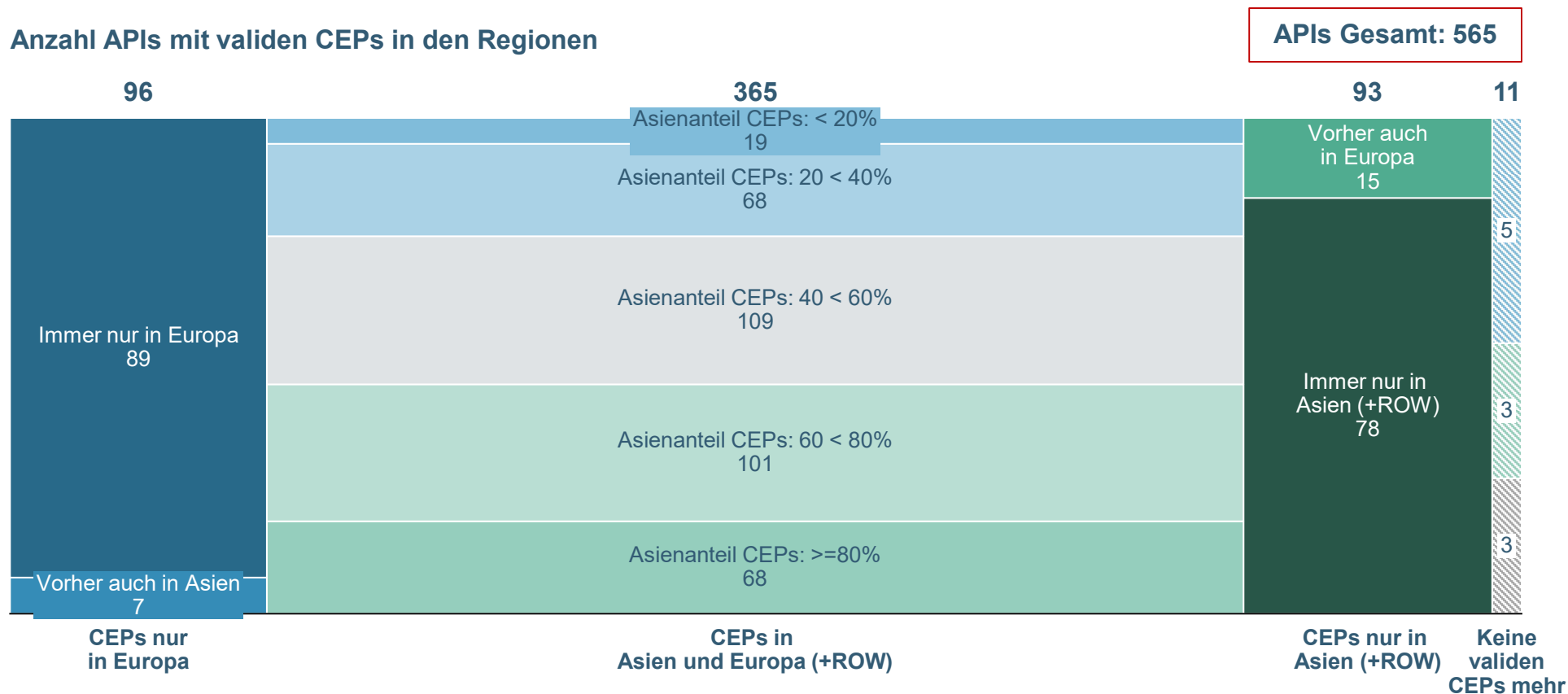
China: Verteilung CEPs nach Provinzen



¹) Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)
 Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

HEUTE WERDEN 93 DER IN EUROPA BENÖTIGTEN WIRKSTOFFE MIT EINEM CEP AUSSCHLIESSLICH AUSSERHALB EUROPAS HERGESTELLT

ÜBERSICHT GLOBALE VERTEILUNG DER API-HERSTELLUNG (STAND 2020)¹

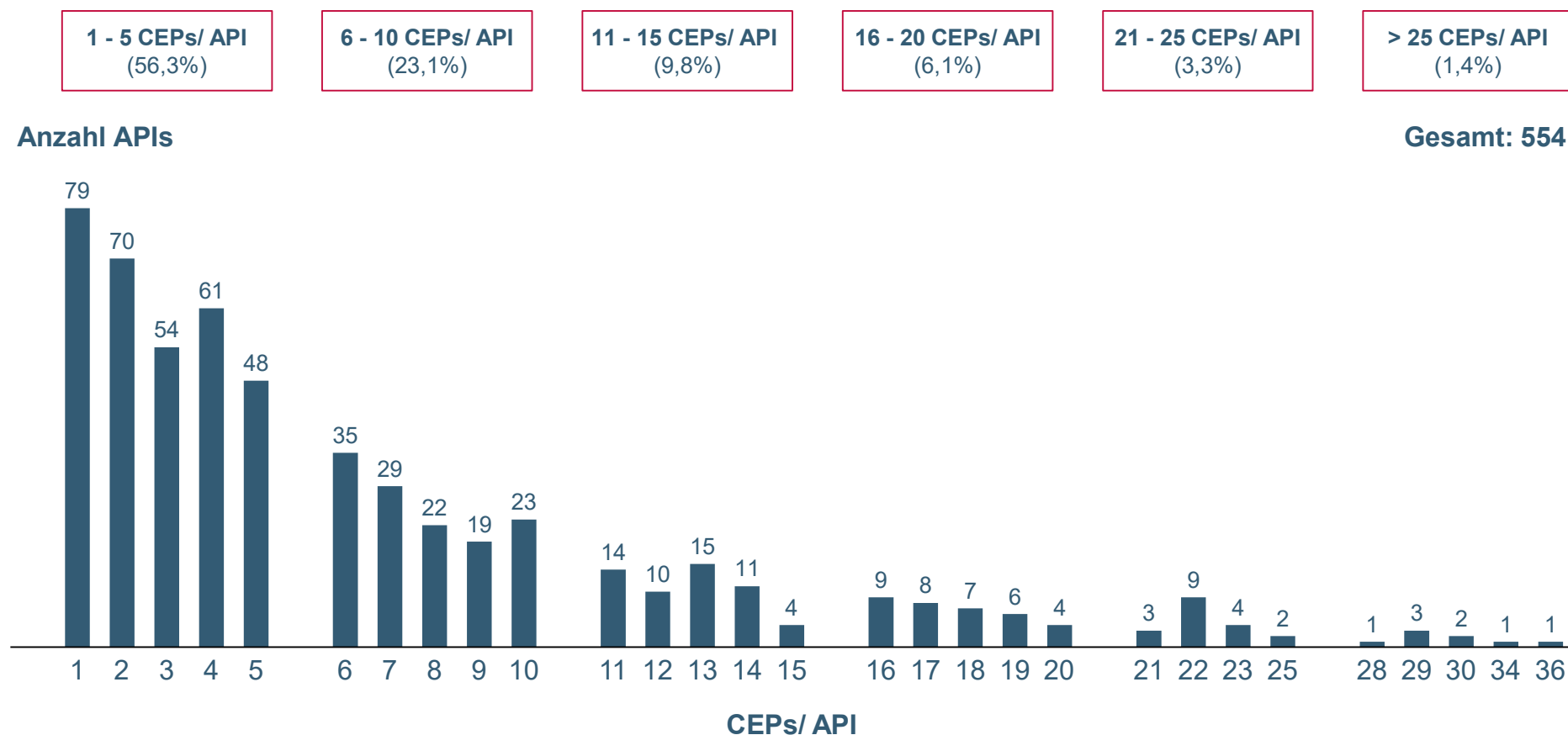


¹) Anzahl aller betrachteten APIs mit validen CEPs im jeweiligen Kalenderjahr (APIs mit ausschließlich abgelaufenen/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

FÜR MEHR ALS DIE HÄLFTE DER APIS GIBT ES MIT EIN BIS FÜNF CEPS NUR WENIGE HERSTELLER

ÜBERSICHT ANZAHL API JE GRUPPE „CEPS/ API“ WELTWEIT (STAND 2020)¹



¹⁾ Anzahl aller betrachteten APIs mit validen CEPS im jeweiligen Kalenderjahr (APIs mit ausschließlich abgelaufenen/ zurückgezogene CEPS sind bereits ausgeschlossen)

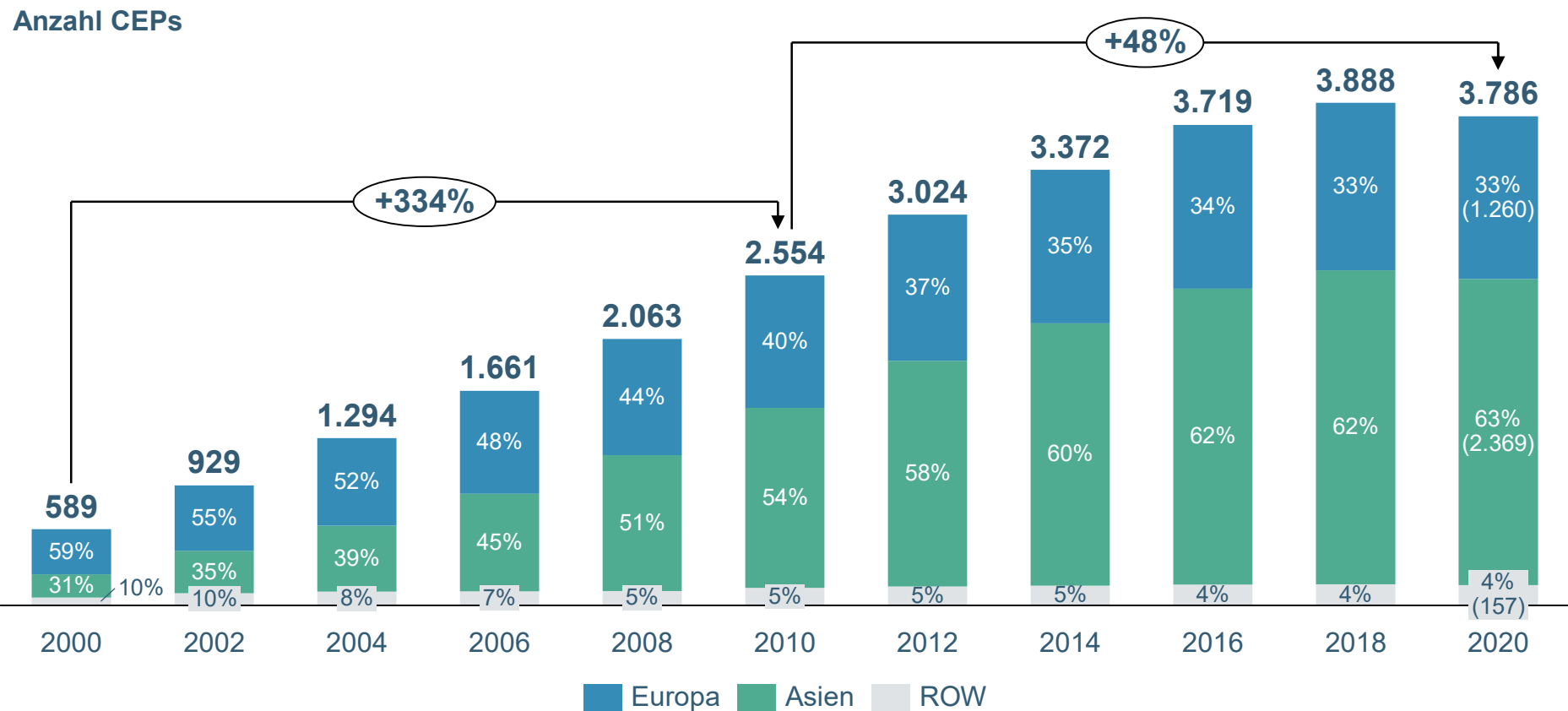
Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

EUROPA STARTETE AUS STARKER POSITION, ABER DANN STETIGER ZUWACHS DER API PRODUKTION UND DEREN HERSTELLER IN ASIEN

- 5 **Europa ist aus einer dominanten Position gestartet** – aber der **starke Zuwachs** von **neuen CEPs** in **Asien**, **hauptsächlich** in **Indien** und **China**, **hat zu einer Verlagerung** nach **Asien** geführt
- 6 Als **Gründe** für die **Abwanderung** sind **Preisdruck** und **regulatorische Rahmenbedingungen** in **Europa** hervorzuheben
- 7 **Viele** der **Trends** waren in den Jahren **um 2000 am stärksten** und haben sich **inzwischen abgeschwächt**. **Europa** ist nun **hauptsächlich** Produzent **komplexer APIs** mit **kleineren Volumina**
- 8 Bei den **Herstellern von APIs** ergibt sich ein **ähnliches Bild**. Die **steigende Anzahl asiatischer Hersteller** führt bei **gleichzeitiger Stagnation** der **europäischen Hersteller** zu einer **klaren Verschiebung Richtung Asien**
- 9 Die **Entwicklungen** in **China** und **Indien** **verlaufen** zwar **ähnlich**, weisen aber **dennoch deutliche Unterschiede** auf, was **Zunahme** von **CEPs** und **Anzahl Hersteller** betrifft

SEIT 20 JAHREN KONTINUIERLICHER ASIEN-SHIFT: DAS VERHÄLTNISS ZWISCHEN EUROPA UND ASIEN HAT SICH VOLLSTÄNDIG UMGEKEHRT

ENTWICKLUNG DER ANZAHL VALIDER CEPS (2000 – 2020)¹



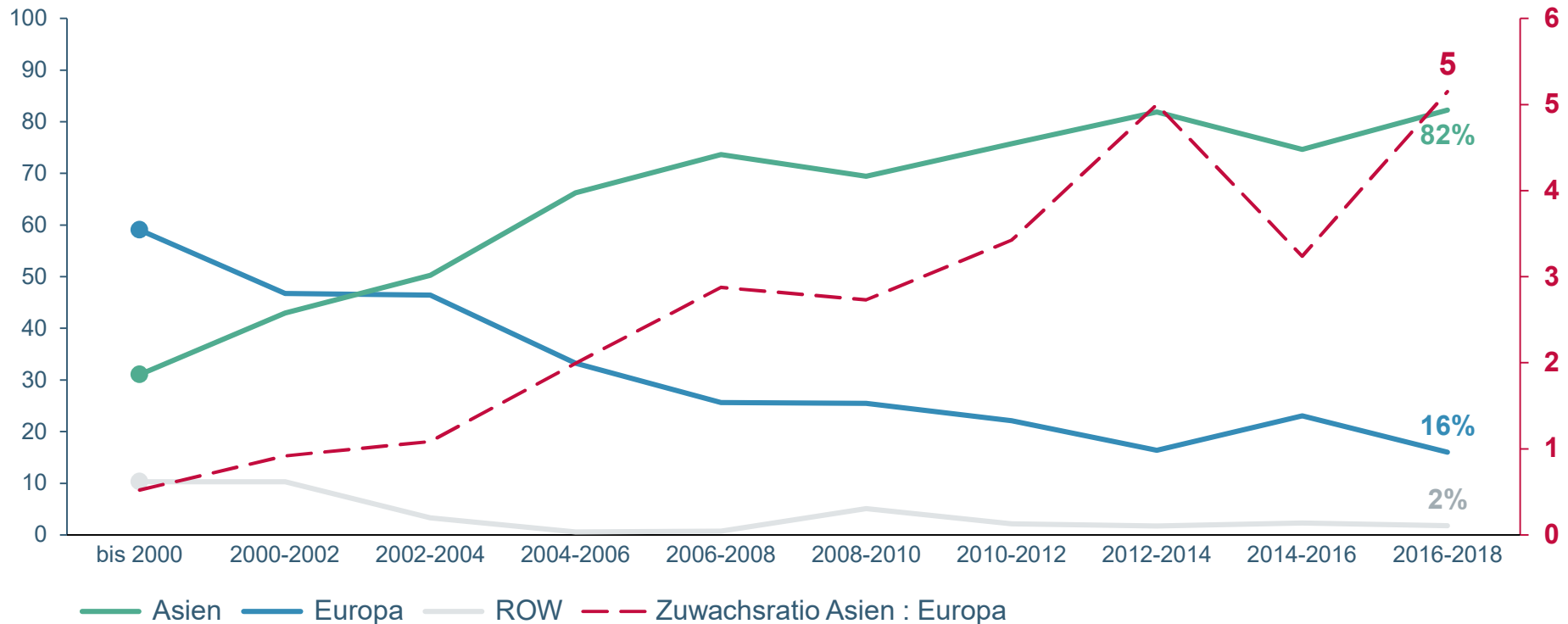
¹) Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

ASIATISCHER ANTEIL AM CEP-ANSTIEG DER LETZTEN 10 JAHRE BETRUG 70–80%

ANTEIL AM ANSTIEG DER WELTWEIT VALIDEN CEPS (2000 – 2018)^{1,2}

Anteil am CEP- Zuwachs
(in %)



¹⁾ Nettozuwachs aller validen CEPs für die betrachteten APIs in der jeweiligen Spanne (abgelaufene/ zurückgezogene CEPs wurden abgezogen)

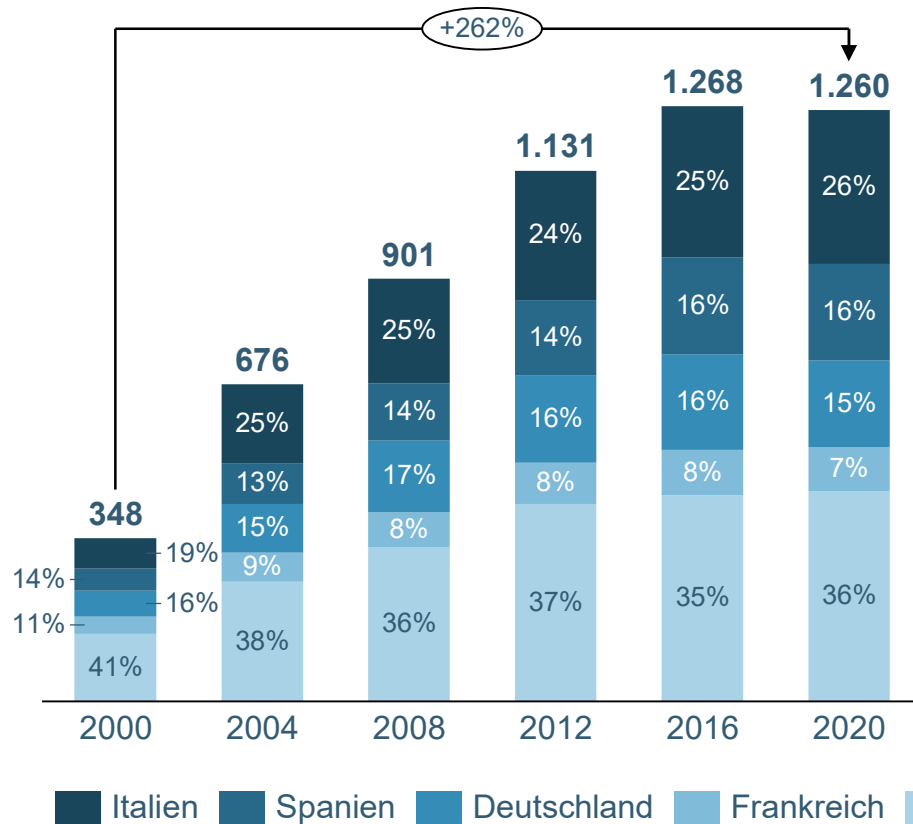
²⁾ Nach aktuellem Datenstand Rückgang in 2020, daher nicht darstellbar

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

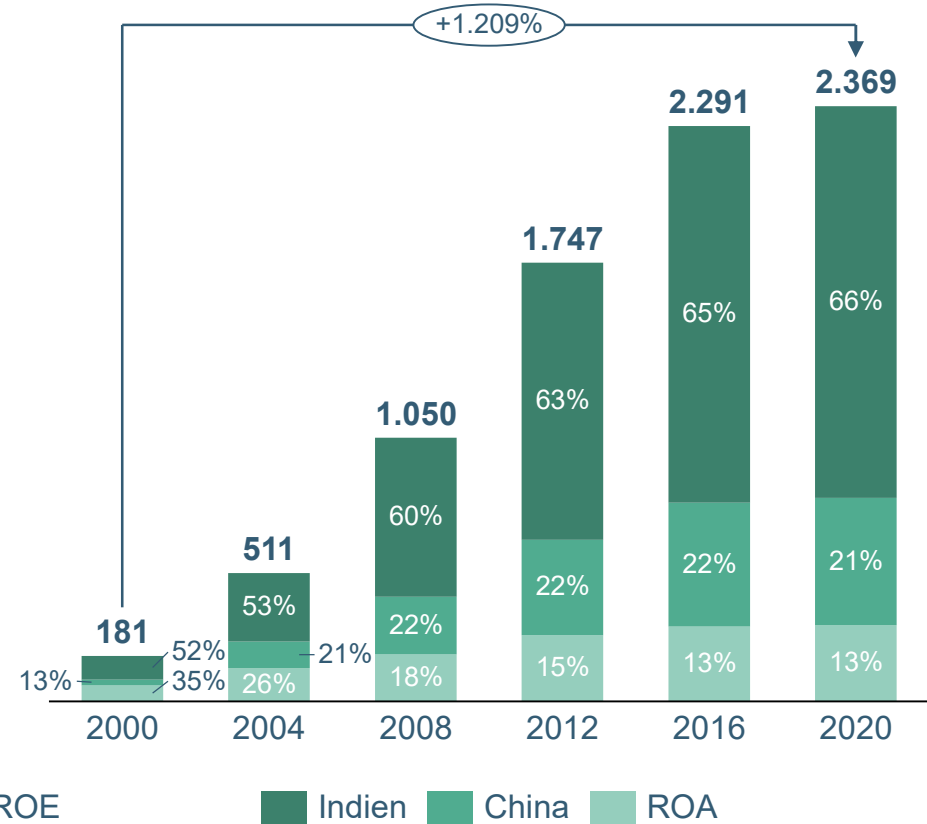
IN EUROPA BLEIBEN DIE VERHÄLTNISSE ZWISCHEN DEN LÄNDERN STABIL, INNERHALB ASIENS WACHSEN INDIEN UND CHINA STÄRKER ALS DER REST

ENTWICKLUNG DER ANZAHL VALIDER CEPS (2000 – 2020)¹

Europa: Entwicklung Anzahl CEPs



Asien: Entwicklung Anzahl CEPs



¹) Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)
Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

VOR ALLEM PREISDRUCK UND REGULATORISCHE RAHMENBEDINGUNGEN IN EUROPA WERDEN FÜR ABWANDERUNG VERANTWORTLICH GEMACHT

ZITATE ZUR PROBLEMURSACHE: ABWANDERUNG NACH ASIEN

„Auf dem Generikamarkt herrscht **hoher Preisdruck durch Rabattverträge**. Daher sind viele Generikafirmen gezwungen, Wirkstoffe günstig in Asien zu kaufen“

„Kunden akzeptieren nicht, dass es wichtig ist, in Europa zu produzieren. **Sie sind nicht bereit, mehr zu zahlen**. Indische Preise können nie erreicht werden“

„Manche APIs werden nicht in Europa produziert, weil die **Produktionskosten den Weltmarktpreis um das Zehnfache übersteigen**“

„Einige **Hersteller verlassen** aufgrund von **zu hohem Konkurrenzdruck den Markt**. Die Abhängigkeit von wenigen Herstellern mündet in die API-Knappheit“

„In Europa gibt es **sehr strenge Sicherheitsauflagen** zur Gründung eines biotechnologischen Betriebs. Dies führt zu hohem Zeitaufwand und hohen Kosten. Diese Investitionen lohnen sich bei der Konkurrenz nicht“

„AOK Tender, the winner takes it all. **Asiatischer Hersteller gewinnt alles**, obwohl weder Forecast Planung noch Supply Chain existiert. **Lieferengpässe sind vorprogrammiert**“

„**Bewilligungsprozess in Europa zu langsam**, während in Indien neue Kapazitäten problemlos aufgebaut werden“

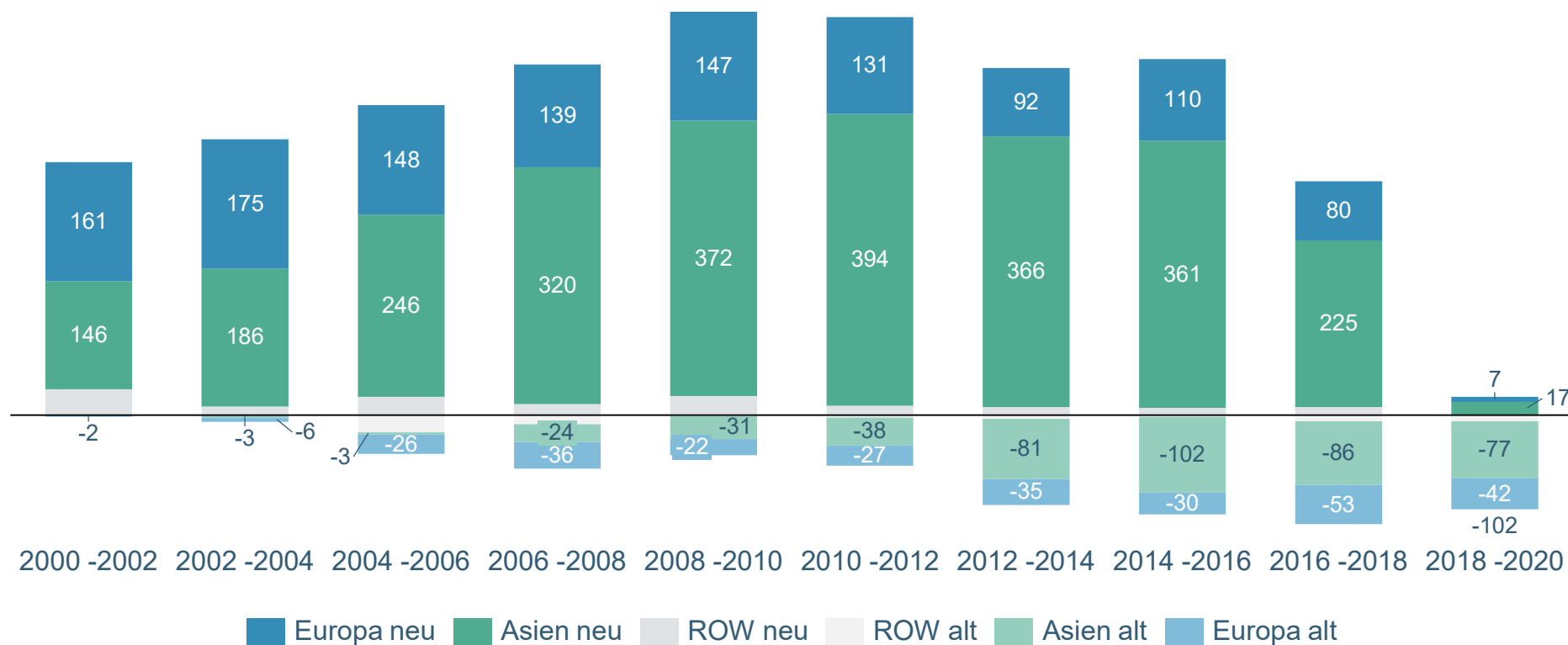
„**Hohe Kostenstruktur** in Europa auch **durch geringe Produktionsmengen**“

„**Unfares Verhalten Chinas** [starke Verflechtung zwischen Staat und Wirtschaft] und **falsche europäische Regelungen** geben **Wettbewerbsvorteil für China**“

UM 2010 HERUM ERREICHT DIE ZAHL DER NEU AUSGESTELLTEN CEPS IHREN HÖHEPUNKT – IN ASIEN WIE IN EUROPA

HISTORIE NEUE UND ABGELAUFENE CEPS NACH REGIONEN (2000-2020)

Anzahl CEPS

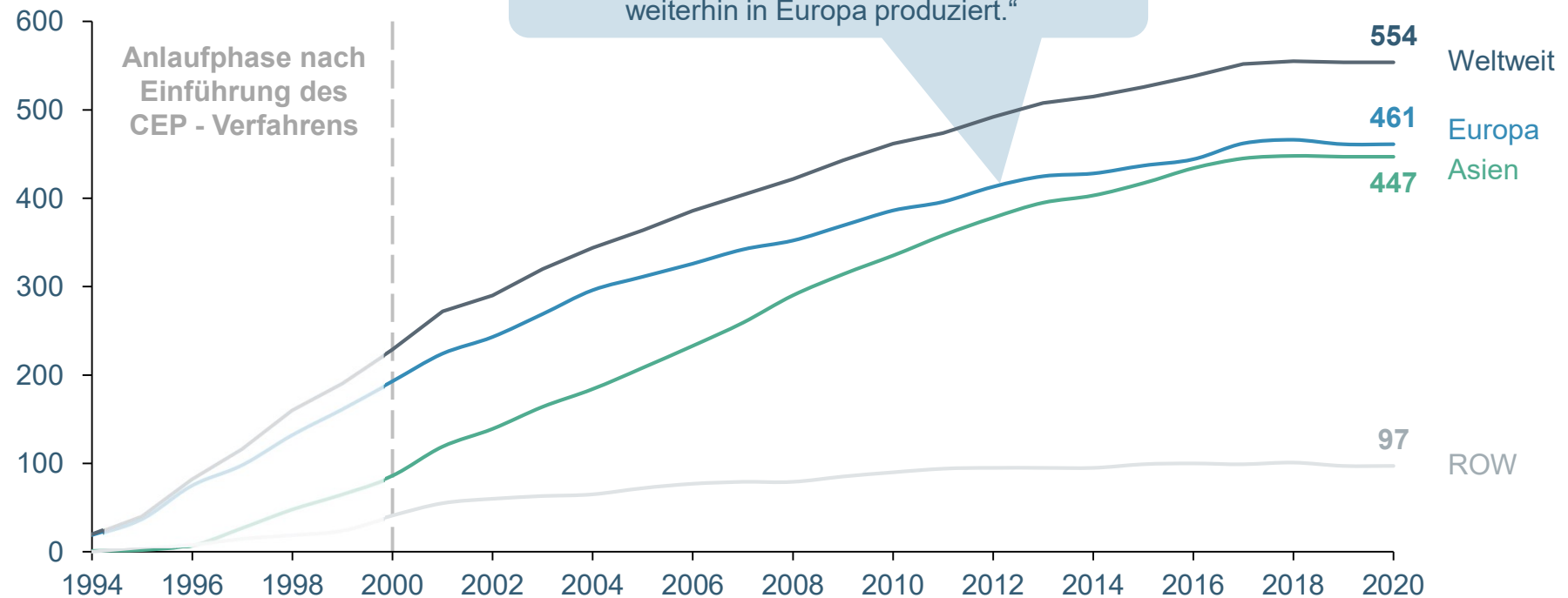


Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

HAUPTTREIBER FÜR STEIGENDE CEPS WAREN NEU HINZUGEKOMMENE APIS, DERZEIT STELLT SICH EIN PLATEAU EIN

ENTWICKLUNG ANZAHL APIS MIT VALIDEN CEPS JE REGION (1994 – 2020)¹

Anzahl APIs mit validen CEPS



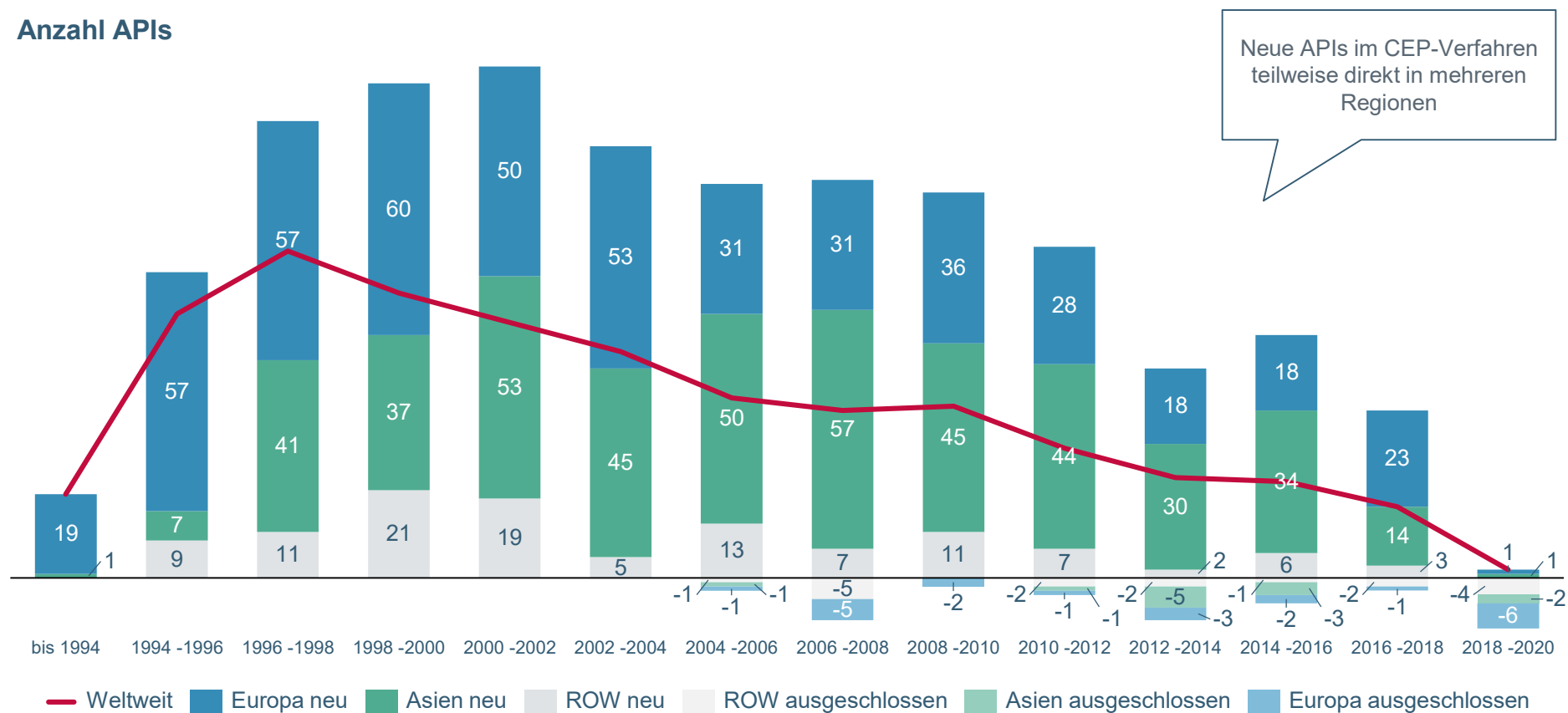
¹) Anzahl aller betrachteten APIs mit validen CEPS im jeweiligen Kalenderjahr (APIs mit ausschließlich abgelaufenen/ zurückgezogene CEPS sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

GRÖSSTE ANZAHL APIS ZWISCHEN 1996 – 1998 IN DAS CEP VERFAHREN AUFGENOMMEN, IN DER JÜNGSTEN VERGANGENHEIT MEHR AUSSCHLUSS

DETAIL HISTORIE NEUE UND WEGGEFALLENE APIS (1994-2020)

Anzahl APIs

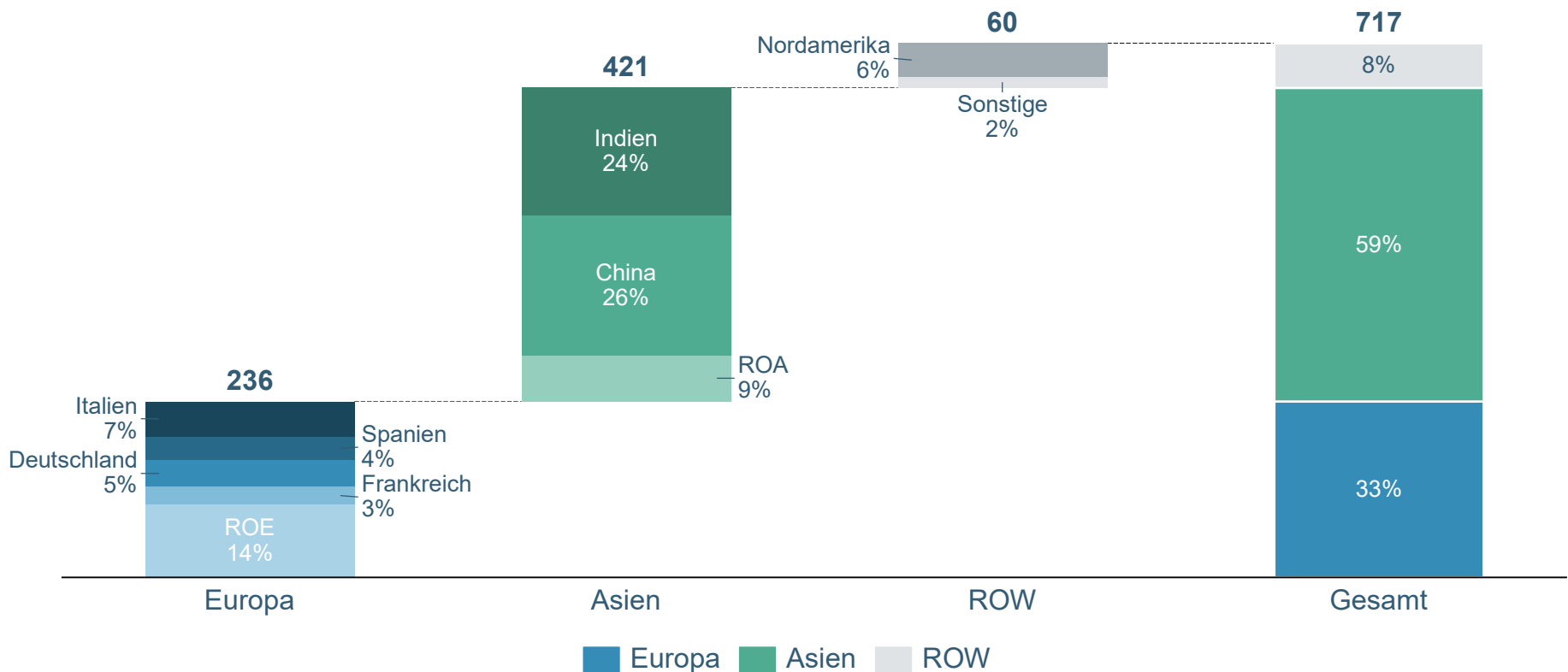


Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

BEI DER VERTEILUNG DER HERSTELLER ERGIBT SICH EIN ÄHNLICHES BILD WIE BEI DEN CEPS; IN ASIEN SIND FAST DOPPELT SO VIELE WIE EUROPA

ÜBERSICHT GLOBALE VERTEILUNG DER HERSTELLER (STAND 2020)¹

Anzahl Hersteller

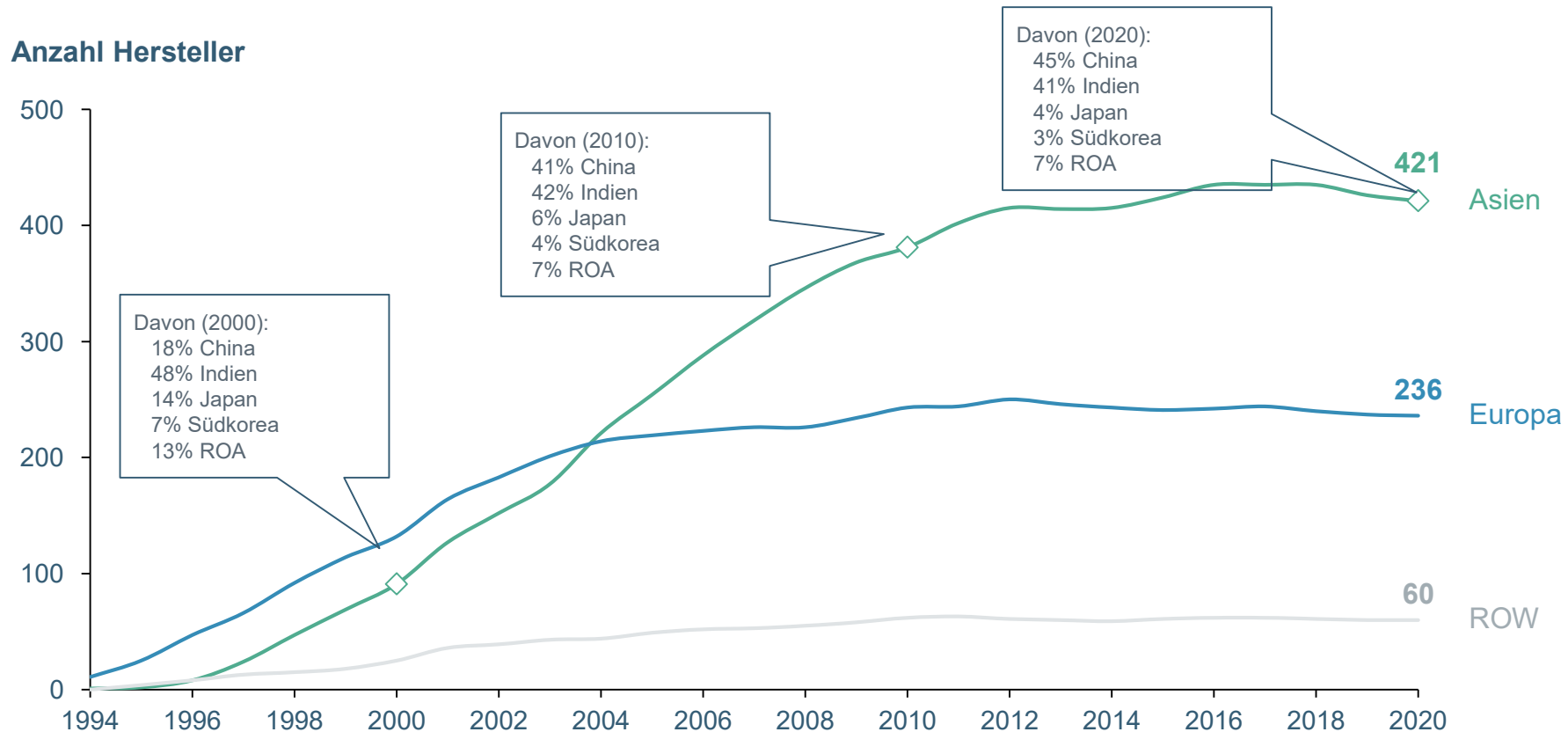


¹⁾ Anzahl aller Hersteller mit validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (Hersteller mit ausschließlich abgelaufenen/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

MIT DEM ANSTIEG DER APIS WUCHS ZUNÄCHST AUCH DIE ANZAHL VON HERSTELLERN, IN EUROPA BEREITS STAGNATION SEIT 2004

ENTWICKLUNG ANZAHL AKTIVER HERSTELLER (1994 - 2020)¹



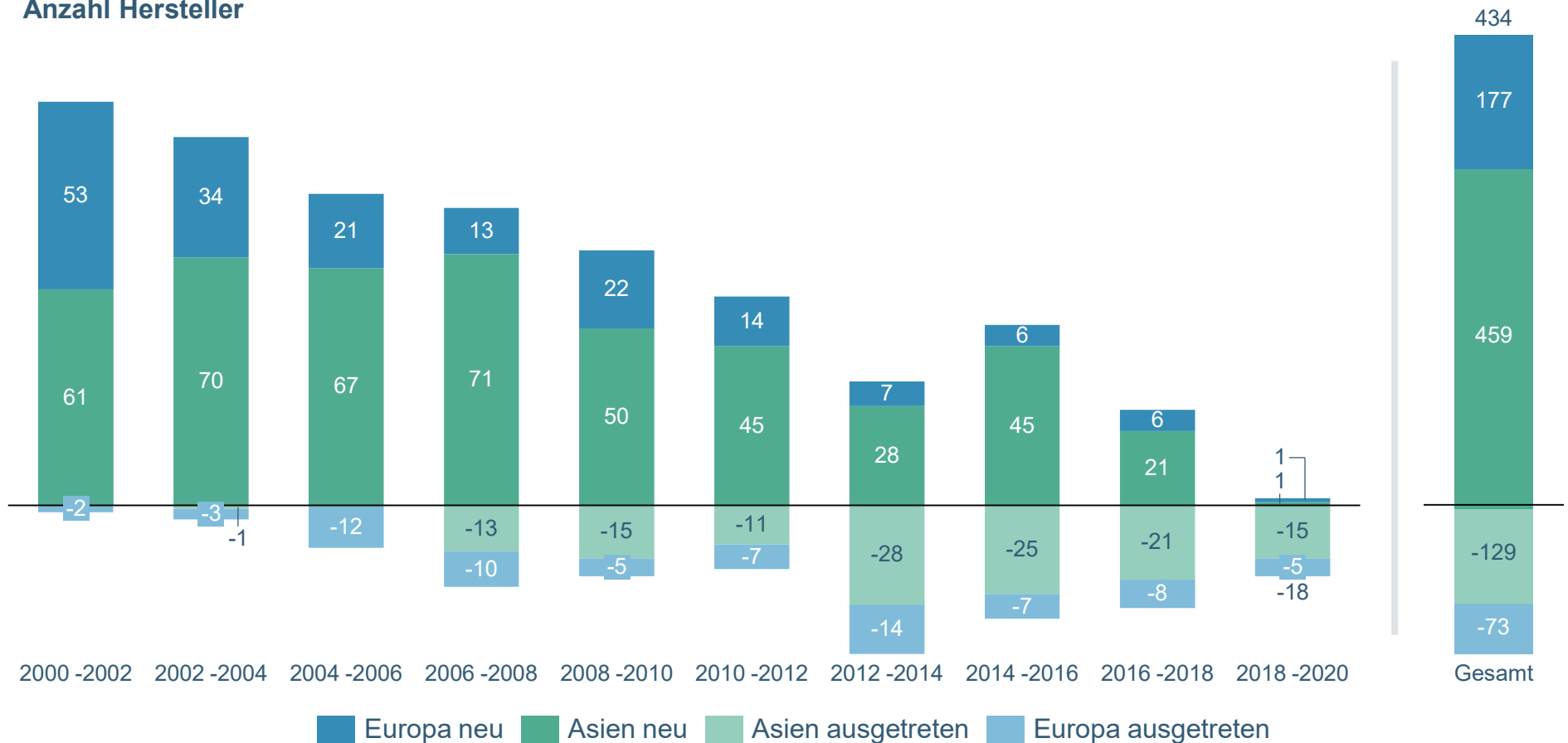
¹) Anzahl aller Hersteller mit validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (Hersteller mit ausschließlich abgelaufenen/zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

NETTO-ZUWACHS ASIATISCHER HERSTELLER IM VERGLEICH ZU EUROPA 3X HÖHER, BEDINGT DURCH DEUTLICH MEHR NEUE MARKTTESILNEHMER

HISTORIE NEUE UND AUSGETRETENE HERSTELLER (2000-2020)

Anzahl Hersteller

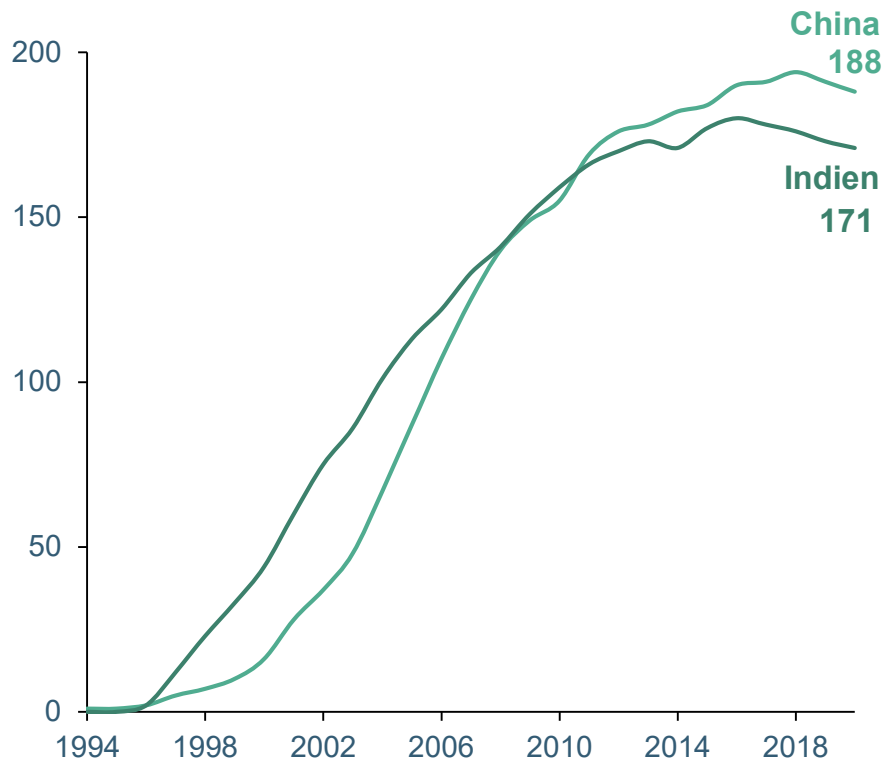


Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

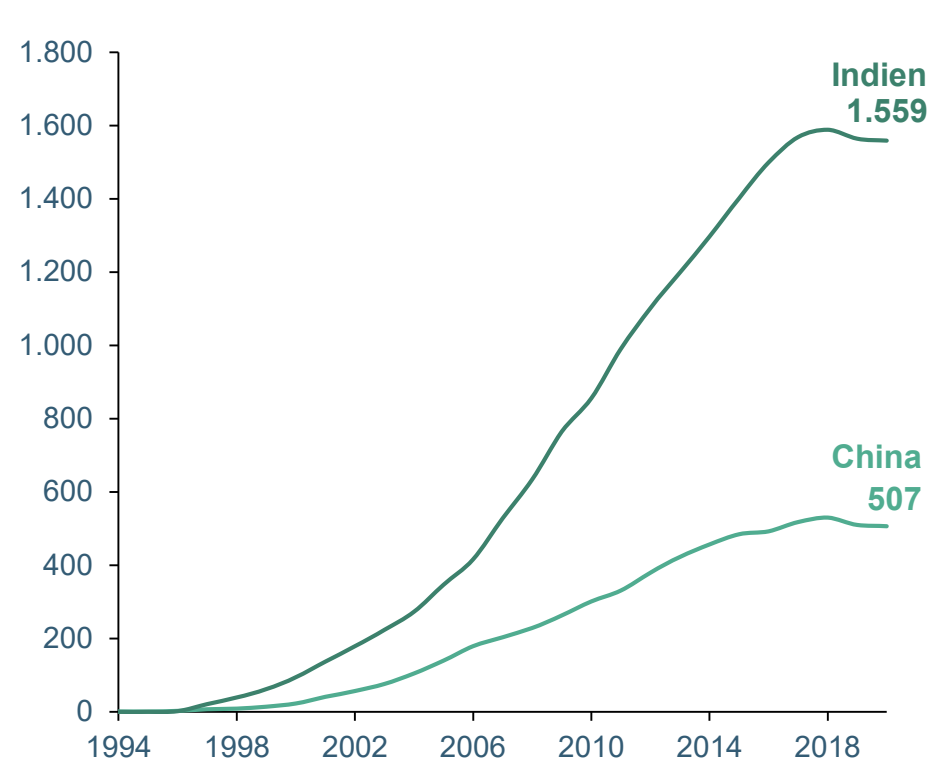
ENTWICKLUNGEN IN CHINA UND INDIEN VERLAUFEN ÄHNLICH, ABER CHINA MIT DEUTLICH WENIGER CEPS

INDIEN UND CHINA: ENTWICKLUNG ANZAHL AKTIVER HERSTELLER & VALIDER CEPS¹

Anzahl Hersteller



Anzahl CEPS



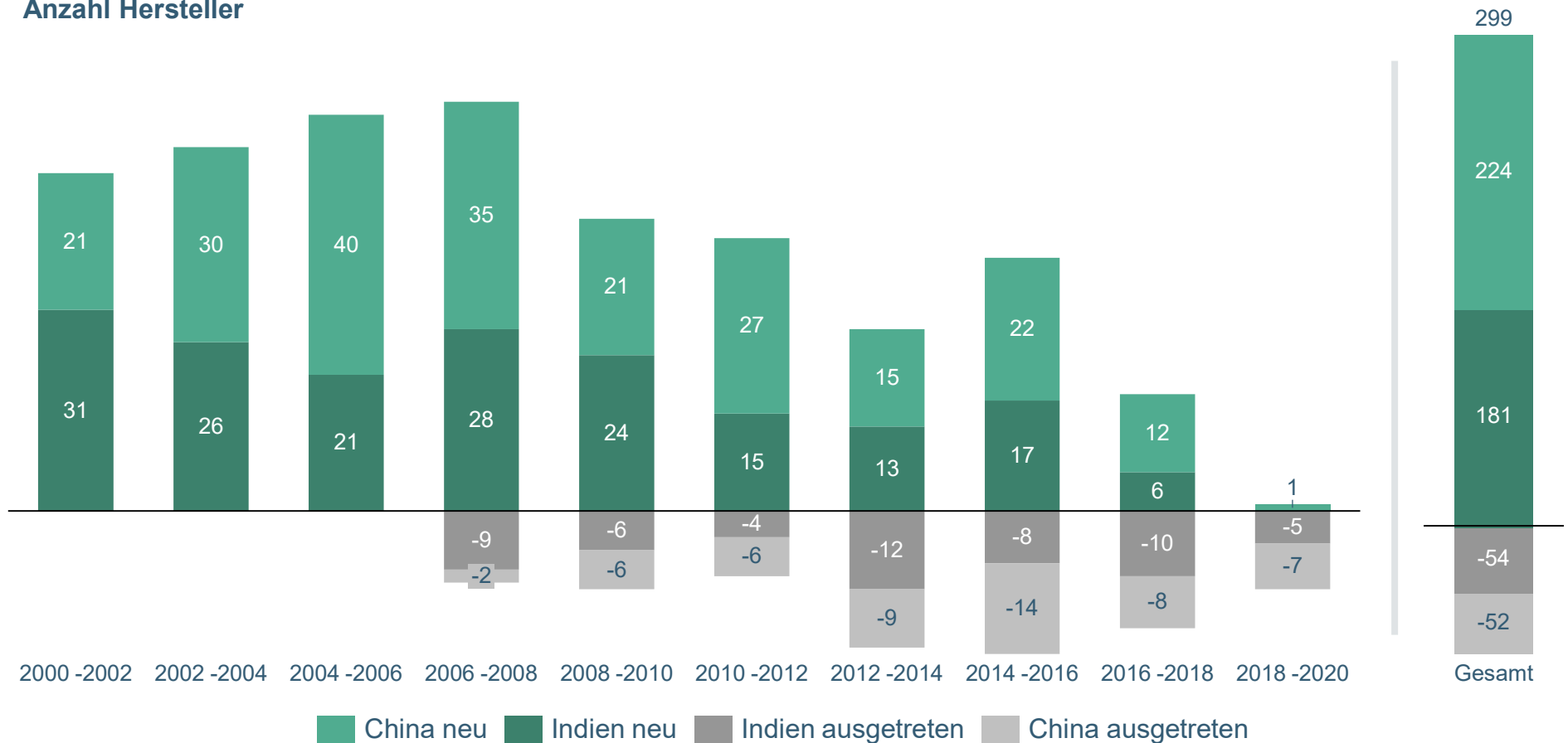
¹) Anzahl aller Hersteller mit validen CEPS im jeweiligen Kalenderjahr für die betrachteten APIs (Hersteller mit ausschließlich abgelaufenen/ zurückgezogene CEPS sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

ANZAHL NEUER CHINESISCHER HERSTELLER STEIGT ÜBER DIE JAHRE DURCHGEHEND STÄRKER ALS IN INDIEN

INDIEN UND CHINA: HISTORIE NEUE UND AUSGETRETENE HERSTELLER (2000-2020)

Anzahl Hersteller



Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

EUROPÄISCHE HERSTELLER HABEN EHER GRÖßERES PORTFOLIO BEI KLEINEREN VOLUMINA; BEI ASIATISCHEN HERSTELLERN IST ES UMGEKEHRT

10

Viele Hersteller in Indien und China bieten ein recht **kleines Portfolio** an, dass sie **aber stetig erweitern**

11

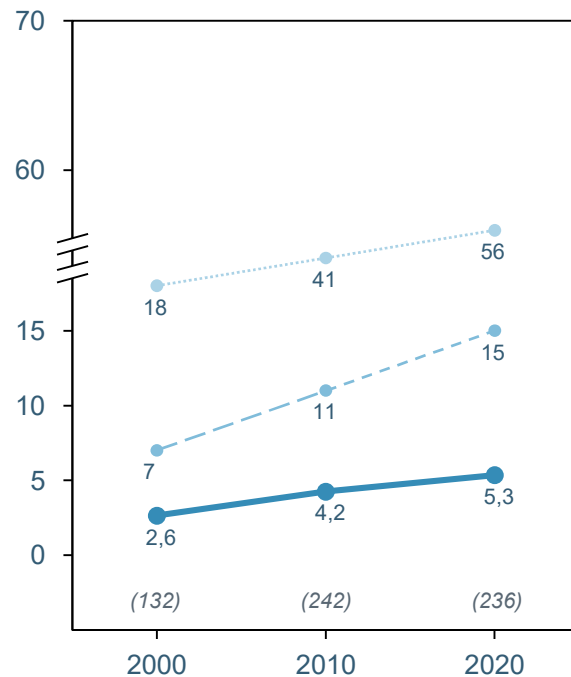
Produktportfolios der Hersteller unterscheiden sich in Indien und China. Indische Hersteller sind **tendenziell größer** und **fokussieren** sich mehr auf **großvolumige APIs**

ÜBER DIE ZEIT ERWEITERTEN HERSTELLER IN EUROPA UND ASIEN IHRE PRODUKT-PORTFOLIOS UND HALTEN HEUTE MEHR CEPS...

ENTWICKLUNG DER CEPS/ HERSTELLER (2000 – 2020)¹

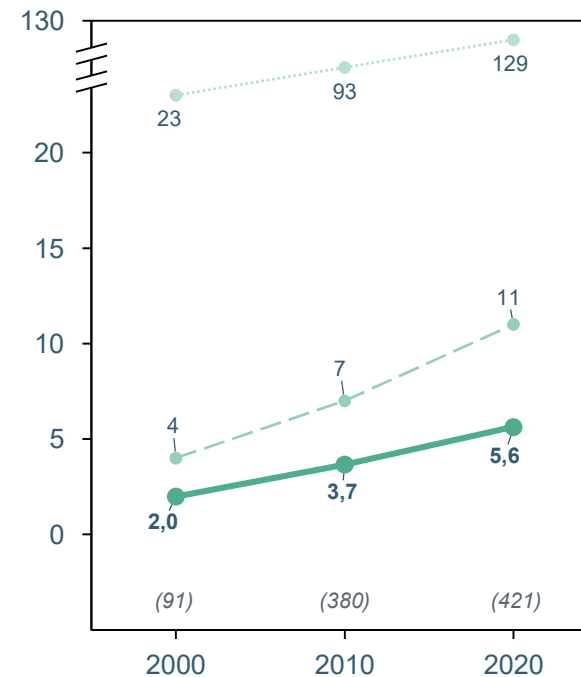
Europa

Anzahl CEPS/ Hersteller



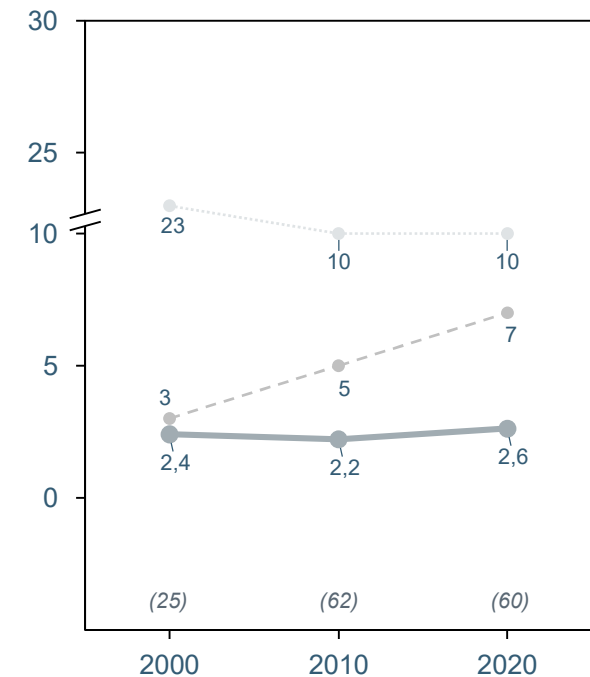
Asien

Anzahl CEPS/ Hersteller



ROW

Anzahl CEPS/ Hersteller

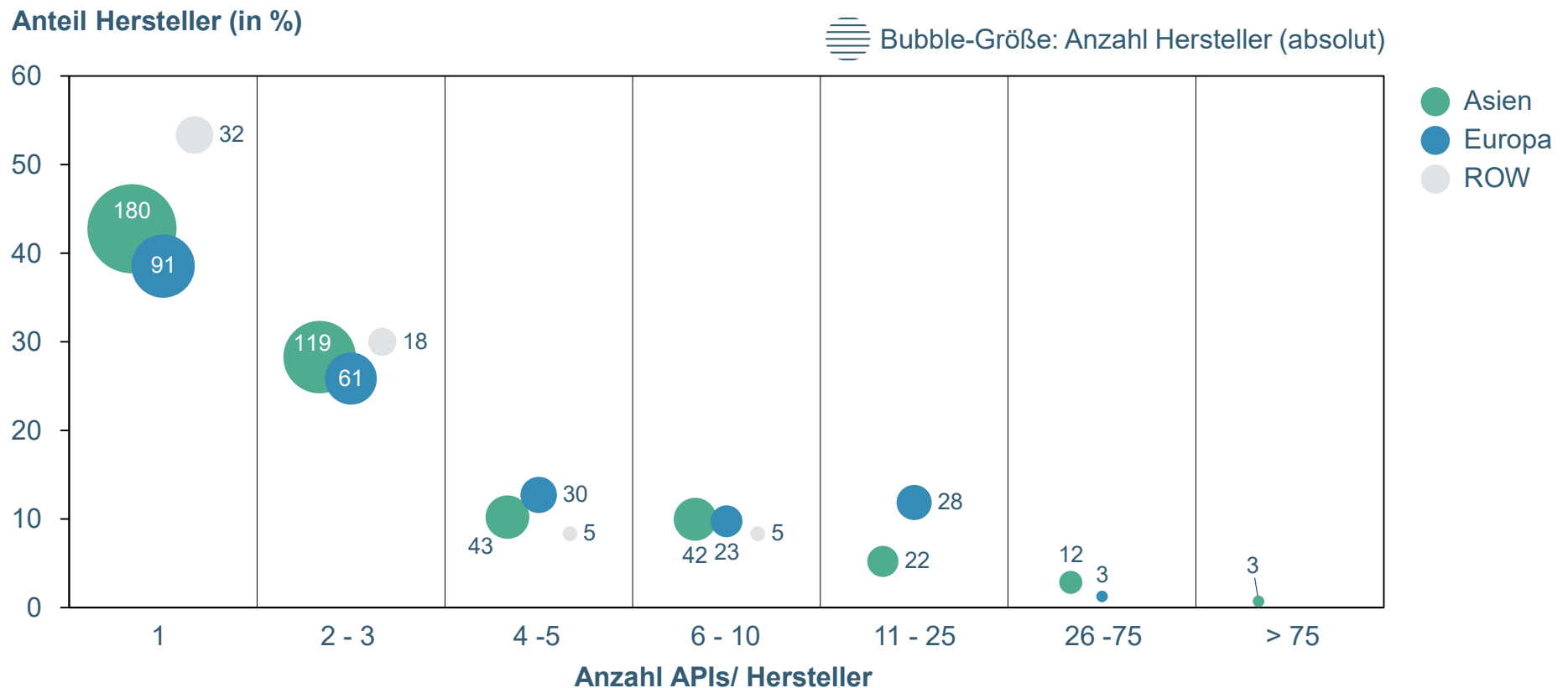


(Zahl) Anzahl Hersteller — Durchschnitt CEPS/ Hersteller - - - Mindestanzahl CEPS der Top10 Hersteller CEPS des größten Herstellers

¹) Berücksichtigt sind alle validen CEPS im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPS sind bereits ausgeschlossen)
Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

... RUND 70 % DER HERSTELLER HABEN ABER WEITERHIN EIN KLEINES PORTFOLIO VON 1 – 3 WIRKSTOFFEN

VERTEILUNG HERSTELLER NACH ANZAHL APIS/ STANDORT (STAND 2020)¹

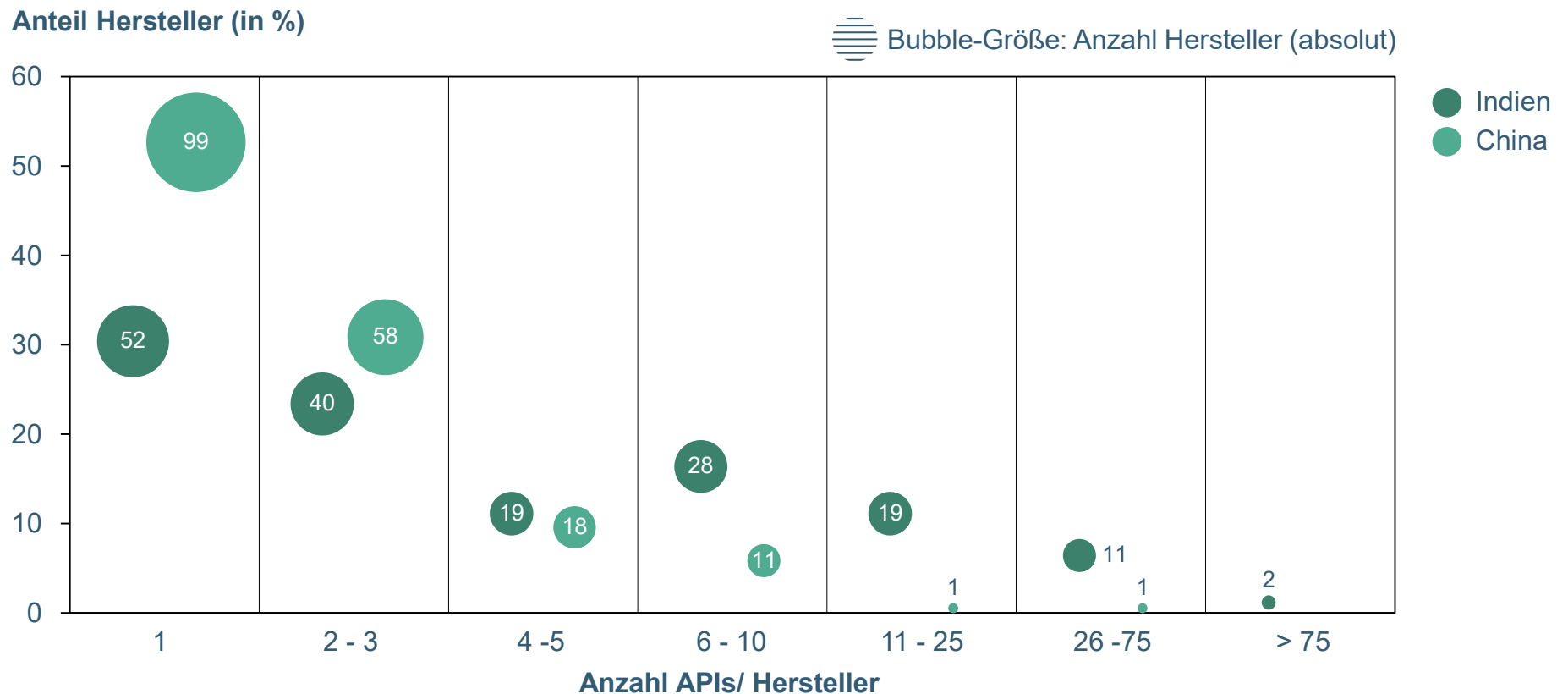


¹) Anzahl aller Hersteller mit validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (Hersteller mit ausschließlich abgelaufenen/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

INNERHALB ASIENS HABEN INDISCHE HERSTELLER GRÖßERE PORTFOLIOS:
35% DER INDISCHEN HERSTELLER MIT 6 ODER MEHR APIS, IN CHINA NUR 7%

VERTEILUNG INDIEN UND CHINA NACH ANZAHL APIS/ HERSTELLER (STAND 2020)¹



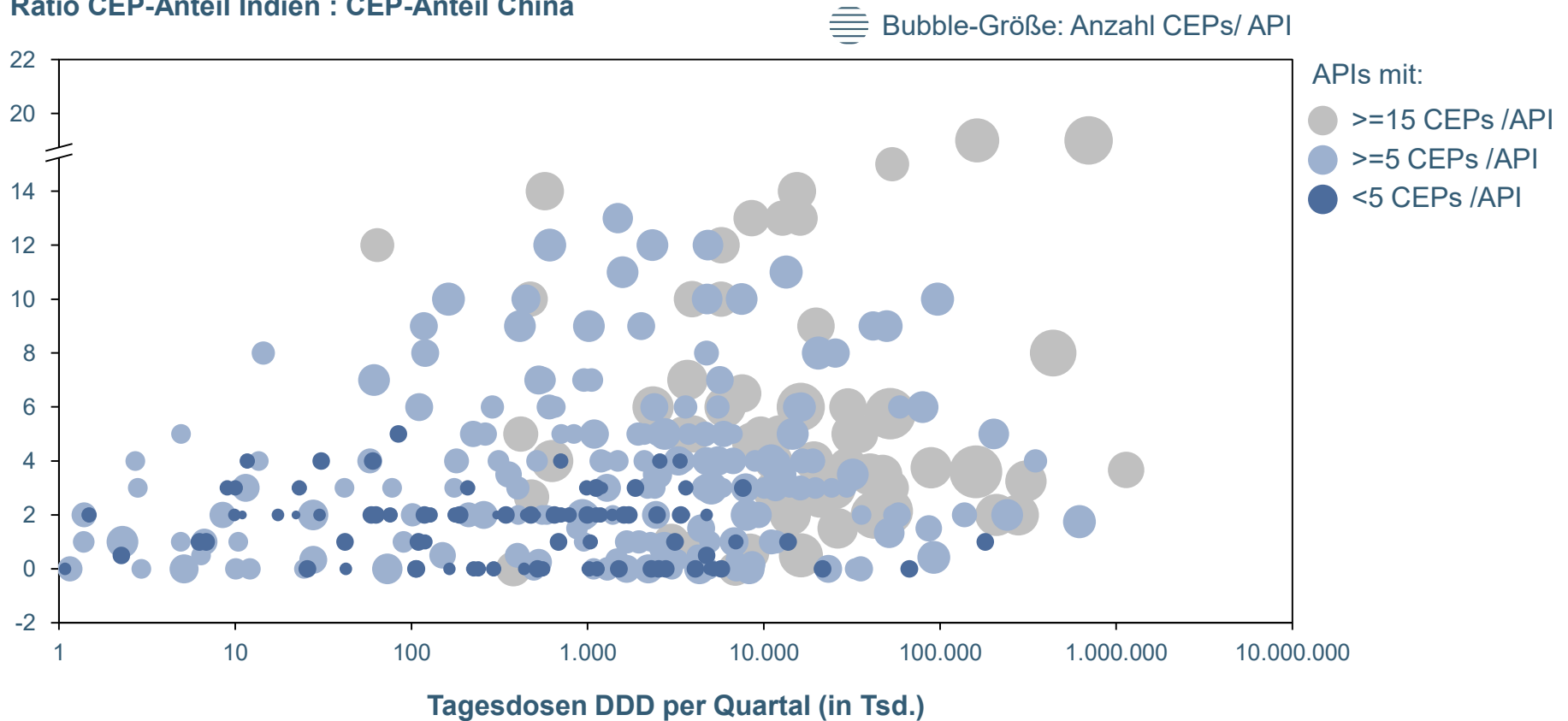
¹⁾ Anzahl aller Hersteller mit validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (Hersteller mit ausschließlich abgelaufenen/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

IM DIREKTEN VERGLEICH ZU CHINA IST INDIEN BESONDERS STARK BEI DEN APIS MIT MITTLEREN UND HOHEN TAGESDOSEN VERTRETEN

CEP-RATIO INDIEN: CHINA IN ABHÄNGIGKEIT DER TAGESDOSEN JE API (STAND 2020)^{1,2}

Ratio CEP-Anteil Indien : CEP-Anteil China



¹⁾ Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

²⁾ Alle betrachteten APIs mit einer Tagesdosis Q4 2019 > 1 Tsd. DDD im Retail-Bereich und einem summierten Anteil von Indien und China > 0%; n = 337

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020; Basisliste Pro Generika

AUS DEN CEP-DATEN LÄSST SICH AB 2000 EINE ZUNEHMENDE AKTIVITÄT IN ASIEN ABLEITEN

12

Die **API Hersteller** in **Asien** waren **seit 2000 wesentlich aktiver als europäische Hersteller** – insbesondere **Indien** und **China** zeigen eine **starke Dynamik**

13

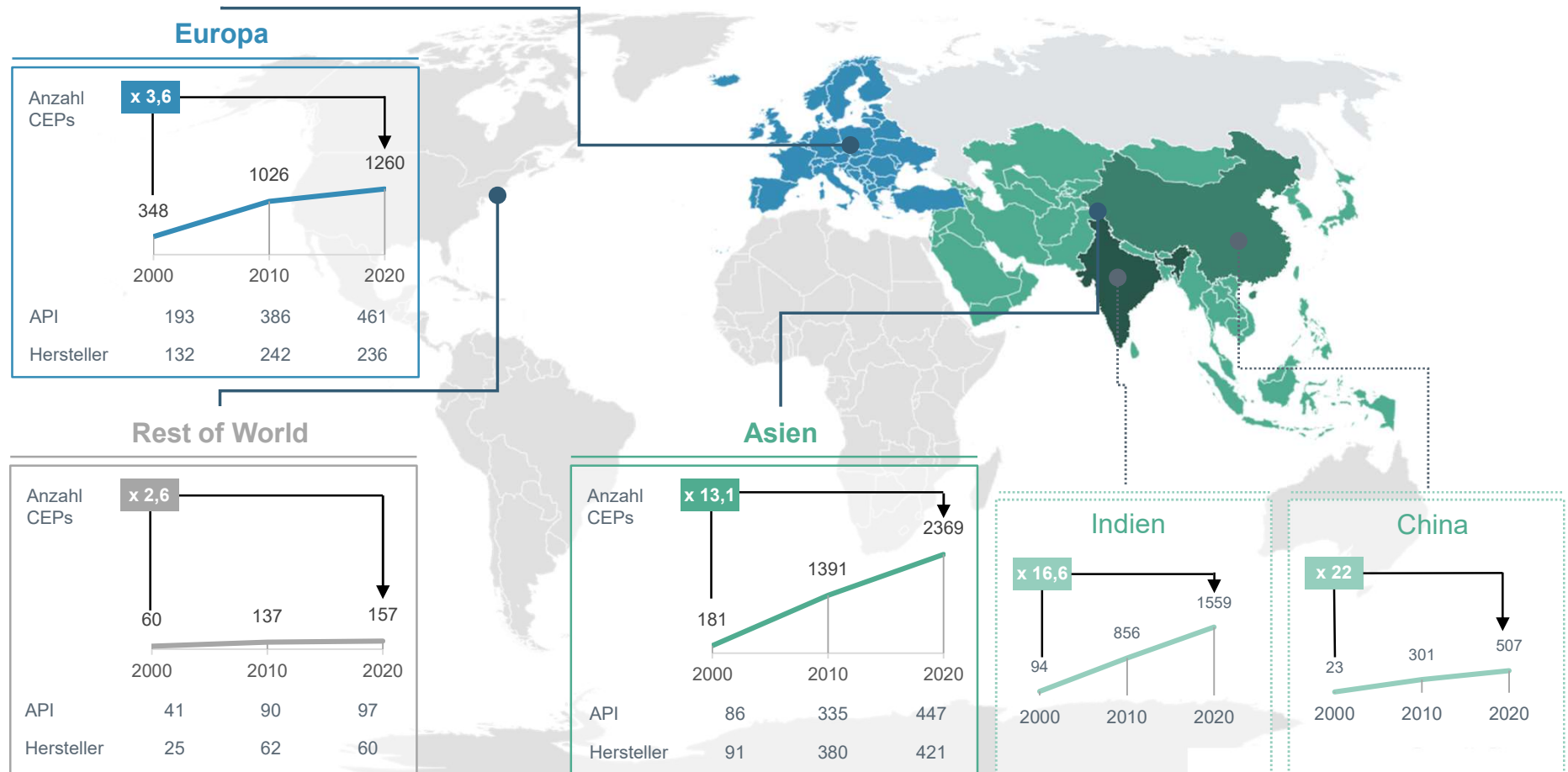
Die **Wachstumstreiber** waren in **Europa** und **Asien** **ähnlich**. Der **Zuwachs** an **CEPs** wurde **durch Patentausläufe** und die damit **einhergehende Zunahme** der **generischen APIs**, **andererseits durch neu hinzugekommene Hersteller** vorangetrieben. **Beiden Trends** wird in **Zukunft weniger Dynamik** unterstellt

14

Je später ein **API** in das **CEP-Verfahren** eintritt, **desto kleiner** ist von Anfang an der **Anteil europäischer Hersteller**. Während **ältere APIs** nach **Patentablauf hauptsächlich in Europa hergestellt** wurden und **asiatische Hersteller** nur **langsam** in den **jeweiligen Markt** eintraten, sind **asiatische Hersteller** bei **neueren APIs** von **Anfang an dominierend**

IN ASIEN GIBT ES MEHR CEPS UND MEHR HERSTELLER, ABER IN ETWA DIE GLEICHE ANZAHL AN APIS

ÜBERBLICK CEPS, APIS UND HERSTELLER IN DEN REGIONEN (2000 – 2020)¹

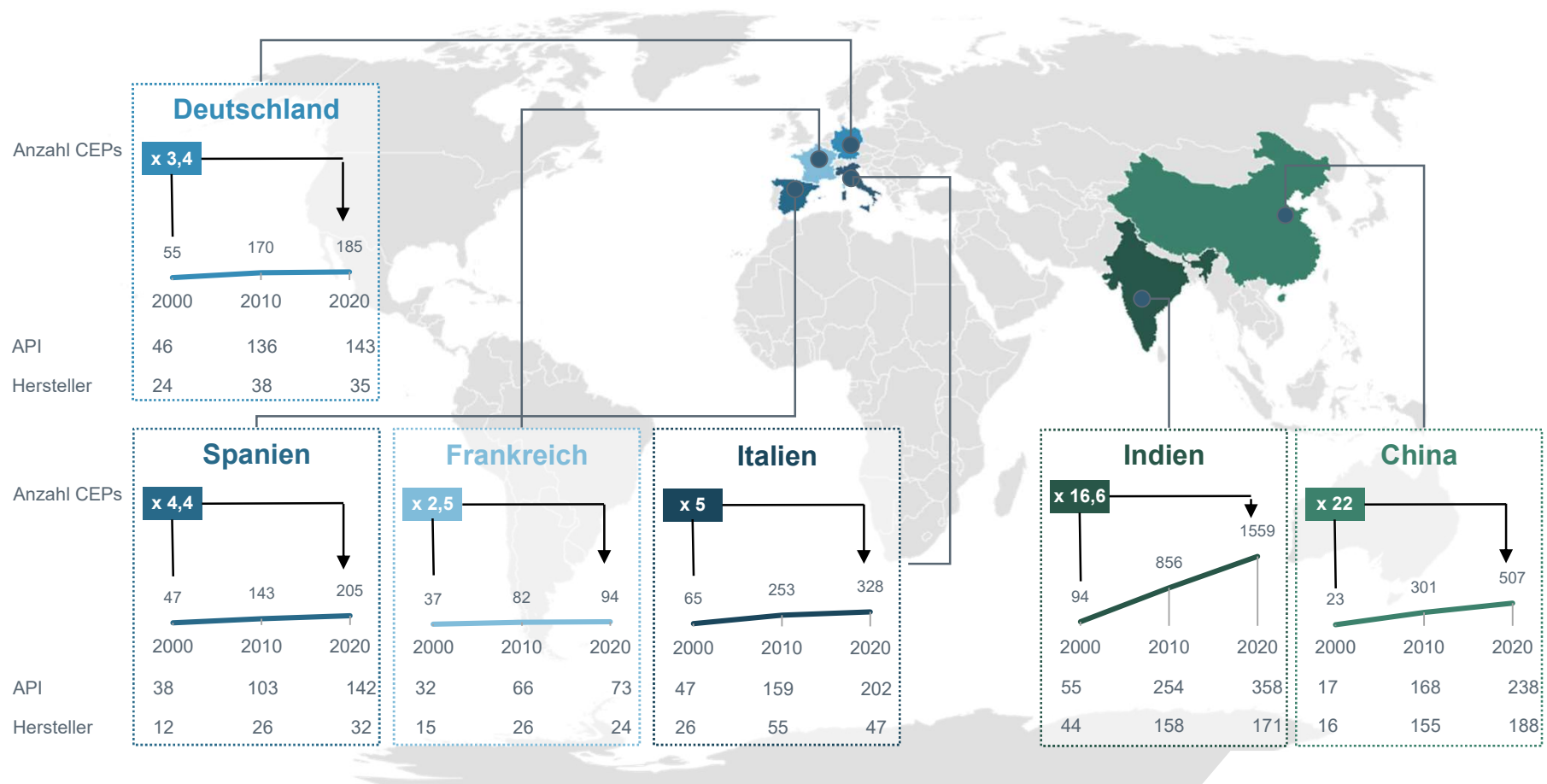


¹) Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

STÄRKSTES RELATIVES WACHSTUM IN CHINA UND SCHWÄCHSTES IN FRANKREICH

ÜBERBLICK CEPS, APIS UND HERSTELLER DER TOP LÄNDER (2000 – 2020)¹



¹⁾ Anzahl aller validen CEPS im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPS sind bereits ausgeschlossen)

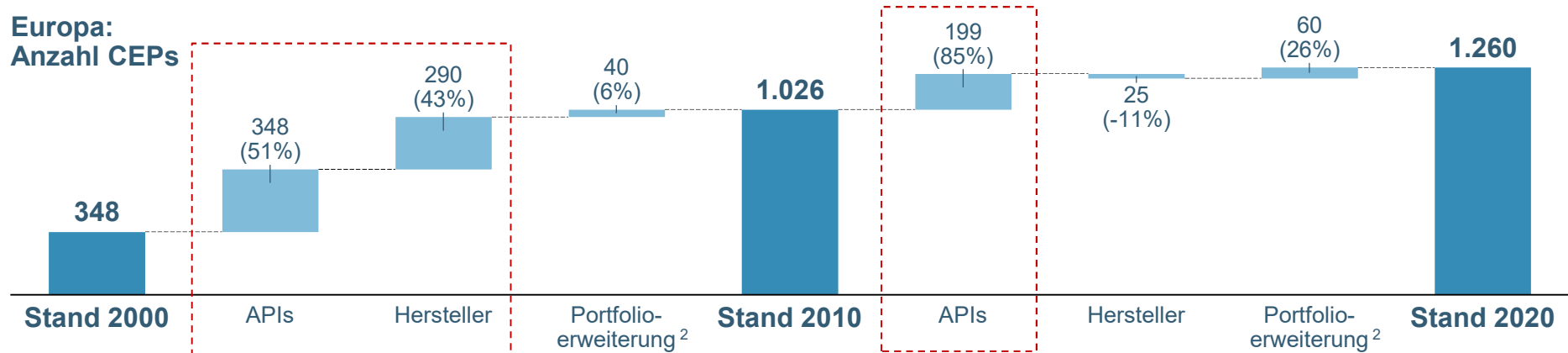
Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

EINTRITT NEUER HERSTELLER UND AUSBAU DES PRODUKTPORTFOLIOS SIND STARKE WACHSTUMSTREIBER IN ASIEN

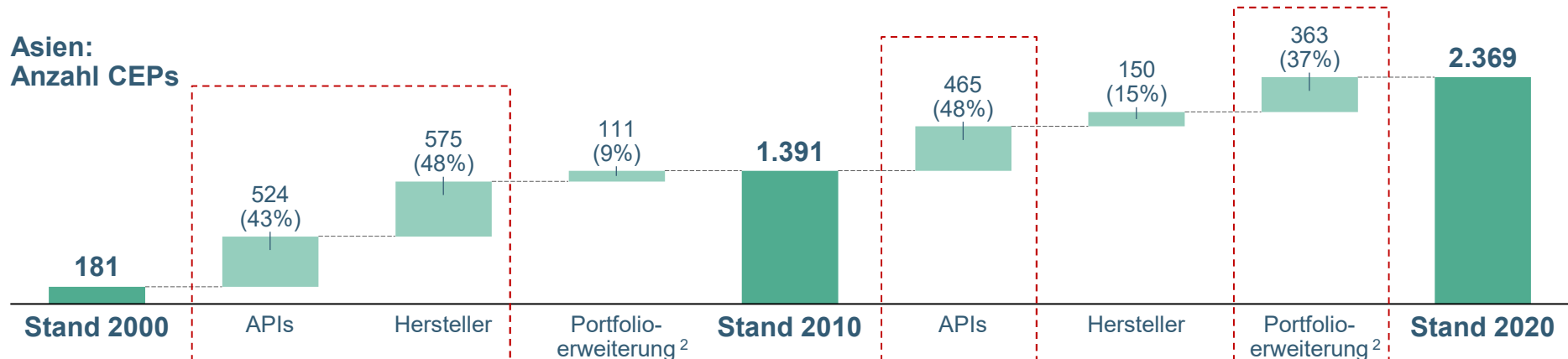
TREIBER FÜR VERÄNDERUNG DER CEP ANZAHL (2000 – 2020)¹

Haupttreiber

Europa:
Anzahl CEPs



Asien:
Anzahl CEPs



¹) Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

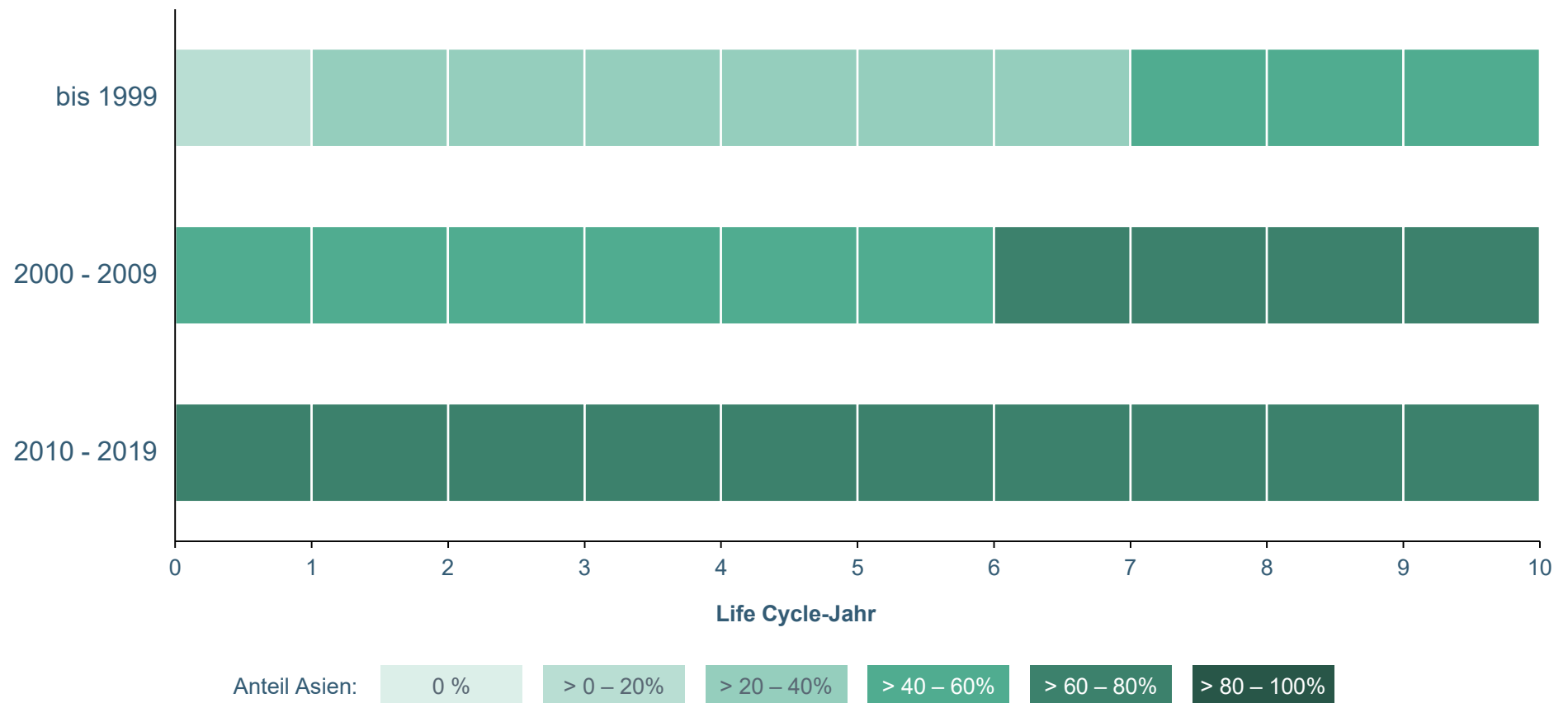
²) inkl. CEPs durch neue Herstellungsverfahren; dadurch halten Hersteller vereinzelt auch mehr CEPs für ein bestimmtes API

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

JE SPÄTER DER EINTRITT DES APIS IN CEP VERFAHREN, DESTO WENIGER EUROPÄISCHE HERSTELLER GIBT ES

ENTWICKLUNG DES ANTEILS ASIATISCHER HERSTELLER NACH LIFE CYCLE

Erstes Jahr des APIs im CEP Verfahren



Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

ANALYSEN AUF EBENE DER ATC-KLASSEN BESTÄTIGT DIESE ERGEBNISSE

15

Die **Untersuchung** anhand von **ATC Klassen bestätigt** alle **Ergebnisse**, wobei **innerhalb** der **ATC Klassen beträchtliche Unterschiede** auftreten

16

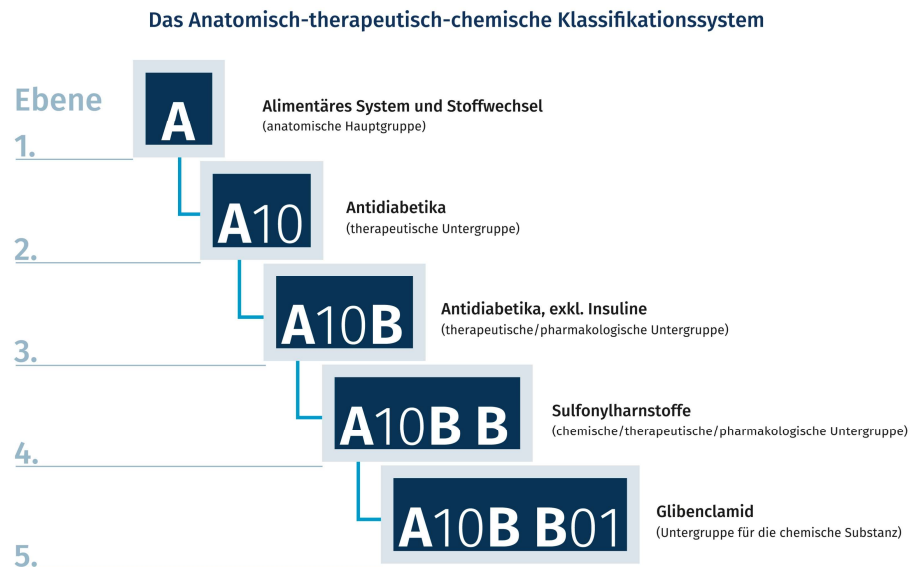
Ausgewählte APIs wurden **detailliert untersucht**, die **Ergebnisse bestätigen** die **Erkenntnisse für** das **Gesamtportfolio**

- Mit **Zunahme** des **Volumens** der einzelnen **Produkte** treten **verstärkt asiatische - insbesondere indische - Hersteller** in den Vordergrund
- Die **Analysen** realer **Produktionsvolumina** für den **europäischen Bedarf decken** sich im **Mittel sehr gut** mit den auf **Anzahl** der **CEPs basierenden Auswertungen**. Im **Einzelfall** kann es zu **Abweichungen** kommen
- **Es scheint**, dass die **Treiber** für eine **Standortwahl** recht **stark** wirken: So werden die **APIs** hauptsächlich **entweder** in **Europa** oder in **Asien hergestellt**, bei **wenigen APIs** gibt es ein **ausgeglichenes Europa zu Asien Verhältnis**
- **Ältere APIs** sind **historisch** in **Europa stark** und zeigen nur **langsame Abwanderung** nach **Asien**, während **jüngere APIs** bereits **beim Eintritt** ins **CEP-Verfahren hohen Anteil asiatischer Hersteller** aufweisen und/ **oder** eine **Abwanderung schneller** erfolgt

AUFFÄLLIGKEITEN INNERHALB DER WIRKSTOFFKLASSEN WERDEN GEMÄSS ATC KLASSIFIZIERUNG UNTERSUCHT

ÜBERSICHT ATC KLASSIFIZIERUNG

Übersicht der ATC-Logik



Nach: WHO, Introduction to Drug Utilization Research, Oslo 2003

Grafik: Wido, 2018

Anwendung in Analysen: 1. ATC-Ebene

- A - Alimentäres System und Stoffwechsel
- B - Blut und blutbildende Organe
- C - Kardiovaskuläres System
- D - Dermatika
- G - Urogenitalsystem und Sexualhormone
- H - Systemische Hormonpräparate, exkl. Sexualhormone und Insuline
- J - Antiinfektiva (systemisch)
- L - Antineoplastische und immunmodulierende Mittel
- M - Muskel- und Skelettsystem
- N - Nervensystem
- P - Antiparasitäre Mittel, Insektizide und Repellenzien
- R - Respirationstrakt
- S - Sinnesorgane

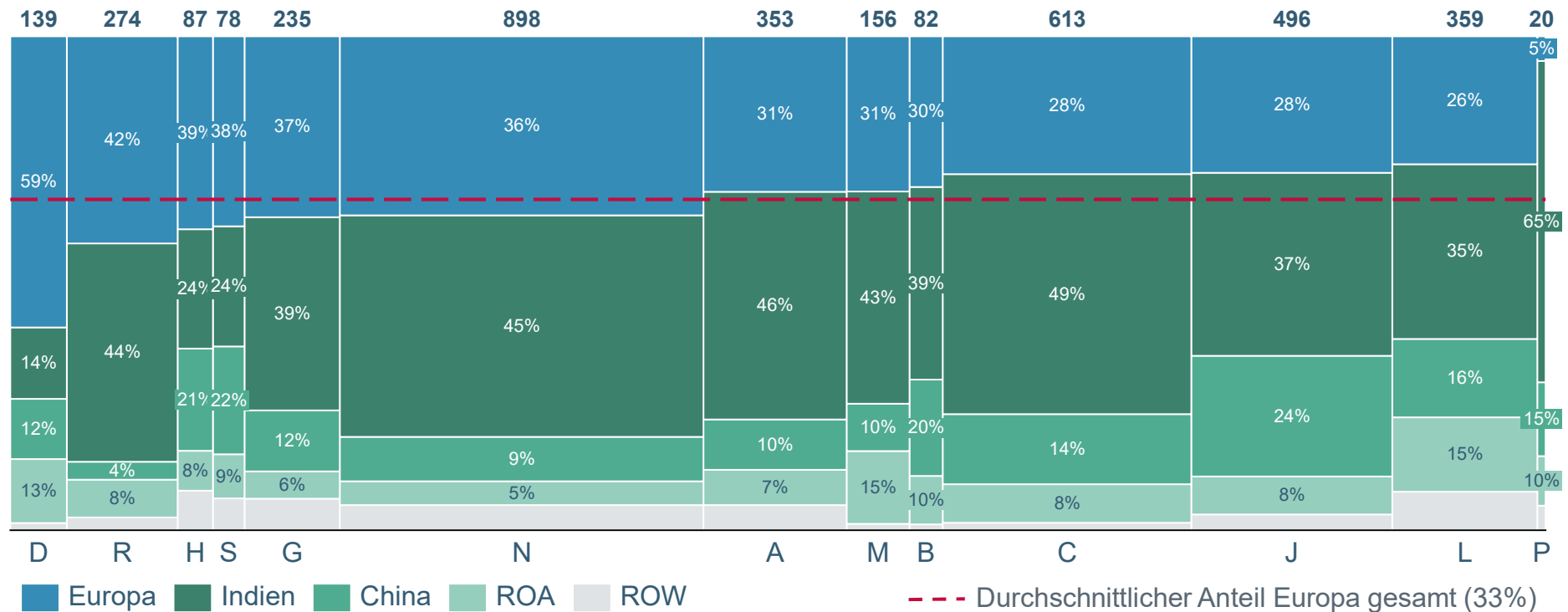
Quelle: https://www.wido.de/fileadmin/Dateien/Bilder/Publikationen_Produnkte/Arzneimittel-Klassifikation/wido_arz_atc_klassifikation.jpg, Stand 30.04.2020

DETAILSICHT DER API-ATC KLASSEN ZEIGT DEUTLICHE UNTERSCHIEDE – GEFAHR DES KNOW-HOW VERLUSTS INSBESONDERE IN C, J, L UND P

GLOBALE VERTEILUNG DER VALIDEN CEPS NACH ATC*-KLASSEN (STAND 2020)¹

Anzahl CEPs (und ihre globale Verteilung (in%))

Gesamt: 3.786



*) A - Alimentäres System und Stoffwechsel; B - Blut und blutbildende Organe; C - Kardiovaskuläres System; D – Dermatika; G - Urogenitalsystem und Sexualhormone; H - Systemische Hormonpräparate, exkl. Sexualhormone und Insuline; J – Antiinfektiva (systemisch); L - Antineoplastische und immunmodulierende Mittel; M - Muskel- und Skelettsystem; N – Nervensystem; P - Antiparasitäre Mittel, Insektizide und Repellenzien; R – Respirationstrakt; S – Sinnesorgane

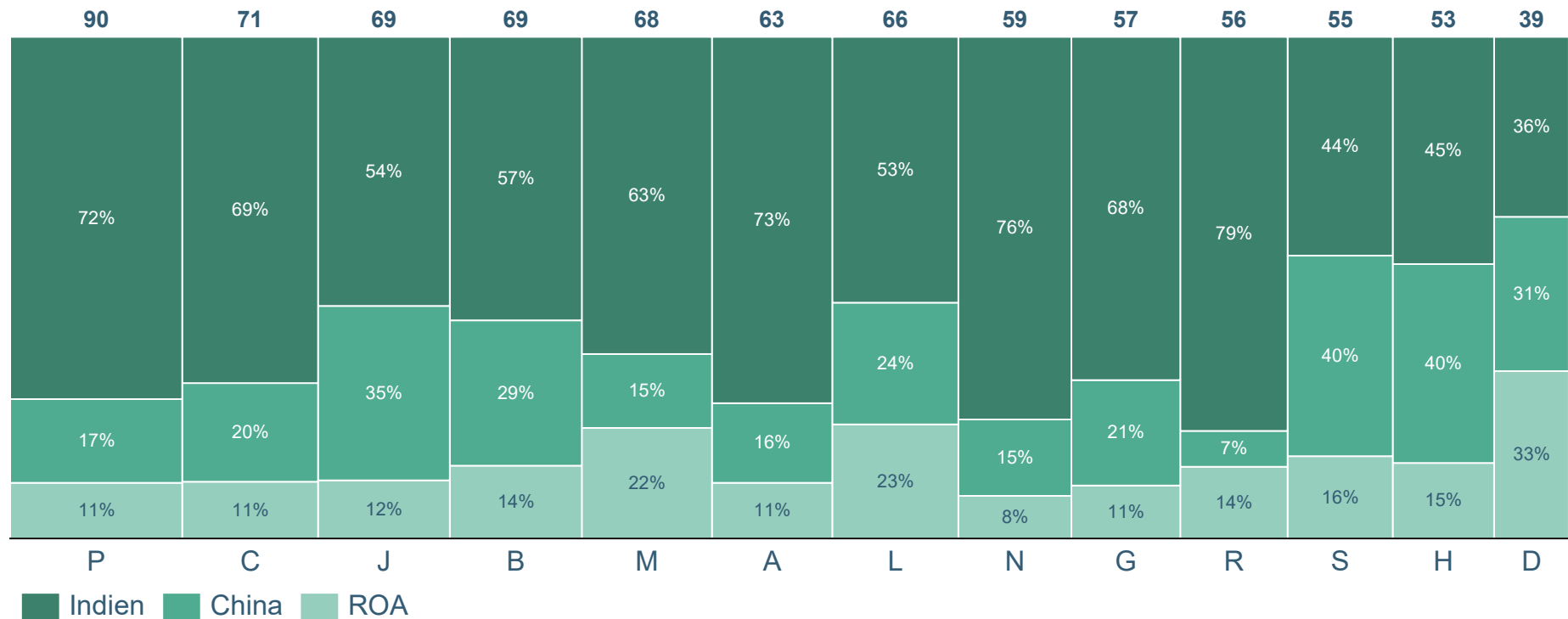
¹) Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

AUCH INNERHALB ASIENS GIBT ES DEUTLICHE UNTERSCHIEDE IN DER VERTEILUNG

VERTEILUNG DER VALIDEN CEPS IN ASIEN NACH ATC*-KLASSEN (STAND 2020)¹

Anzahl CEPs (und ihre Verteilung innerhalb Asiens (in%))



*) A - Alimentäres System und Stoffwechsel; B - Blut und blutbildende Organe; C - Kardiovaskuläres System; D – Dermatika; G - Urogenitalsystem und Sexualhormone; H - Systemische Hormonpräparate, exkl. Sexualhormone und Insuline; J – Antiinfektiva (systemisch); L - Antineoplastische und immunmodulierende Mittel; M - Muskel- und Skelettsystem; N – Nervensystem; P - Antiparasitäre Mittel, Insektizide und Repellenzien; R – Respirationstrakt; S – Sinnesorgane

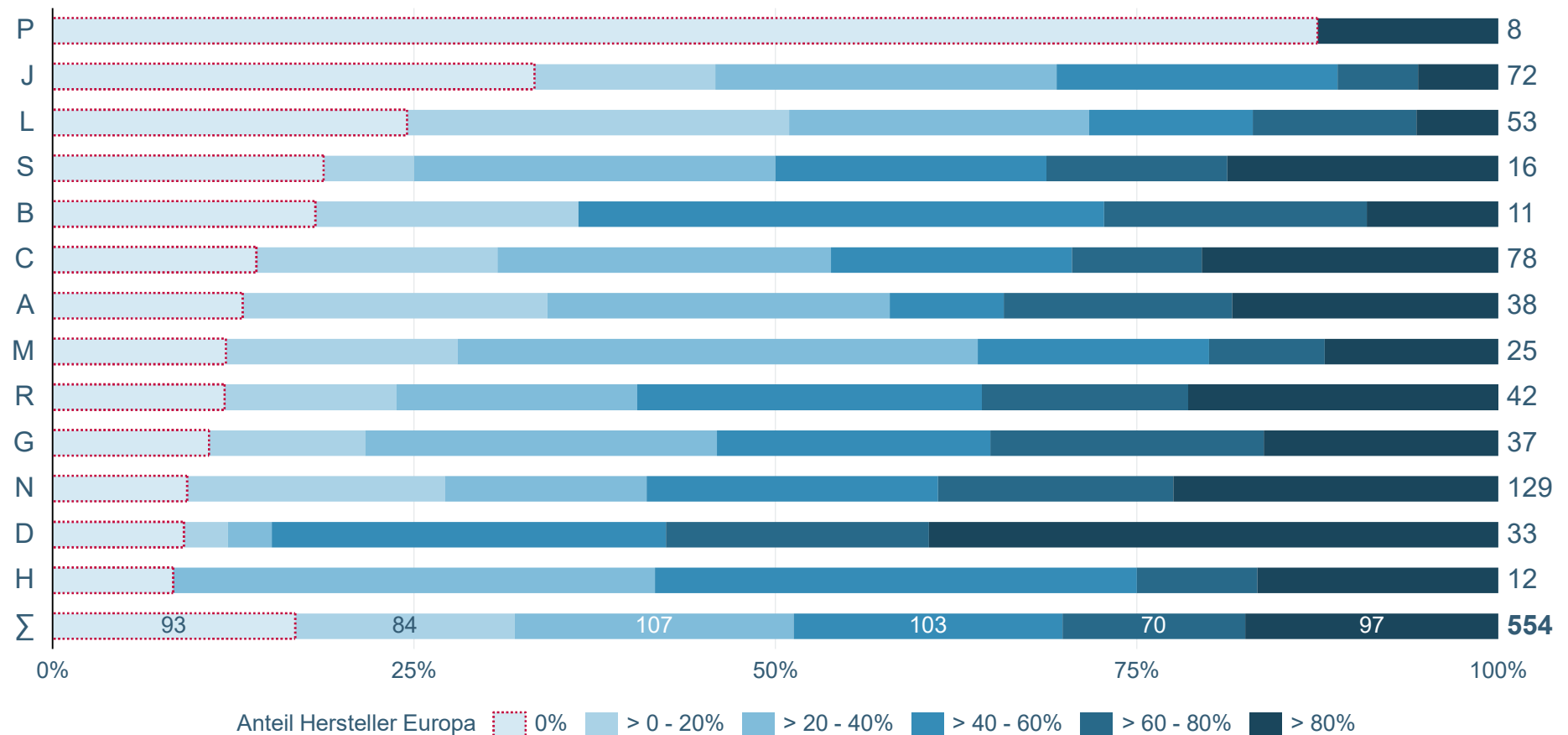
¹⁾ Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

BEI JEDEM 6. API STEHT EUROPA IN EINER BESONDERS KRITISCHEN ABHÄNGIGKEIT ZU ASIATISCHEN LIEFERANTEN (KEINE CEPS IN EUROPA)

ANTEIL EUROPÄISCHER HERSTELLER VON APIS NACH ATC KLASSEN (STAND 2020)¹

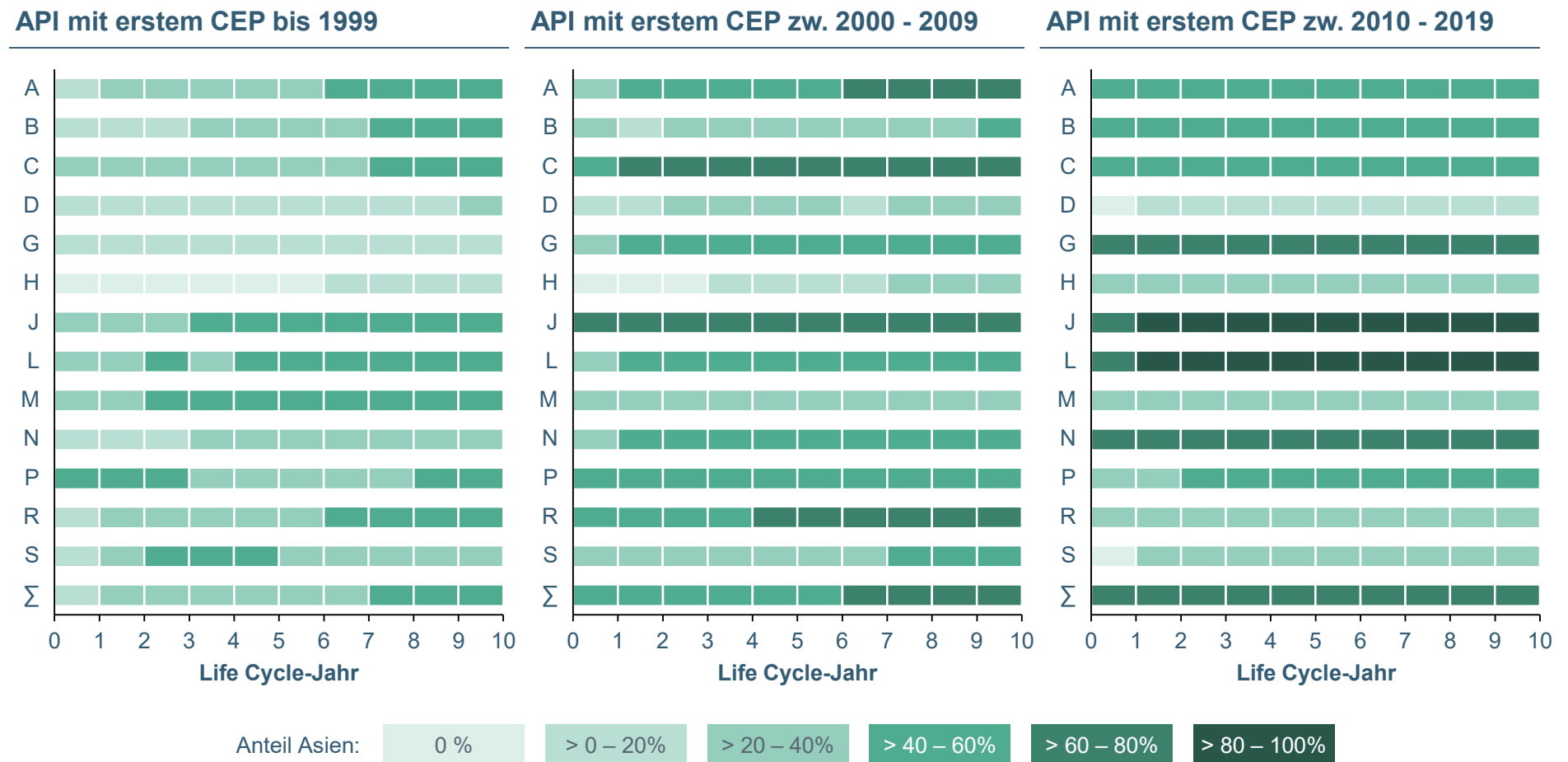
Anteil APIs mit x% Hersteller in Europa



¹) Anzahl aller APIs mit validen CEPS im jeweiligen Kalenderjahr für die betrachteten APIs (APIs mit abgelaufenen/ zurückgezogenen CEPS ausgeschlossen)
 Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

JE SPÄTER EIN API INS CEP-VERFAHREN EINGETRETEN IST, DESTO HÖHER IST DER ASIATISCHE ANTEIL

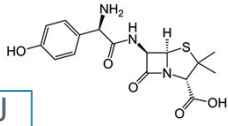
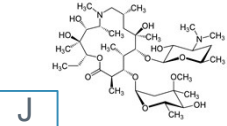
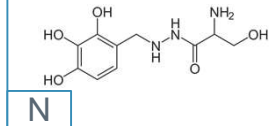
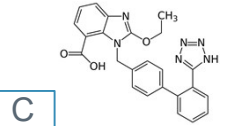
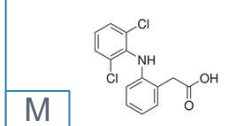
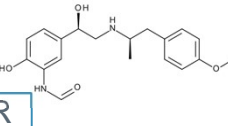
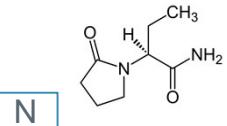
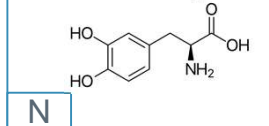
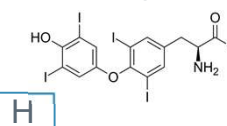
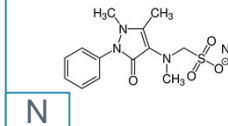
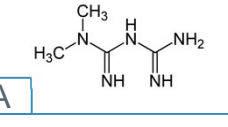
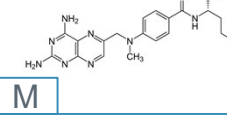
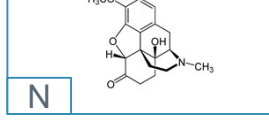
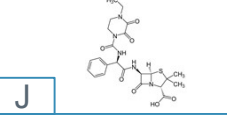
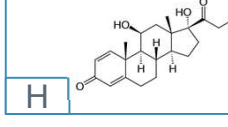
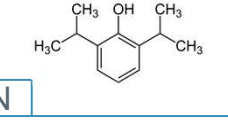
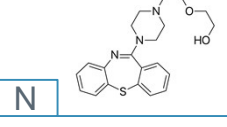
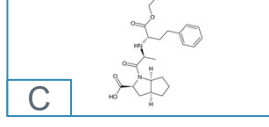
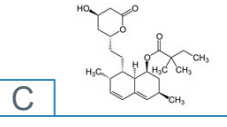
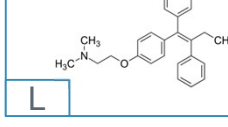
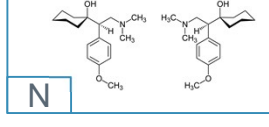
ENTWICKLUNG ANTEIL ASIATISCHER HERSTELLER NACH LIFE CYCLE



Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

21 APIS WURDEN FÜR EINE DETAILBETRACHTUNG AUSGEWÄHLT

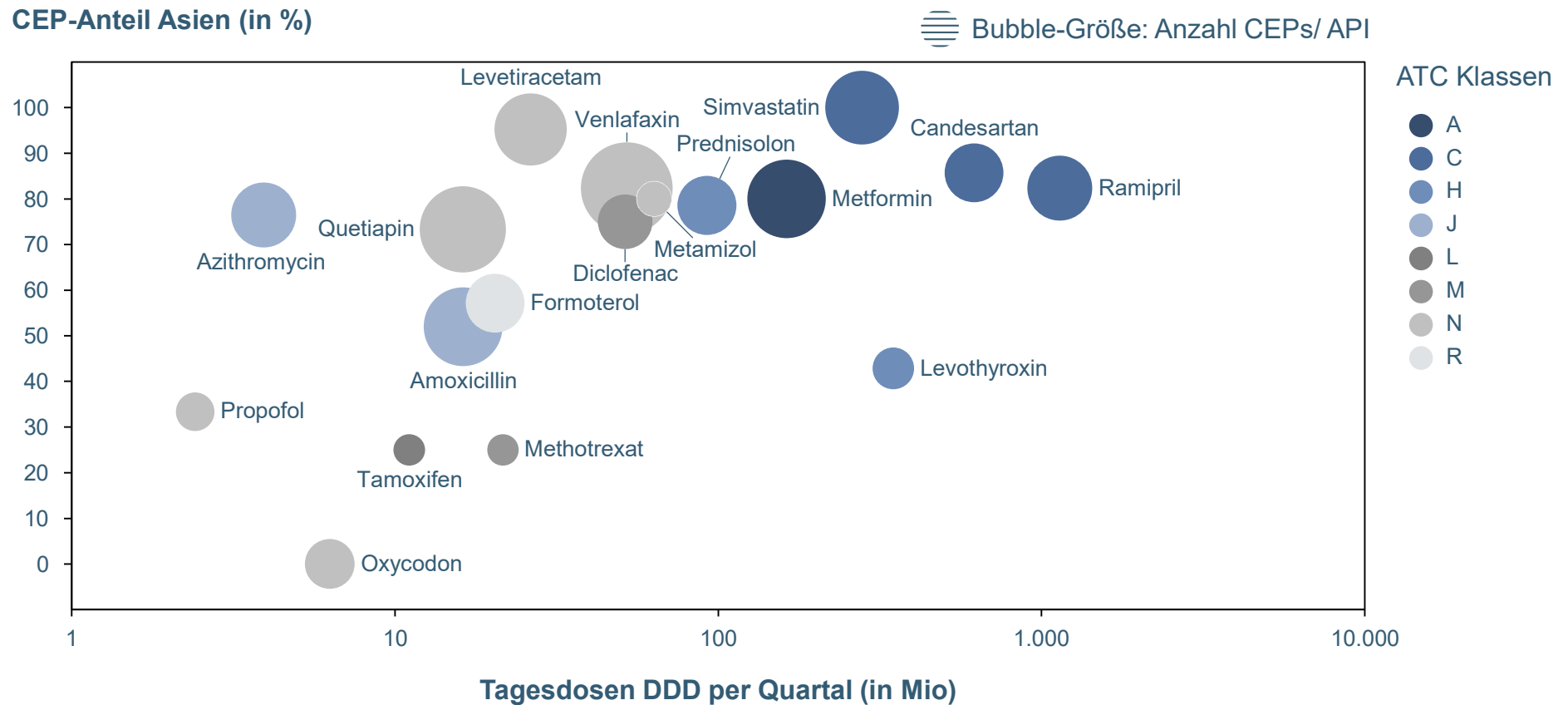
EXEMPLARISCHE AUSWAHL

Amoxicillin  J	Azithromycin  J	Benserazid  N	Candesartan  C	Diclofenac  M
Formoterol  R	Levetiracetam  N	Levodopa  N	Levothyroxin  H	Metamizol  N
Metformin  A	Methotrexat  M	Oxycodon  N	Piperacillin  J	Prednisolon  H
Propofol  N	Quetiapin  N	Ramipril  C	Simvastatin  C	Tamoxifen  L
	Venlafaxin  N			

☐ ATC Klasse

JE HÖHER DAS VOLUMEN EINES WIRKSTOFFS IST, DESTO HÖHER IST DER ANTEIL ASIATISCHER HERSTELLER

EXEMPLARISCHE API-AUSWAHL: CEP-ANTEIL ASIEN:TAGESDOSEN (STAND 2020)^{1,2}



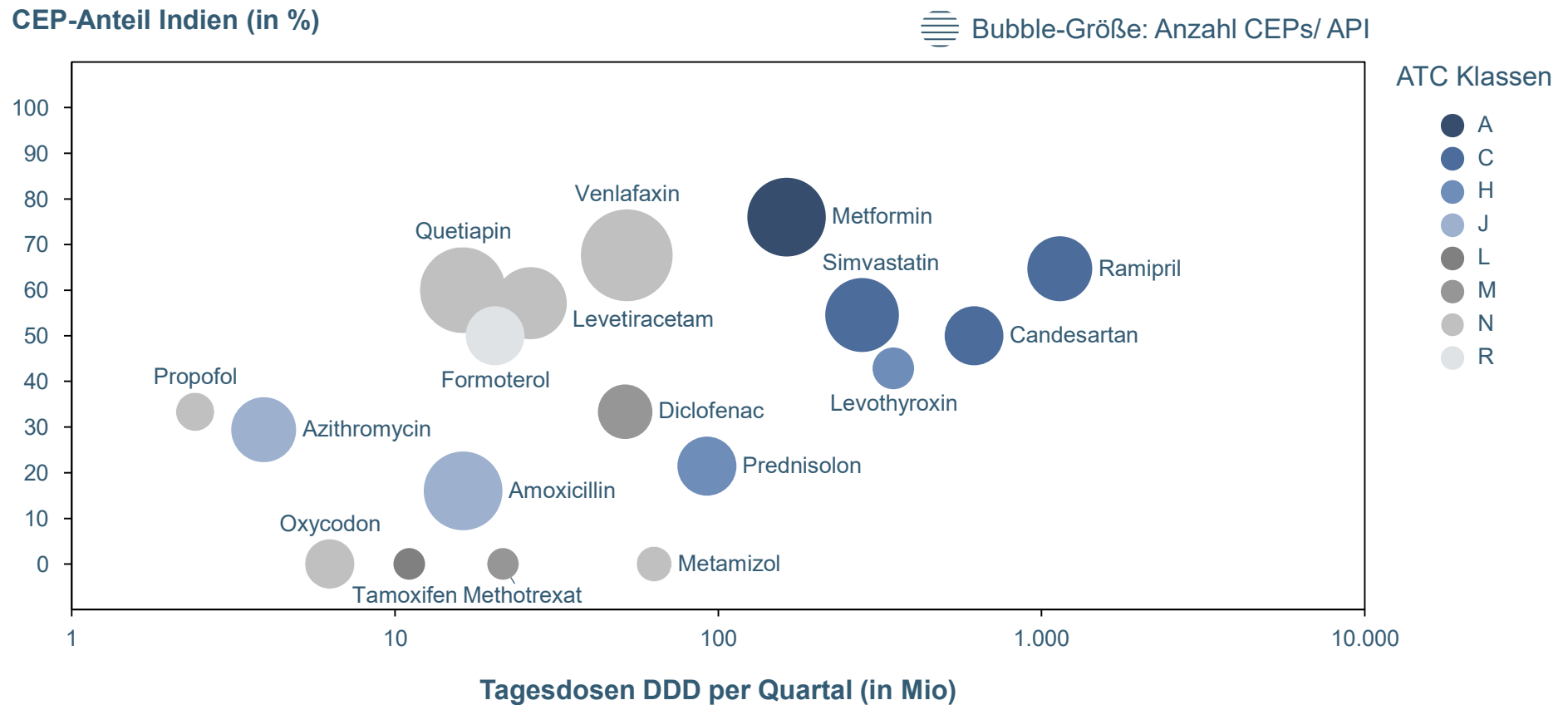
¹⁾ Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die exemplarischen APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

²⁾ Exemplarische API-Auswahl mit einer Tagesdosis Q4 2019 > 1 Mio. DDD im Retail-Bereich (Ausschluss von: Piperacillin, Benserazid, Levodopa); n = 18

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020; Basisliste Pro Generika

... DIESE KORRELATION GILT WIEDERUM INNERHALB ASIENS FÜR DEN INDISCHEN CEP-ANTEILS

EXEMPLARISCHE API-AUSWAHL: CEP-ANTEIL INDIEN:TAGESDOSEN (STAND 2020)^{1,2}



¹⁾ Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die exemplarischen APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

²⁾ Exemplarische API-Auswahl mit einer Tagesdosis Q4 2019 > 1 Mio. DDD im Retail-Bereich (Ausschluss von: Piperacillin, Benserazid, Levodopa); n = 18

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020; Basisliste Pro Generika

DIE MEISTEN APIS WERDEN ENTWEDER HAUPTSÄCHLICH IN EUROPA ODER IN ASIEN PRODUZIERT – WENIGE MIT AUSGEGLICHENEN ANTEILEN

SCHÄTZUNG ANTEIL DES SUPPLIES AM EUROPÄISCHEN BEDARF NACH REGIONEN

Anteil des Supplies in %; (oberhalb der Säule: europäischer Gesamtbedarf in t)



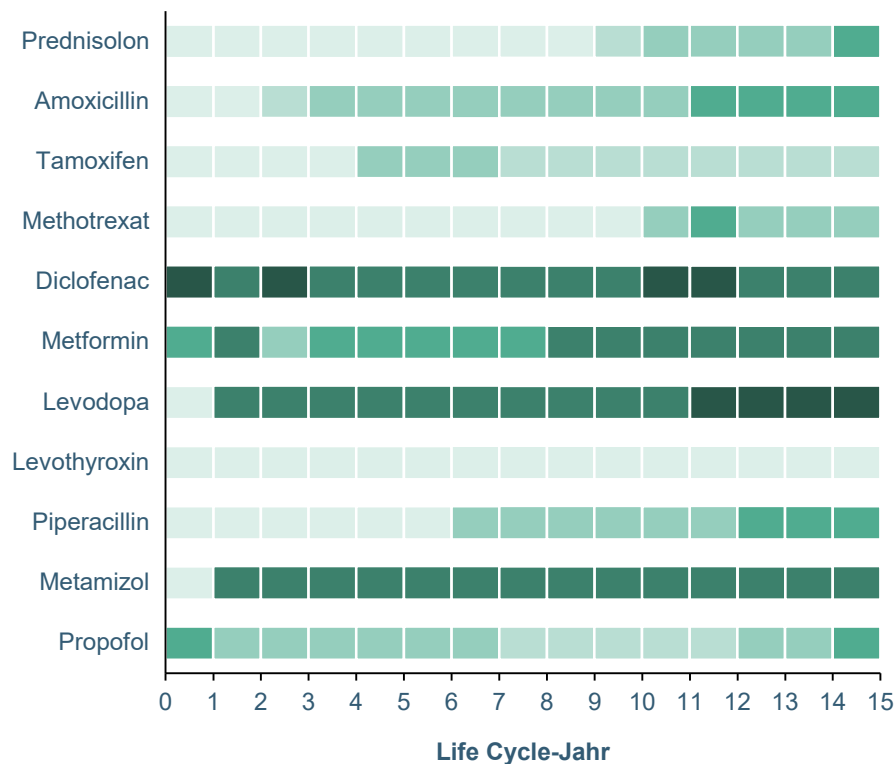
*) Schätzung, Datengrundlage eingeschränkt belastbar; **) API überwiegend in Kombi-Anwendung mit Tazobactam (ausschließlich in Asien hergestellt).

Quelle: Supplier Interviews, Import Data Analysis QYOB market platform, CEP Database, Pharmaoffer; IQVIA

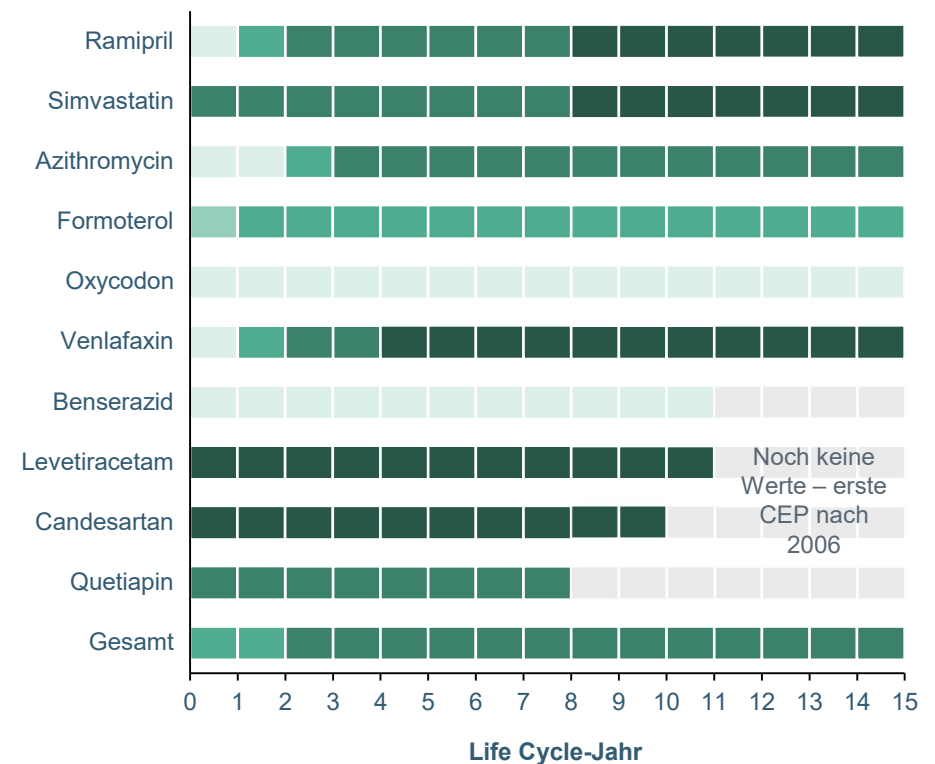
AUCH BEI DER LIFE CYCLE-BETRACHTUNG EINZELNER APIS WIRD DIE VERLAGERUNG DER PRODUKTION NACH ASIEN DEUTLICH

EXEMPLARISCHE AUSWAHL: ANTEIL ASIATISCHER HERSTELLER NACH LIFE CYCLE

Exemplarische Auswahl mit erstem CEP
zwischen 1992 und 2001



Exemplarische Auswahl mit erstem CEP
zwischen 2001 und 2014



Anteil Asien: 0 % > 0 – 20% > 20 – 40% > 40 – 60% > 60 – 80% > 80 – 100%

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

EUROPA HEUTE FOKUSSIERT AUF „NISCHENPRODUKTE“, ABER POTENTIAL UND KAPAZITÄTEN SIND NOCH VORHANDEN

17

Europa ist heute fokussiert auf **APIs** mit **niedrigem Produktionsvolumen**, **technisch komplexer Herstellungsweise** und **Produkte mit besonderen Qualitätsansprüchen**

Studienteilnehmer unterbreiten verschiedene **Verbesserungsvorschläge**.

18

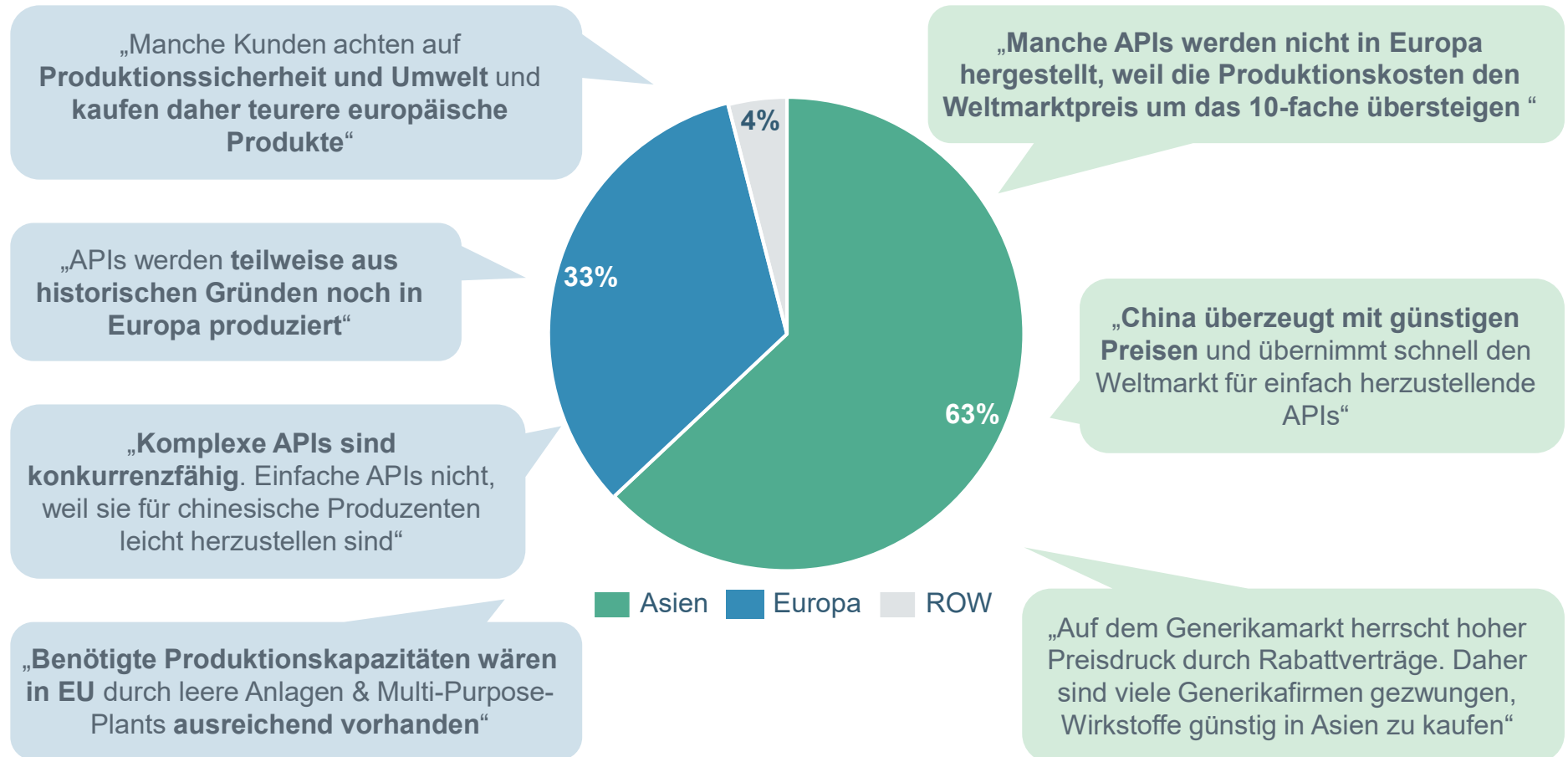
Neben einer **Verbesserung** der **Datenlage** als Basis für **Entscheidungen** werden **Änderungen** auf verschiedenen **Stufen** der **Wertschöpfungskette** vorgeschlagen. **Besonders stark** ist der **Wunsch** nach **Veränderungen** sowohl **arzneimittelrechtlicher** als auch **erstattungsrechtlicher Regulierungen**

19

Konkrete Maßnahmen zeigen Möglichkeiten auf, um die **Abhängigkeit** von **Asien** zu **reduzieren**

EUROPA HEUTE FOKUSSIERT AUF „NISCHENPRODUKTE“; POTENTIAL IST WEITERHIN VORHANDEN

ANZAHL VALIDER CEPS 2020



Stichtag der Datenerhebung ist der 30.04.2020

¹⁾ Anzahl aller validen CEPs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020, Interviews

INTERVIEWPARTNER WEISEN AUF VERBESSERUNGSVORSCHLÄGE HIN

„Gießkannenprinzip funktioniert nicht. Zunächst zu klären, **welche API und Arzneimittel für Patienten** in Europa relevant sind“

„**GKVN müssen von Politikern dazu gebracht werden**, dass nicht nur der Preis sondern auch der **Produktionsstandort eine Rolle bei Vergabe der Arzneimittel** spielt“

„**Bewilligungen in Europa zu langsam**, während in Indien neue Kapazitäten problemlos aufgebaut werden“

„**Registrierungsanforderungen** (für neu und alt) **sollten angepasst werden**: Arzneimittelhersteller müssen **Versorgung durch europäischen API Zulieferer nachweisen**, so dass bei Ausfall von asiatischen Zulieferern europäischer Bedarf gesichert werden kann“

„**API Hersteller** müssten **Produktionsprozesse in Europa aufwendig verbessern**, um **Preise senken zu können**“

„**Alle müssen mitwirken**. Insbesondere **Kunden müssen höhere Preise akzeptieren**, wenn in Europa produziert werden soll“

KONKRETE MASSNAHMEN SOLLEN DIE ABHÄNGIGKEIT VON ASIEN REDUZIEREN

Stärkung des europäischen Netzwerks rückt in den Fokus – Beispiel Kundl (Novartis/Sandoz)



- Werk **Kundl** letzte verbliebene vollständige **Antibiotika-Produktion** in der westlichen Welt
- Novartis und österreichische Bundesregierung **sichern langfristige Produktion von Schlüssel-Antibiotika** in Europa
- Geplantes gemeinsames **Investment von mehr als EUR 150 Millionen** – österreichische **Regierung mit EUR 50 Millionen beteiligt**

Fokus dabei auf versorgungskritische APIs in Europa – Beispiel Sanofi



- Große Initiative von Sanofi zur **Gründung eines eigenständigen Unternehmens zur API Produktion** in Frankreich
- **Zum Ziel gesetzt:**
 - **Zweitgrößter API Hersteller** mit ~ 1Mrd. € Umsatz
 - **Stärkung** des API-Produktionsstandortes **Europa**
 - **Ausgleich der derzeitigen API-Versorgungslücken** in Europa
 - **Reduktion der Abhängigkeit** vom asiatischen API Importen

Quelle: Pressemitteilungen



DR. ANDREAS MEISER
PARTNER

MUNDICARE profitiert von Andreas umfangreichen Erfahrungen aus der akademischen Forschung, der Strategieberatung sowie mit Aufbau und Leitung von Biotech Startups. Er arbeitet an der Schnittstelle zwischen Wissenschaft und Wirtschaft und treibt die Implementierung neuer Lösungsansätze im biotechnologischen Umfeld voran. Vor seiner Partnerschaft bei MUNDICARE war er in verschiedenen Unternehmen verantwortlich für Forschung und Entwicklung und leitete interdisziplinäre Beratungsprojekte mit großen Teams.

FOKUS

- < Strategie: Business Development, Innovation, Market Assessment und Markteintrittsstrategien
- < Umsetzung: Implementierung von Projekten, PMOs in verschiedenen Industrien
- < Regionale Erfahrung: Deutschland, Europa, Asien

MILESTONES

Partner bei MUNDICARE



Zahlreiche Beratungsprojekte mit breitem Industrieportfolio mit Fokus auf Business Development, Implementierung neuer Technologien und der Planung/Implementierung von PMOs



Interim-Leitung von F&E eines mittelständigen Pharmaunternehmens: Entwicklung neuer Produktionsmethoden zur Steigerung der Effizienz



Gründung von Biotechnologie Start-ups: Entwicklung und Vermarktung von neuen Technologien im Bereich der Blauen (Algen-) Biotechnologie



McKinsey & Company: Nach anfänglich breitem Einsatz in verschiedensten Prozessindustrien, Eintritt in die Chemical Practice als Industrie Specialist. Projektmanager mit Portfolio von Engagements aus den Bereichen Chemicals, Climate Change und Biotechnologie. Als Industrieexperte Unterstützung von Teams weltweit hinsichtlich Biochemikalien und Bioenergie. Globales Kundenportfolio mit Relocation nach Asien. Autor von Veröffentlichungen und Vorträge auf verschiedenen internationalen Kongressen



Längere Forschungsaufenthalte in Russland und Lateinamerika



Promotion im Bereich Biotechnologie: Kommerzielle Produktion von Wirkstoffen mittels biotechnologischem Ansatz



Wissenschaftliche Tätigkeit bei Fraunhofer Gesellschaft



Studium der Mikrobiologie/Biotechnologie



Intensive Beschäftigung mit der Chemie, Nationalteam Chemieolympiade



AUS ERFAHRUNG GUT:
DREI KÖPFE, EIN TEAM, EIN NETZWERK

Spezialisten und Teamplayer, Vor- und Querdenker, Problemlöser und Aufräumer, Analytiker und Macher – jeder Partner ein Experte, das ganze Team ein Brückenschlag über die gesamte Wertschöpfungskette. Mundicare vereint Vielfalt und Multitasking, Gesundheitsindustrie und Unternehmensberatung, Beratungsansatz und Realität.

DR. ANDREAS MEISER – DR. MICHAEL MEHLMANN – BJÖRN KOMISCHKE

WE LOOK FORWARD TO YOUR INQUIRY

+49 163 49 65 770
andreas.meiser@mundicare.de

MUNDICARE GmbH
Zenettistrasse 2
80337 München
Germany

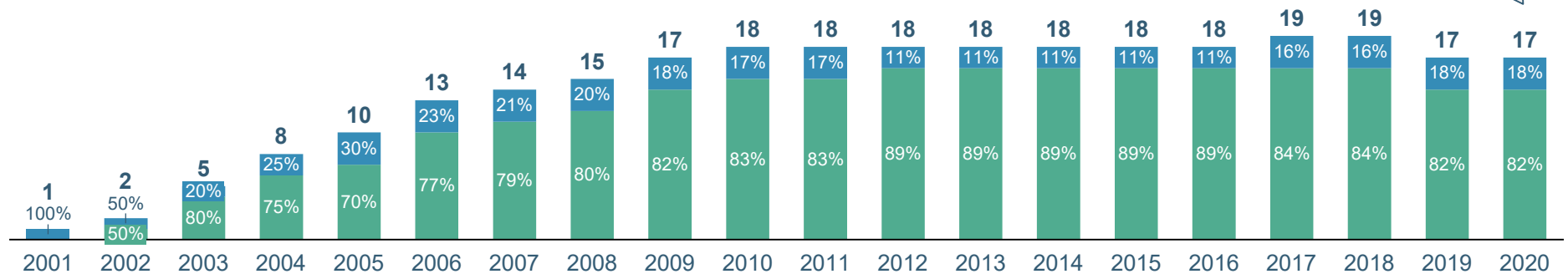


BACK UP

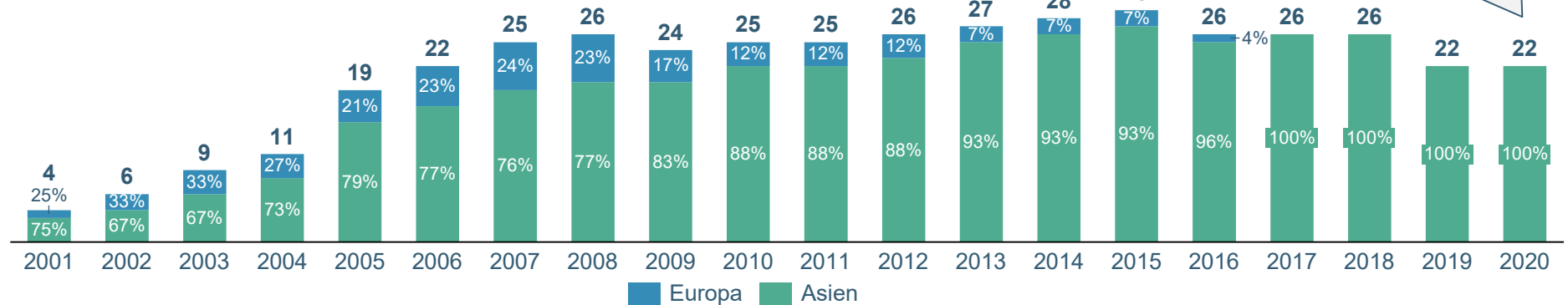
DIE HOCHVOLUMIGEN APIS RAMIPRIL UND SIMVASTATIN SCHON WENIGE JAHRE NACH ERSTEM CEP IN GROSSER ABHÄNGIGKEIT ASIENS

ENTWICKLUNG DER ANZAHL VALIDER CEPS (2001 – 2020)¹

Ramipril: Anzahl CEPs



Simvastatin: Anzahl CEPs



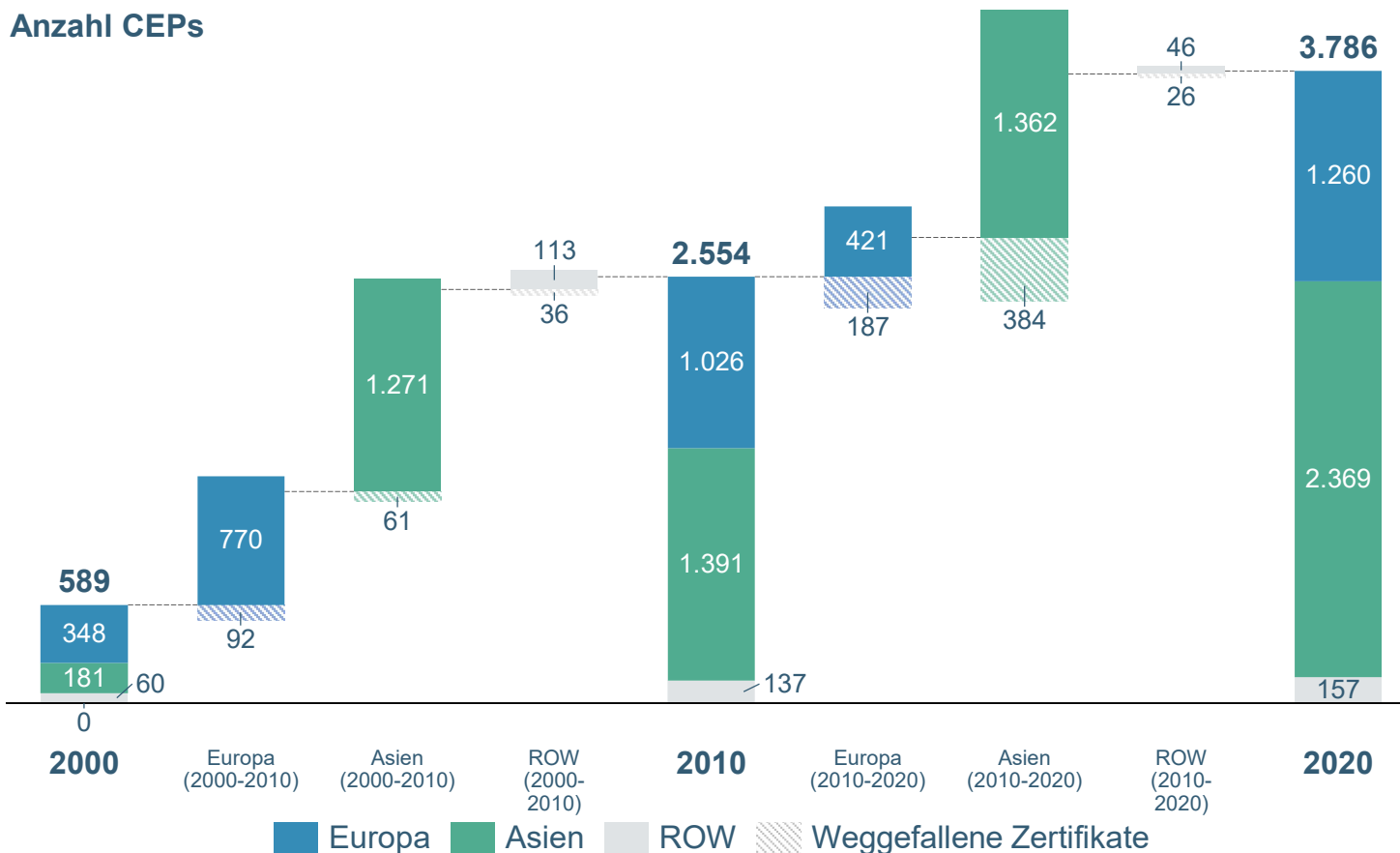
¹⁾ Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

HÖHERE ABLAUFQUOTE ASIATISCHER CEPS WIRD MIT EINEM SIGNIFIKANT STÄRKEREN ANSTIEG DER NEUZULASSUNGEN AUSGEGLICHEN

ENTWICKLUNG DER ANZAHL VALIDER API ZERTIFIKATE (2000 – 2020)¹

Anzahl CEPS



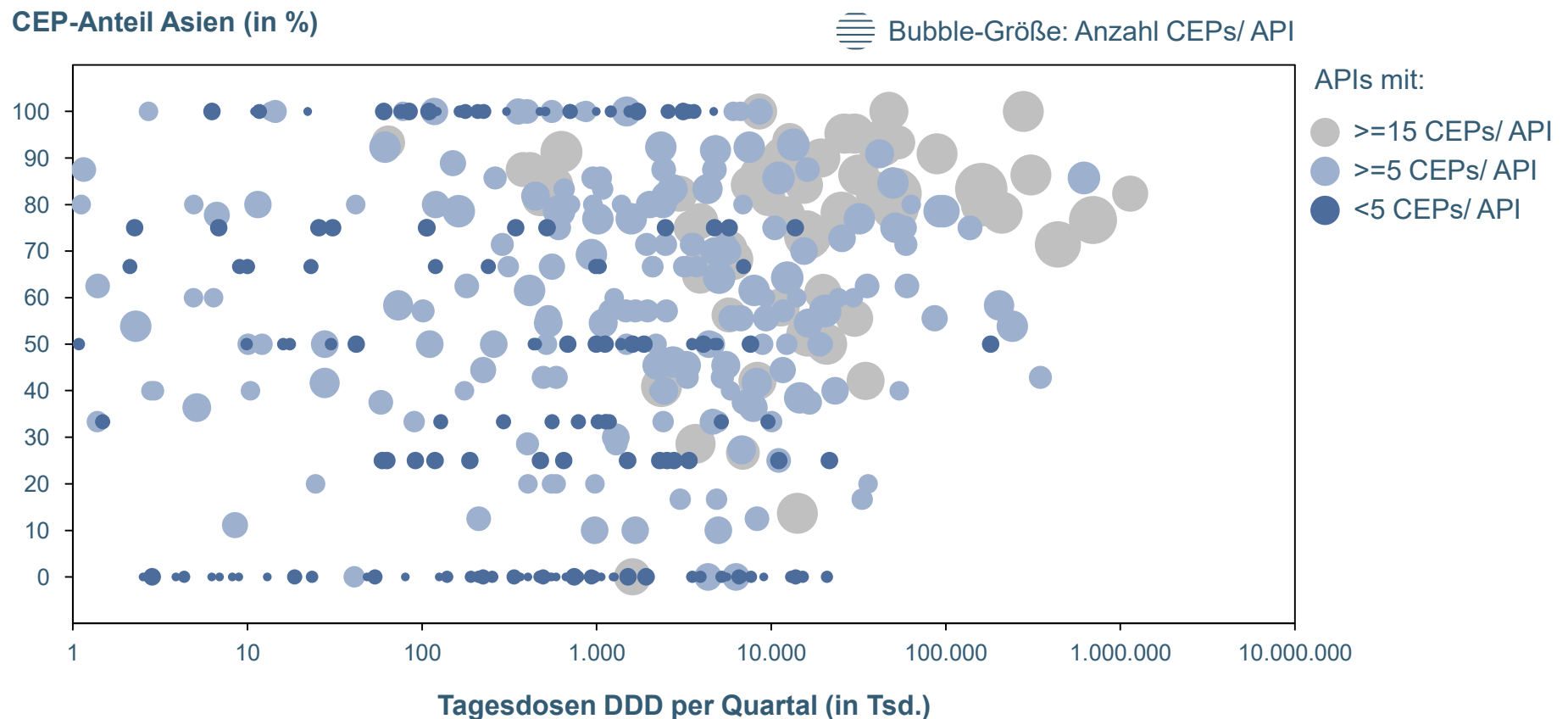
- **Anzahl der neuen CEPS** innerhalb der letzten 10 Jahre **sinkt in Europa um 45%** (in Asien Anstieg um 7%) im Vergleich zur Vorperiode
- **In Europa sind 18% der CEPS** zwischen 2010 und 2020 **abgelaufen** (Asien: 27%)
- **Verhältnis abgelaufener Zertifikate zu neuer CEPS in Europa** deutlich schlechter als in Asien (Europa: 1 : 2,2 vs. Asien: 1: 3,5)

¹⁾ Anzahl aller validen CEPS im jeweiligen Kalenderjahr 2000; 2010; 2020 für die betrachteten APIs (abgelaufene/ zurückgezogene CEPS sind bereits ausgeschlossen)

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020

TREND AUCH NOCH IN DER BETRACHTUNG EINER GRÖßEREN ANZAHL VON WIRKSTOFFEN ERKENNBAR, JEDOCH ETWAS VERWÄSSERTER

CEP-ANTEIL ASIEN IN ABHÄNGIGKEIT DER TAGESDOSEN JE API (STAND 2020)^{1,2}



¹⁾ Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

²⁾ Dargestellt sind alle APIs mit einer Tagesdosis Q4 2019 > 1 Tsd. DDD im Retail-Bereich; n = 410

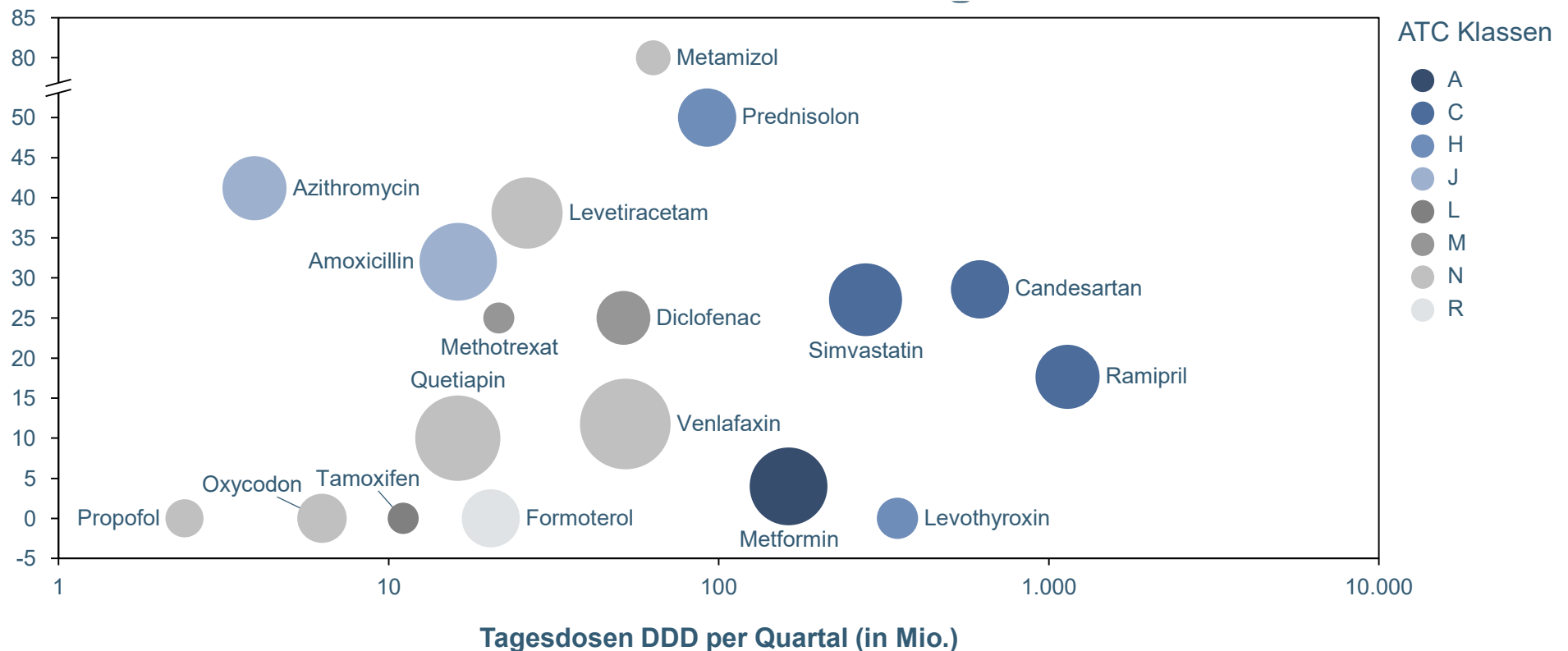
Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020; Basisliste Pro Generika

... CHINAS ANTEIL AN CEPS FÜR GROSSVOLUMIGE APIS IST ETWAS GERINGER ALS DER INDISCHE

EXEMPLARISCHE API-AUSWAHL: CEP-ANTEIL CHINA ZU TAGESDOSEN (STAND 2020)^{1,2}

CEP-Anteil China (in %)

Bubble-Größe: Anzahl CEPs/ API



¹⁾ Anzahl aller validen CEPs im jeweiligen Kalenderjahr für die betrachteten APIs (abgelaufene/ zurückgezogene CEPs sind bereits ausgeschlossen)

²⁾ Exemplarische API-Auswahl mit einer Tagesdosis Q4 2019 > 1 Mio DDD im Retail-Bereich (Ausschluss von: Piperacillin, Benserazid, Levodopa); n = 18

Quelle: Certificate Database, European Directorate for the Quality of Medicine & HealthCare, Stand 30.04.2020; Basisliste Pro Generika

ANTEIL EUROPÄISCHER HERSTELLER AM EU-SUPPLY IM MITTEL VERGLEICH- BAR ZUM ANTEIL CEPS; BEI EINZELNEN APIS JEDOCH ABWEICHEND

VERGLEICH ANTEIL EU-SUPPLY VS. ANTEIL CEPS

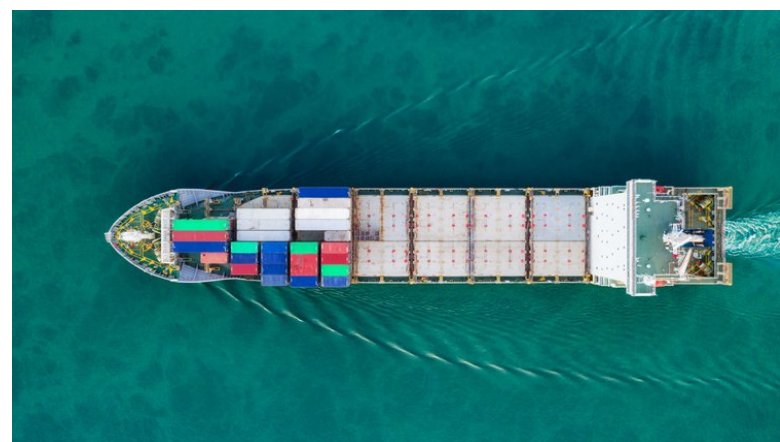
API	Im CEP Verfahren seit	#CEPs Gesamt	EU-Supply			CEP Verteilung ¹		
			Europa	China	Indien	Europa	China	Indien
Benserazid	2010	2	100,00%	0,00%	0,00%	100,00%	0,00%	0,00%
Propofol	2001	6	100,00%	0,00%	0,00%	60,00%	0,00%	40,00%
Methotrexat	1996	4	95,00%	5,00%	0,00%	75,00%	25,00%	0,00%
Levothyroxin	1998	7	95,00%	0,00%	5,00%	57,14%	0,00%	42,86%
Tamoxifen	1995	4	95,00%	0,00%	5,00%	100,00%	0,00%	0,00%
Oxycodon	2005	10	90,00%	0,00%	10,00%	100,00%	0,00%	0,00%
Formoterol	2005	14	85,00%	0,00%	15,00%	46,15%	0,00%	53,85%
Levodopa	1998	9	60,00%	30,00%	10,00%	0,00%	66,67%	33,33%
Amoxicillin	1994	25	30,00%	65,00%	5,00%	47,83%	34,78%	17,39%
Quetiapin	2014	30	30,00%	10,00%	60,00%	27,59%	10,34%	62,07%
Metamizol	2000	5	20,00%	80,00%	0,00%	20,00%	80,00%	0,00%
Azithromycin	2002	17	20,00%	65,00%	15,00%	25,00%	43,75%	31,25%
Metformin	1997	25	20,00%	5,00%	75,00%	13,04%	4,35%	82,61%
Piperacillin	1998	10	15,00%	85,00%	0,00%	55,56%	33,33%	11,11%
Prednisolon	1992	14	10,00%	80,00%	10,00%	23,08%	53,85%	23,08%
Levetiracetam	2010	21	10,00%	45,00%	45,00%	4,76%	38,10%	57,14%
Ramipril	2001	17	10,00%	10,00%	80,00%	17,65%	17,65%	64,71%
Diclofenac	1997	12	10,00%	5,00%	85,00%	30,00%	30,00%	40,00%
Venlafaxin	2005	34	10,00%	5,00%	85,00%	15,63%	12,50%	71,88%
Candesartan	2011	14	5,00%	90,00%	5,00%	15,38%	30,77%	53,85%
Simvastatin	2001	22	0,00%	40,00%	60,00%	0,00%	33,33%	66,67%
Durchschnitt			43%	30%	27%	40%	24%	36%

1) Gewichtung zwischen Europa, China, Indien; CEPs von ROA und ROW wurden hier in der Verteilung nicht berücksichtigt

Quelle: Supplier Interviews, Import Data Analysis QYOB market platform, CEP Database, Pharmaoffer; IQVIA-Bedarfsanalyse

26.02.2020

Arzneimittelproduktion im Lichte der Lieferengpässe



Die Arzneimittelproduktion ist ein komplexer Vorgang mit vielen einzelnen Schritten. Die Wirkstoffherstellung ist dabei nur der erste Schritt einer langen und oft globalisierten Fertigungskette. Mit einer Produktion in Deutschland bzw. Europa lässt sich die Wahrscheinlichkeit einer zuverlässigen, verbesserten, kontinuierlichen Versorgung der Bevölkerung mit Arzneimitteln erhöhen.

Im Gesundheitssystem ist das Wissen darüber, welche Herausforderungen mit der Herstellung von Arzneimitteln verbunden sind, häufig begrenzt. Die Arzneimittelproduktion ist ein komplexer Vorgang mit vielen einzelnen Schritten. Die Wirkstoffherstellung ist dabei nur der erste Schritt einer langen und oft globalisierten Fertigungskette. Dabei kann die Produktion durch ein Unternehmen selbst oder im Zuge von Lohnherstellung für sich selbst und/oder andere Unternehmen erfolgen. Wirkstoffe und Hilfsstoffe bilden die wichtigen Ausgangsstoffe für die Herstellung eines Arzneimittels. Gibt es nur wenige Bezugsquellen hierfür, ist der Produktionsprozess sehr häufig anfällig für Störungen durch Lieferschwierigkeiten. Der Produktionsprozess selbst ist in verschiedene Teilschritte untergliedert:

- Ausgangspunkt sind Hilfsstoffe und Wirkstoff(e), die in eine gebrauchsfertige Form mit den gewünschten Eigenschaften zu bringen sind.
- Anschließend wird unverpackte sogenannte „Bulkware“ bspw. in Form von Tabletten, Flüssigkeiten oder Salben gefertigt, die dann in eine Primärverpackung (z. B. Blister, Flasche oder Tube) verbracht werden.
- Danach folgt die Endverpackung (Faltschachtel) und Qualitätsprüfung des fertigen Produktes.
- Abschließend ist eine Endfreigabe vor dem Vertrieb notwendig.

Neben der durch den Wirkstoff vermittelten Wirkung sind pharmazeutische Eigenschaften wie z. B. der Weg der Verabreichung (u. a. oral, kutan, parenteral), der Ort der Freisetzung oder die Geschwindigkeit der Freisetzung für die Wirksamkeit und Verträglichkeit entscheidend. Der gesamte Herstellungsprozess in allen seinen Teilschritten unterliegt höchsten Anforderungen an die Sicherstellung der Qualität und Dokumentation und wird behördlich überwacht.

Dies bedeutet eine aufwändige Analytik, die sowohl bei der Eingangskontrolle der Ausgangsmaterialien als auch beim Produkt erfolgen muss. Insbesondere im Bereich der sterilen Herstellung müssen zudem hohe Hygieneanforderungen beachtet werden. Die o. g. Teilschritte können dabei ganz oder teilweise in verschiedenen Ländern und entweder in eigenen Betrieben oder über Lohnherstellung auf allen Kontinenten erfolgen, was zu komplexen Lieferketten führt.

Insbesondere aufgrund des Kostendrucks, vor allem im Bereich der generischen Arzneimittel, werden immer mehr Teilschritte der Produktion nicht mehr in Deutschland bzw. Europa durchgeführt. Dabei ist festzustellen, dass insbesondere die Produktion der Wirkstoffe vor allem in Asien stattfindet.

Die Förderung deutscher und/oder europäischer Produktion (gesamte Produktion an einem Standort bzw. in sehr starker räumlicher Nähe) hat viele Vorteile, denn so

- können Prozesse schneller und lückenlos kontrolliert bzw. dokumentiert werden,
- ist ein flexibles Agieren bei Bedarfsschwankungen möglich und reduziert so die Abhängigkeit von ausländischen Lohnherstellern und deren Verfügbarkeiten und Vorgaben,
- entstehen keine längeren Transportwege und Lieferzeiten, so dass die Arzneimittel schneller zur Verfügung stehen,
- wird der Schutz des eigenen Know-hows sichergestellt, was bei komplexeren Darreichungsformen eine wichtige Rolle spielt,
- wird die Abhängigkeit von politischen Unwägbarkeiten oder höherem Eigenbedarf durch aktuelles Krankheitsgeschehen (Epidemien), z. B. in Asien, gesenkt,
- besteht keine Abhängigkeit von asiatischer Preispolitik. Die Gewährleistung hoher Qualitätsstandards führt auch in Asien zu teilweise wenigen Anbietern, die dann die Preise vorgeben. Dies vor dem Hintergrund, dass ein Zulassungsinhaber nicht einfach einen gemeldeten Hersteller wechseln kann, weil dies nicht nur ein sehr teurer Vorgang ist, sondern es auch sehr komplex ist, einen Alternativlieferanten aufzubauen bzw. im Zulassungsverfahren einzuschließen. Hier spielen die geforderten Nachweise z.B. beim Änderungsmanagement eine Rolle,
- wird die Abhängigkeit von Auswirkungen möglicher Handelsstreitigkeiten z. B. mit asiatischen Ländern gesenkt,
- werden die hohen Produktionsstandards in Europa und Deutschland über die Gewährleistung der Produktqualität hinaus auch hinsichtlich Arbeitsschutz, Entlohnung und Umweltschutz eingehalten.

Mit einer Produktion in Deutschland bzw. Europa lässt sich die Wahrscheinlichkeit einer zuverlässigen, verbesserten, kontinuierlichen Versorgung der Bevölkerung mit Arzneimitteln erhöhen. Aufgrund der engmaschigen behördlichen Überwachung „vor Ort“ sind die Prozesse viel besser kontrollierbar. Damit kann ein Beitrag zur Gewährleistung der öffentlichen Gesundheit geleistet werden und der im Rahmen der Daseinsvorsorge vorhandene Anspruch der Menschen auf eine Versorgung mit lebenswichtigen Arzneimitteln besser durchgesetzt werden.

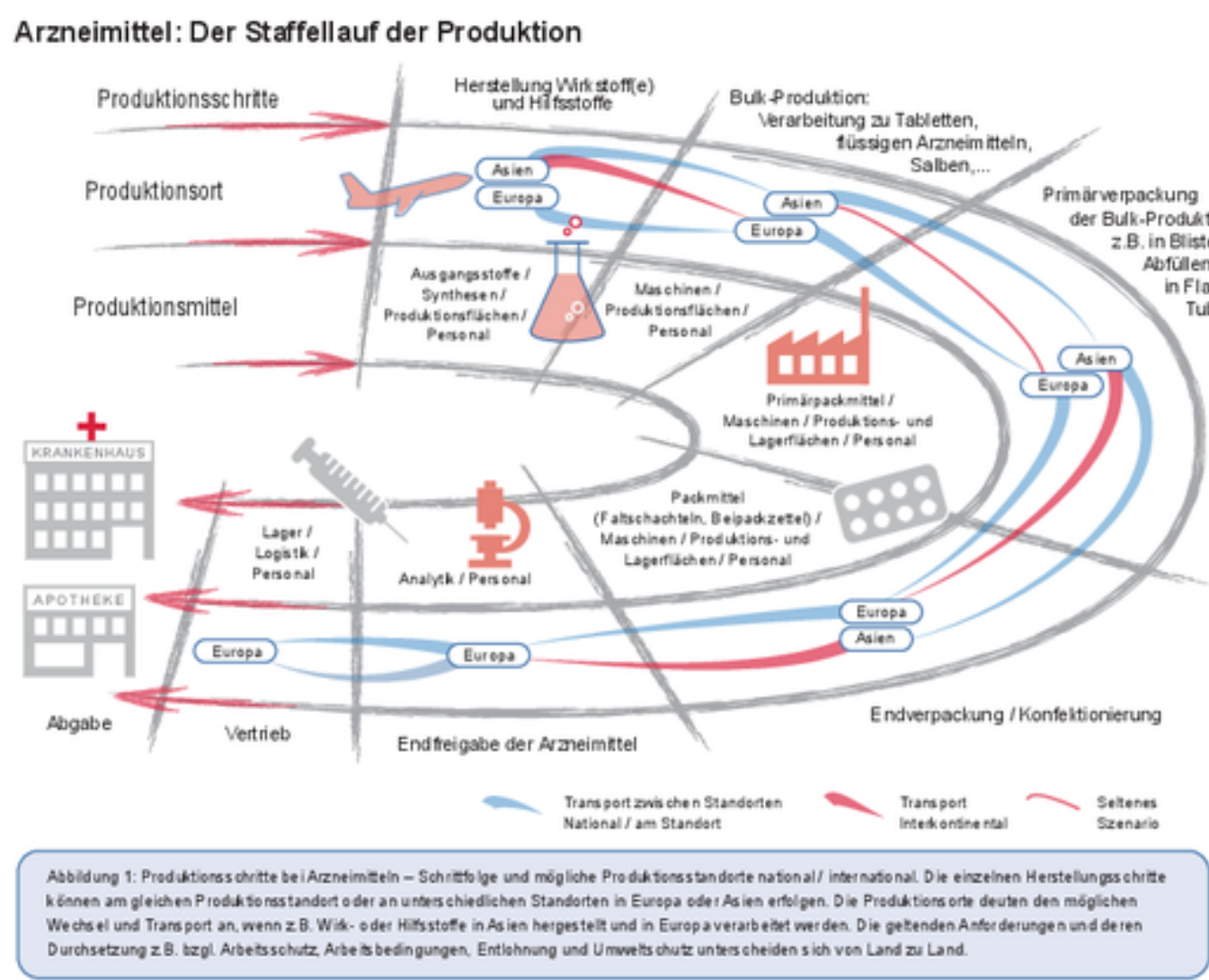
Vor allem aber würde ein erhöhter Produktionsanteil in Europa dazu führen, dass wieder mehr Anbieter auf dem Markt verfügbar sind. Wenn ein Anbieter aufgrund technischer Schwierigkeiten dann nicht liefern kann, sind andere Unternehmen vorhanden, die einspringen können. Dies ist bei der aktuell gegebenen Marktkonzentration insbesondere bei der Herstellung vieler Wirkstoffe auf wenige Anbieter v. a. in Asien immer seltener der Fall.

Um mit einer Produktion in Deutschland bzw. Europa die Versorgungssicherheit mit Arzneimitteln zu erhöhen, bedarf es u. a. auch der Modifikation der bestehenden Ausschreibungsregelungen für Rabattverträge und einer konkreten Verankerung von Vorgaben im SGB V.

- Zum einen kann ein Punktesystem für die Teilschritte der Produktion zugrunde gelegt werden, um die essentiellen bzw. einzelnen Schritte in der Produktion in Deutschland bzw. Europa entsprechend zu honorieren.
- Darüber hinaus sollten Wirkstoffe/Arzneimittel, die in den letzten zwei Jahren mehrfach ein Versorgungsdefizit aufgewiesen haben, für die Dauer von zwei bis drei Jahren nicht mehr ausgeschrieben werden. Damit stünden diese vollständig zur Versorgung der Bevölkerung zur Verfügung und es würden Anreize geschaffen, die Versorgung in Deutschland zu verbessern.
- Bei der Zuschlagserteilung müssen die Krankenkassen verpflichtet werden, in einem echten Mehrbietermodell (Vorteile des Mehrbietermodells siehe BPI-Positionspapier) mindestens einen Bieter mit deutscher bzw. EU-Produktion bei insgesamt drei Zuschlägen zu berücksichtigen, wobei Ein-Partner-Zuschläge grundsätzlich untersagt sind.

Grundsätzlich sollte die noch in Deutschland/Europa bestehende Wirkstoffherstellung vor weiterer Abwanderung gesichert werden. Die Fertigproduktherstellung ist ohne größere Probleme wieder verstärkt realisierbar in Europa, die grundlegenden Strukturen sind vorhanden, politisch könnte man das durch verstärkte Förderungen unterstützen. Bei der Wirkstoff-Herstellung hat Deutschland/Europa durch deren Abwanderung in andere Teile der Welt sehr viel verloren.

Dadurch ist das „Zurückholen“ der Wirkstoffproduktion nur bedingt realisierbar, zumal dann große Investitionen notwendig würden. Auch dies müsste ggf. entsprechend gefördert werden (z. B. wie in Irland durch die Irish Development Agency) und ist eine längerfristige Aufgabe. Schlussendlich sind im Vergleich zu Asien in Deutschland/Europa höhere Herstellungskosten und ein höherer regulatorischer Aufwand vorhanden, so dass man im Bereich der Gesetzlichen Krankenversicherung auch bereit sein muss, für die Lieferfähigkeit und Patientenversorgung entsprechende Mehrkosten in Kauf zu nehmen.



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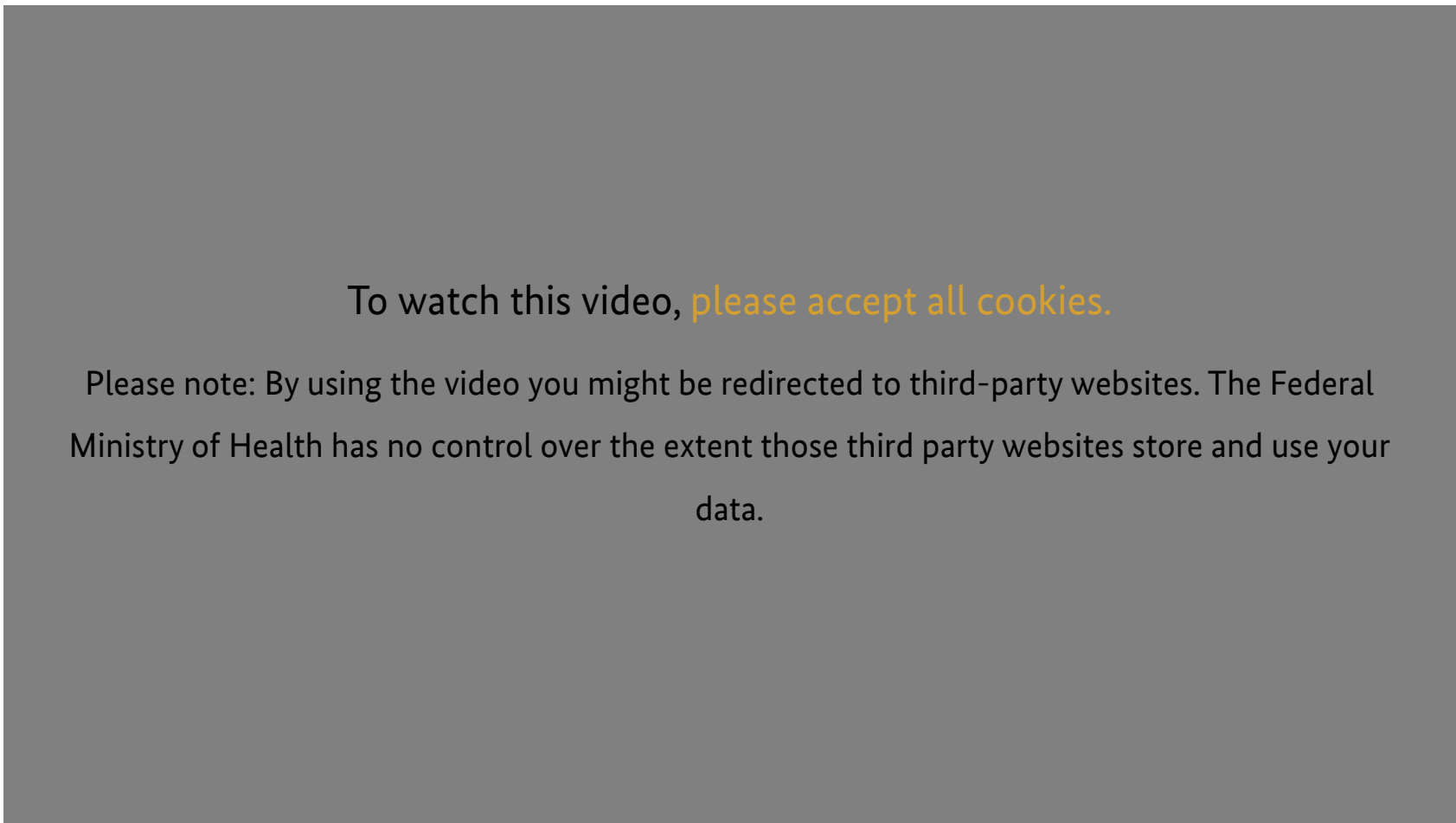
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Informal Meeting of Health Ministers

Minister of Health Jens Spahn: “Strengthening Europe’s resilience together”

16 July 2020



The EU Health Ministers called upon the European Commission to expand the European Centre for Disease Prevention and Control (ECDC) into a forceful response centre for international health crises and to submit a strategy for how the manufacture of important medicinal products can be relocated to the European Union. These are key results of the Informal Meeting of the Health Ministers of the 27 EU Member States held today in Berlin. The video conference chaired by Federal Minister Jens Spahn was attended in person by the representatives of Germany's Trio Presidency partners: the Portuguese Minister of Health Marta Temido and the Slovenian Minister of Health Tomaž Gantar.

Federal Minister of Health, Jens Spahn: “The coronavirus pandemic has once more shown us Europeans the importance of standing shoulder to shoulder in a time of crisis. We must be better prepared to be able to ward off dangers together. Europe must become more independent from other countries when it comes to manufacturing important medicinal products. We need a European health crisis authority that is robust and better equipped. This is the only way it can quickly respond to an emergency and support the member states. Together we will succeed in strengthening Europe’s resilience.”

The projects in detail:

- To be able to respond to international health crises faster in future, the ECDC is to be expanded and given additional powers. To this end, a Health Task Force is to be set up within the ECDC that will also be able to support member states in preparing their crisis management. Going forward, a standardised EU-wide electronic surveillance system at the ECDC and in the member states, with common criteria and threshold values, is to provide real-time evaluation and analysis of health threats as well as model forecasts. Together, the ECDC and the member states are to draft an EU guideline on regional pandemic planning. For the corresponding ECDC expansion to go ahead, the EU Commission will be called upon to table a legislative proposal by the end of this year.
- The fact that the manufacture of active substances for essential medicinal products is increasingly concentrated outside the EU, and is in some cases limited to a handful of manufacturing sites, increases the risk of supply shortages – and not only amidst a health crisis. This is why ensuring the supply of medicinal products is another key priority of Germany’s Presidency of the Council of the European Union. Measures such as providing financial incentives to preserve or relocate the manufacture of active substances for critical medicinal products to Europe are therefore to be jointly examined and an EU-wide data exchange on manufacturing sites facilitated. A dialogue, coordinated and institutionalised by the European Medicines Agency, is to be initiated between the member states and other actors at EU level. In close coordination with the member states, the European Commission is called upon to submit by October 2020 its announced EU Pharmaceutical Strategy that takes into account these concrete measures.
- Europe is to also make full use of the potential of digitalisation in the EU’s health sector. This above all means improved access to and sharing of health data within the EU. To achieve this, a common Health Data Space is to be created that enables the privacy-compliant access to and exchange of health data for research, diagnosis and treatment. The EU Commission and member states will develop common framework conditions for this Health Data Space.

More Information

- > [EU2020](#)
Everything you need to know about the German EU Presidency is available on our overview page
- > [Réunion informelle des ministres de la santé](#)
Here can be found the French language version of this press release

16 July 2020

Studie zur Versorgungssicherheit mit Antibiotika: Wege zur Produktion von Antibiotikawirk- stoffen in Deutschland bzw. der EU

Ergebnisbericht

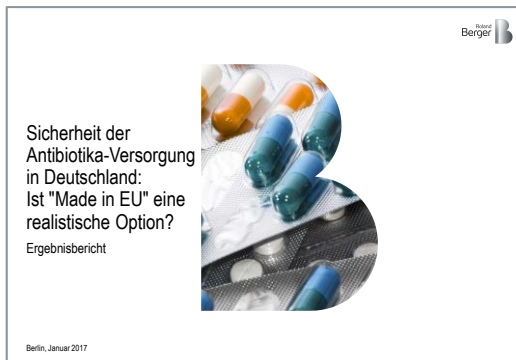


Basierend auf der Studie 2016 werden Ansätze zur Rückverlagerung/Neuaufbau lokaler Antibiotikawirkstoffproduktion untersucht

Hintergrund und Methodik der aktuellen Studie (Juni - November 2018)

Hintergrund

- > Aufgrund des niedrigen Preisniveaus generischer Antibiotika ist lokale Produktion in Deutschland nicht mehr wirtschaftlich
- > Lieferengpässe im deutschen Markt durch Produktionskonzentration in Niedriglohnländern
- > Risiko für Versorgungssicherheit erhöht sich durch Abhängigkeit von ausländischer Produktion
- > Zunehmende Diskussion über Rückführung der Produktion nach Deutschland bzw. in die EU als Hebel zur Sicherung der Versorgung



Studie zur Analyse einer Relokalisierung der Antibiotikawirkstoffproduktion nach Deutschland

- 1 Überblick der **Hintergründe** für die **Notwendigkeit** des **Wiederaufbaus lokaler Produktionskapazitäten**
- 2 Beschreibung des **rückzuführenden Produktionsprozesses** und der **notwendigen Kapazitäten**
- 3 Berechnung verschiedener Szenarien und folgende Analyse der **Wirtschaftlichkeit** der Relokalisierung einer **lokalen Antibiotikawirkstoffproduktion**
- 4 Evaluation **möglicher Betreibermodelle** für die Rückführung der Antibiotikawirkstoffproduktion

Die Studie 2016 ergab, dass lokale Produktionskapazitäten die Abhängigkeit reduzieren und die Versorgungssicherheit erhöhen könnten

Ergebnisse Studie 2016: Übersicht zur aktuellen Situation und erwartete Effekte

Situation

- > **Hoher Importanteil** in Deutschland verarbeiteter **Intermediates** und **Antibiotika-Wirkstoffe**
- > **Abhängigkeit von ausländischen Intermediate- und Wirkstoff-Produzenten**, vorwiegend aus Non-EU Low-Cost-Ländern
- > **Gefährdung der Versorgung** mit Antibiotika und **Auftreten von Lieferengpässen**



Vorschlag

Einstieg in Stakeholder-Diskussion über eine partielle **Rückverlagerung/Neuaufbau der Produktion von Intermediates und Wirkstoffen** für (generische) Antibiotika **nach/ in Deutschland bzw. EU**

Erwarteter Effekt

- + **Reduktion der (politischen) Abhängigkeit** durch Produktion in Non-EU-Ländern
- + Sicherstellung der kontinuierlichen **Versorgung durch Antibiotika** in Deutschland
- + **Erhalt/Aufbau von Produktionskapazitäten und -wissen**, welche relevant für die **Produktion von Antibiotika** sind
- + **Weitere positive Ausstrahlungswirkung** möglich
 - **Export von Intermediates und Wirkstoffen in EU-Nachbarländer**, insbesondere im Falle von Lieferausfällen bei Non-EU-Produzenten
 - **Stärkung des Standorts Deutschland** gegenüber dem internationalen Wettbewerb
 - Generierung **zusätzlicher Wertschöpfung** für die **inländische Wirtschaft** sowie **Schaffung von Arbeitsplätzen** durch den Betrieb von Produktionsanlagen

Die derzeitige Abhängigkeit entstand durch eine sukzessive Auslagerung der Antibiotikawirkstoffproduktion in das Non-EU-Ausland

Verlagerungshistorie: Verlagerung der Produktion von Intermediates und Wirkstoffen

Gezielter Aufbau von Produktionskapazitäten in China

- > **Subventionierung der lokalen Produktion von Intermediates und Wirkstoffen** zur Sicherstellung chinesischer Unabhängigkeit in der Antibiotika-Produktion in den 1980er Jahren
- > Umfangreicher Aufbau von Produktionskapazitäten für **Human- und Veterinärwirkstoffe**
- > **Kontinuierlicher Effizienzgewinn und Ausbau der Kapazitäten**, auch nach Erfüllung des nationalen Bedarfs, somit **Entstehung von Überkapazitäten**
- > Erzielung von **Skaleneffekten**

Zunehmender Anteil an generischen Antibiotika nach Patentausläufen in Deutschland

- > **Anstieg der Kosten** für die **lokale Produktion** von Intermediates und Wirkstoffen aufgrund zunehmend anspruchsvoller Audits bei relativ veralteten Produktionsanlagen sowie Kostennachteilen
- > **Reduktion der (kostenintensiven) lokalen Kapazitäten in der Wirkstoff-/Intermediate-Produktion** durch Originatoren nach Patentausläufen
- > Bedarf an **ökonomischen Produktionskapazitäten** für Intermediates und Wirkstoffe generischer Antibiotika
- > **Ausbau der Produktion von Intermediates und Wirkstoffen** im Ausland aufgrund des Kostendrucks

Verfügbarkeit von Low-Cost
Produktionskapazitäten in China

Bedarf an wirtschaftlichen
Produktionskapazitäten für Deutschland

Die Produktion von Intermediates und Antibiotika-Wirkstoffen
verlagert sich nach China
und in andere Low-Cost-Länder außerhalb der EU

Die Produktion in Non-EU-Ländern wird durch globale und lokale Faktoren bedingt, z.B. durch Kostenvorteile und globalen Preisdruck

Aktuelle Treiber: Verlagerung der Produktion von Intermediates und Wirkstoffen

Preisdruck

- > **Niedrige Preise bei (generischen) Antibiotika** aufgrund von **Preisbildungsmechanismen** der Gesetzlichen Krankenversicherung sowie aufgrund der **Nachfragemacht** von Einkaufsgemeinschaften der Krankenhäuser
- > **Wirtschaftliche Herstellung** der (generischen) Antibiotika somit **nur durch Kosteneinsparungen** in der **Produktion** möglich

Vorhandene Produktionskapazitäten von Intermediates und Wirkstoffen im Ausland

- > Kontinuierlicher **Ausbau und Effizienzsteigerung der Produktionskapazitäten**, u.a. bedingt durch das stetige Wachstum des globalen Wirkstoffmarktes¹⁾
- > Rückgang der Nachfrage nach Veterinär-Antibiotika, somit **Nutzung der Kapazitäten** für die Herstellung von **Human-Wirkstoffen**
- > Notwendigkeit zur **Erreichung einer Mindestproduktionsmenge**²⁾ zur Deckung der Fixkosten und Auslastung vorhandener Kapazitäten

Lokale Faktoren

Nachfrageschwankungen und -spitzen

- > **Schwankungen** in der **Nachfrage** nach (generischen) Antibiotika, welche **durch die Externalisierung von Produktionsschritten flexibler ausgeglichen** werden können

**Weiterhin
Produktion von
Intermediates
und Antibiotika-
Wirkstoffen
in
Low-
Cost-
Ländern
außerhalb
der EU**

Globale Faktoren

Kostenvorteil

- > **Kostengünstige Produktion von Intermediates und Wirkstoffen** aufgrund von
 - **Lohnkostenvorteilen**
 - **Geringeren Produktionsauflagen** (Umwelt, Sicherheit)
 - **Geringeren Produktionskosten** (insbes. für Kühlung und somit Energie)
 - **Mengenskalisierungseffekten**

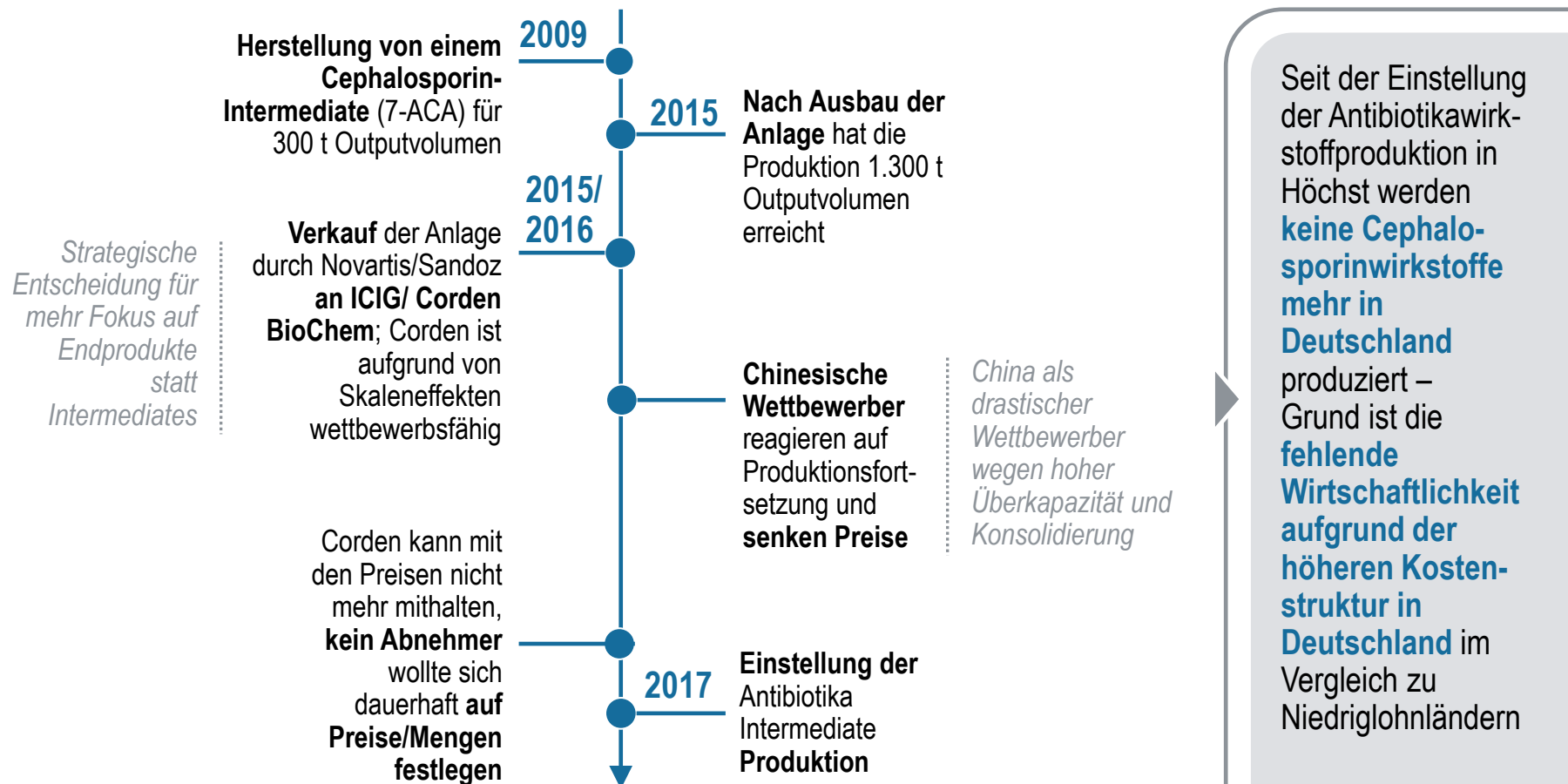
1) Wachstum von ca. 10% p.a. zwischen '12-'16

2) Länger dauernde Fermentierungsprozesse, die nicht kurzfristig unterbrochen bzw. wieder hochgefahren werden können (Dauerbetrieb an 365 Tagen/Jahr)

Quelle: Statista, Experteninterviews, Antibiotikastudie 2016; Roland Berger

Dies führte z.B. auch zur Produktionseinstellung von Cephalosporin-intermediates in Höchst – Produktion nicht mehr wirtschaftlich

Beispiel 7-ACA Produktionsstätte Höchst



Als Resultat werden Penicilline weitgehend in Niedriglohnländern produziert – Deutschland hängt "am Tropf"

Abhängigkeit von Intermediate-/Wirkstoff-Produzenten – Bsp. Amoxicillin-haltige Antibiotika

Fermentierung von 6-APA

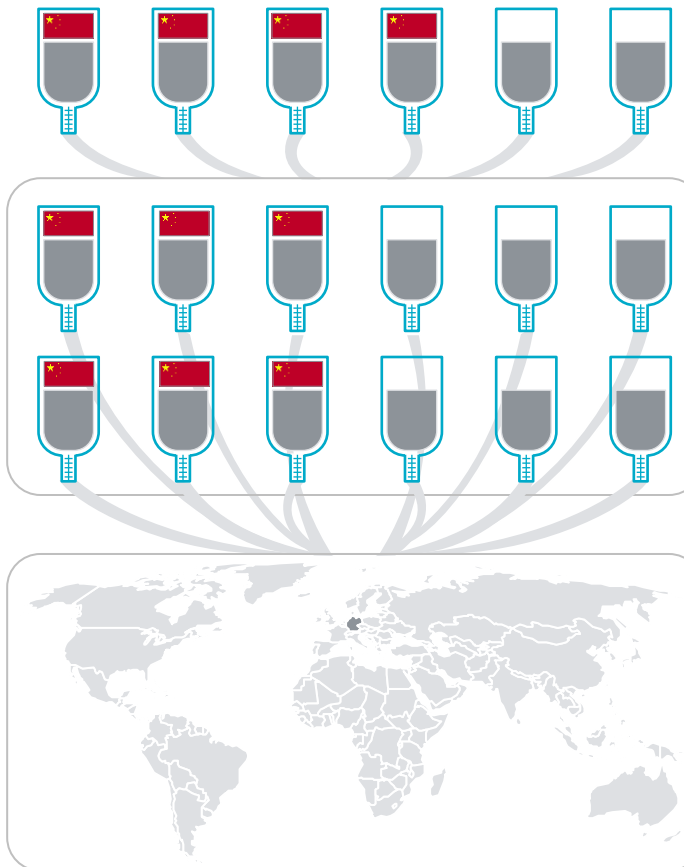
- > **Vier** relevante Produktionsstätten in **China** + **zwei** relevante Produktionsstätten **außerhalb von China**¹⁾

Chemische Synthese von Amoxicillin Trihydrate²⁾

- > **Sechs** relevante Produktionsstätten in **China** + **sechs** relevante Produktionsstätten **außerhalb von China**¹⁾

Erzeugung der Amoxicillin-haltigen Antibiotika

- > **Erzeugung aller** in Deutschland/ weltweit vertriebenen **Amoxicillin-haltigen Pharmazeutika** von den **Lieferungen** dieser Produzenten, die **größtenteils in Asien** ansässig sind, **abhängig**



6-APA ist das **Kernmolekül** für die Herstellung von Antibiotika aus der Gruppe der **Penicilline**

Amoxicillin ist einer der **wichtigsten Wirkstoffe** in der Gruppe der **Penicilline**

Amoxicillin-haltige Pharmazeutika sind die am **häufigsten eingesetzten Antibiotika** in **Deutschland**, gemessen an der **DDD**

1) Werden von globalen Arzneimittel-Herstellern betrieben 2) Primär basierend auf 6-APA

Quelle: Quintiles, IMS, Insight Health, Experteninterviews; Antibiotikastudie 2016; Roland Berger

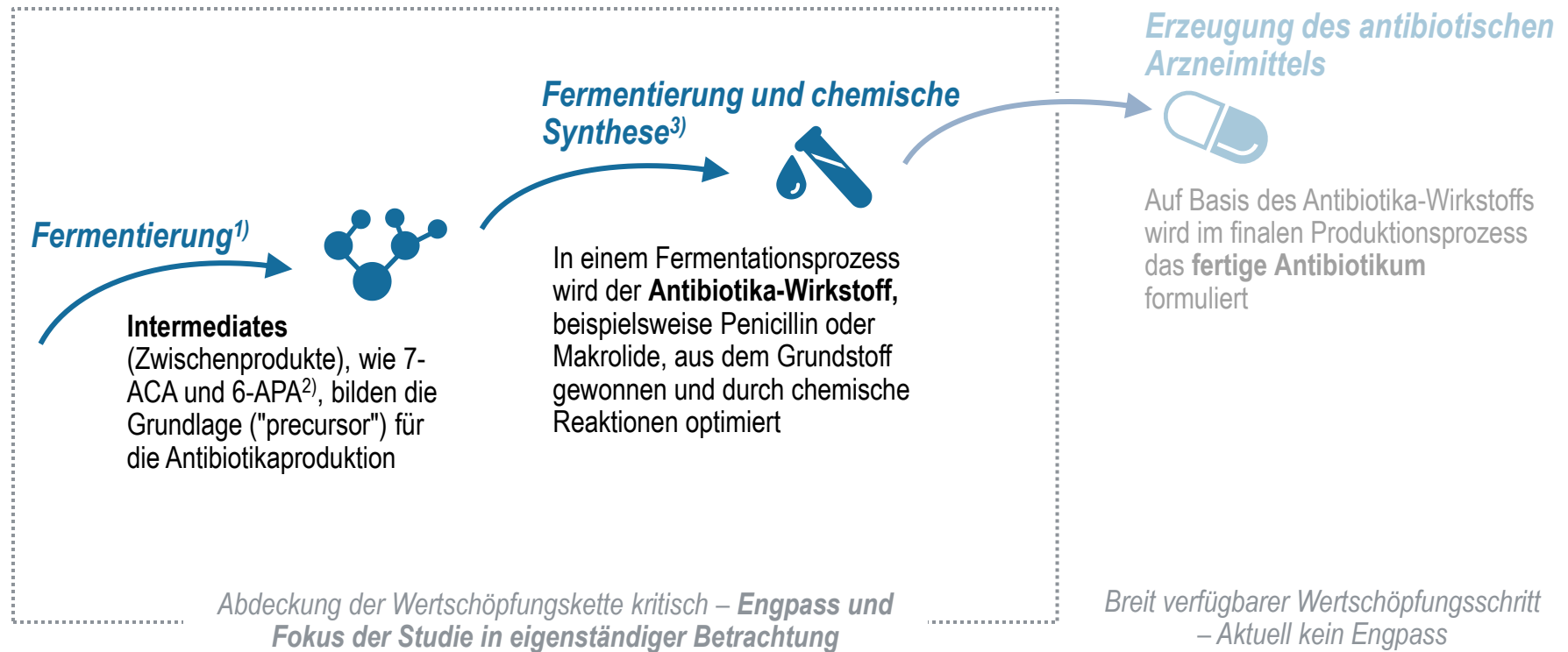
Eine Rückverlagerung/Neuaufbau der Produktion für Antibiotikawirkstoffe wird daher von zahlreichen Stakeholdern gewünscht

Stimmen aus der Studie 2016 zur lokalen Produktion von Intermediates und Wirkstoffen



Lokale Intermediateproduktion unwirtschaftlich – In Europa halten sich kaum Produktionsanlagen für Fermentierung und Synthese

Übersicht über die notwendigen Schritte der Wirkstoffproduktion



1) Herstellung der Grundstoffe

2) "7-aminocephalosporanic acid" und "6-aminopenicillanic acid", welche die Grundlage für halbsynthetisches Cephalosporin bzw. Penicillin bilden

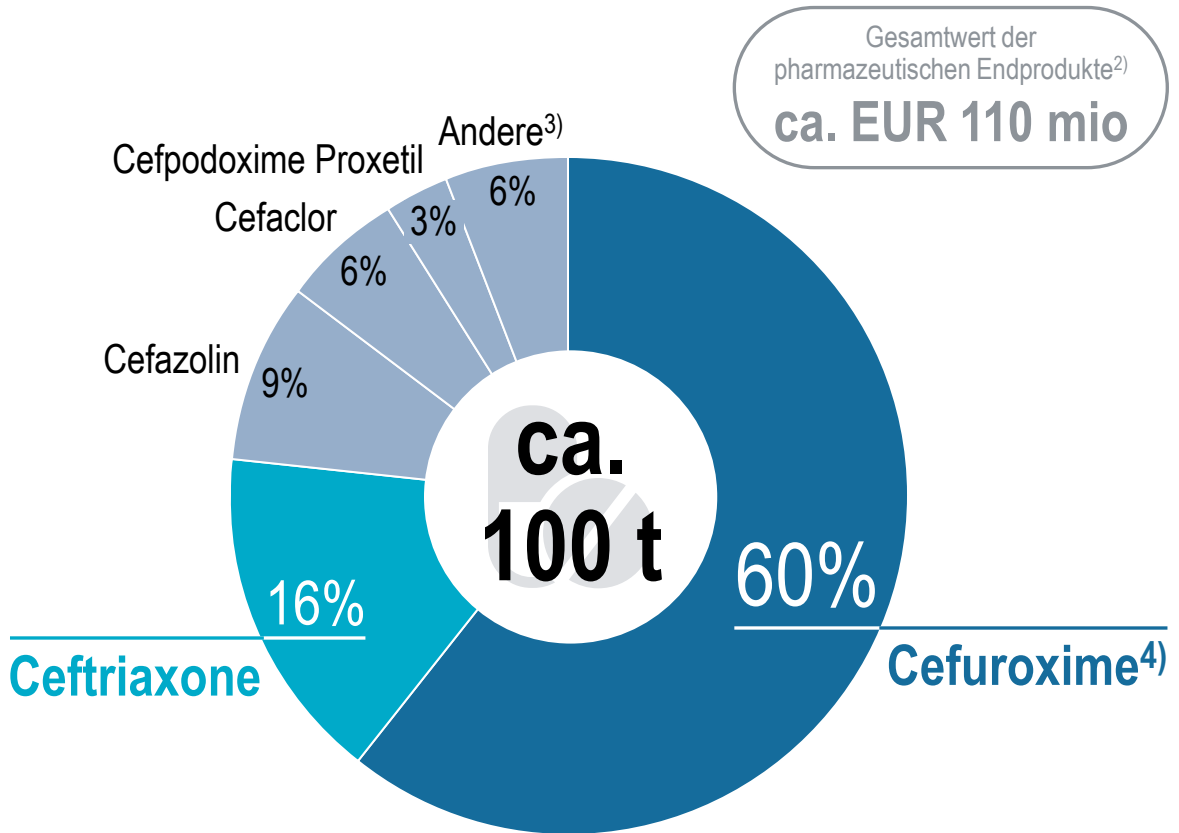
3) Produktion des Wirkstoffs

Quelle: Roland Berger

Derzeit keine lokale Herstellung von Cephalosporinintermediates – Exemplarische Analyse einer Rückführung dieser Wirkstoffproduktion

Generischer Cephalosporinverbrauch in Deutschland¹⁾, 2017 in Tonnen

- > In Deutschland werden seit dem **Produktionsstopp in Höchst** in 2017 **keine generischen Cephalosporine samt ihrer Vorstufen** mehr hergestellt
- > **Cephalosporine** sind ebenso wie (Amino-)Penicilline eine **häufig verbrauchte** und entsprechend **sehr wichtige Antibiotikagruppe**
- > Um die **Abdeckung des deutschen Markts** mit Cephalosporinen **sicherzustellen**, müssen jährlich **ca. 100 t des Wirkstoffs hergestellt werden**



1) Ausschließlich Humanmedizin 2) Zum Herstellerabgabepreis 3) Beinhaltet Ceftazidime, Cefotaxime, Cefixime, Cefadroxil, Cefepime und Cefalexin

4) Sowohl Cefuroxim als auch Cefuroxim Axetil

Die Analyse konzentriert sich auf die Herstellungsschritte von Fermentation über Intermediateherstellung zur Wirkstoffproduktion

Moderner Herstellungsprozess von 7-ACA und Beispiel einer Cefuroxim-Synthese

d Generierung von 7-ACA

- > Das präzipitierte 7-ACA wird gefiltert, mit Methanol und danach Wasser gewaschen und getrocknet

e Synthese zu Cefuroxim

- > Durch Einführen einer Schutzgruppe am freien Amin in 7' Position wird 7-Glutaryl-ACA gewonnen
- > Anschließende Carbamatester-Bildung am 3'OH durch Umsetzung mit Chlorosulfonyl Isocyanat
- > Entfernen der Schutzgruppe an der 7' Position mit Hilfe enzymatischer Hydrolyse (Glutaryl Acylase) der Amidbindung
- > Gewinnung des finalen Produkts durch Acylierung des freienamins mit 2-Furanyl (sin-methoxyimino)Acetic Acid Chlorid

c Enzymatische Hydrolyse II: Cephalosporin-Acylase

- > Durch Verbrauch des gebildeten H_2O_2 entsteht durch irreversible oxidative Decarboxylierung Glutaryl-7-ACA
- > Durch eine immobilisierte Glutaryl-7-ACA-Acylase gelangt man zu 7-ACA

b Enzymatische Hydrolyse I: D-Aminosäure-Oxidase

- > Oxidative Desaminierung der Seitenkette des Cephalosporins C in wässriger Lösung durch das Enzym D-Aminosäureoxidase
- > Unter Verbrauch von O_2 entsteht α -Keteoadipyl-7 ACA, NH_3 und H_2O_2

a Herstellung von Cephalosporin C durch Fermentation

- > Hyphenpilz Acremonium (Schimmelpilz) wird mit Cornsteep-Lösung, Fischmehl, Fleischmehl, Saccharose, Glucose und Ammoniumacetat zusammengelegt
- > Mit Hilfe von anorganischen Salzen entsteht Cephalosporin C



Untersuchung von drei Produktionsszenarien für Cephalosporin-intermediates – Fokus auf Deutschland- und EU-Szenario

Produktion des Bedarfs für DE, EU und darüber hinaus: Drei verschiedene Szenarien

Fokus der Studie

100 t



Niedriges Szenario

Jährliche Produktionsmenge von 100 t, welche ungefähr der lokalen Nachfrage in Deutschland entspricht

500 t



Mittleres Szenario

Jährliche Produktionsmenge von 500 t, welche einen Großteil des europäischen Bedarfs abdecken könnte

1.000 t








Hohes Szenario

Jährliche Produktionsmenge von 1.000 t, welche aus produktions-technischen Gesichtspunkten als Mindestmenge zu wünschen wäre (Skaleneffizienz) – Signifikante Überschreitung lokal/Europa-weit nachgefragter Produktionsmenge

Deutscher Antibiotikakonsum mit ca. 20% des Konsums der Top-5 Märkte Europas – 500 t für europäische Marktabdeckung berechnet

Antibiotikakonsum der Top-5 Märkte Europas als Berechnungsgrundlage

Antibiotikakonsum der Top-5 Märkte Europas (alle Wirkstoffe)

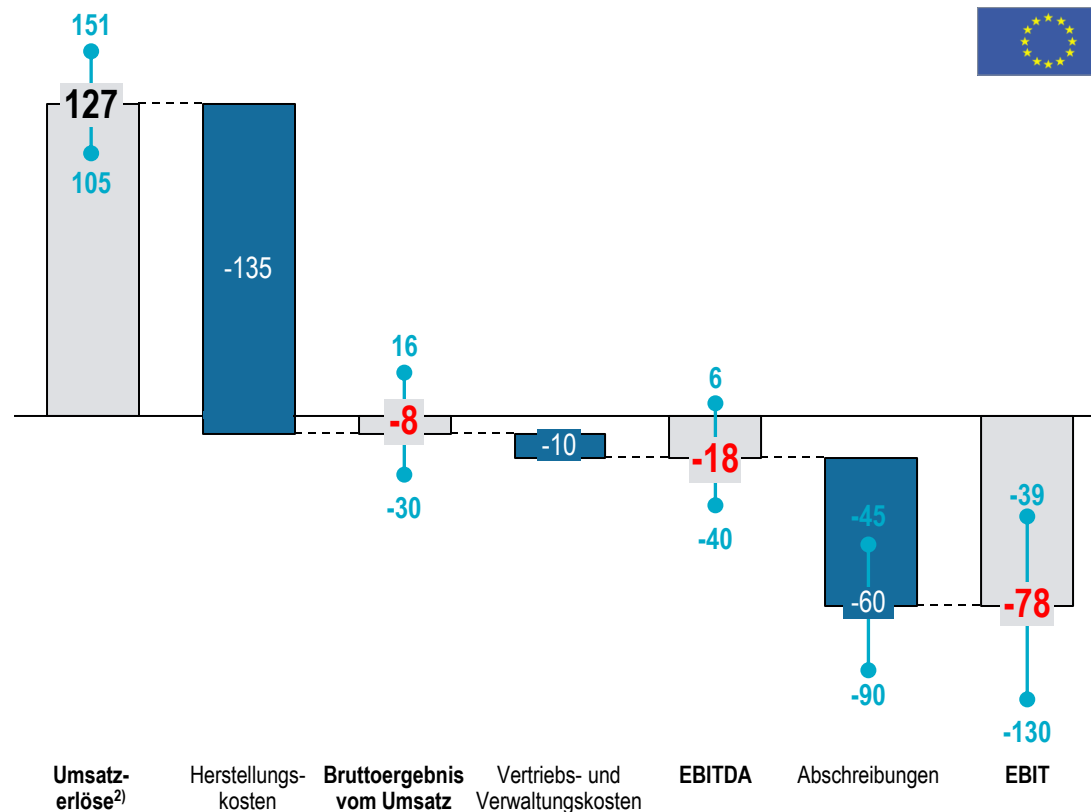
Staat	Absolut [DDD mio]	Prozentual [%]
	ca. 740	29%
	ca. 535	21%
	ca. 448	18%
	ca. 425	17%
	ca. 371	15%
Gesamt	ca. 2.519	100%

Berechnungsgrundlage

- > Der **deutsche Antibiotikakonsum** erreicht knapp **20% des Konsums der Top-5 Märkte Europas**
- > Der **deutsche Jahresverbrauch** von **Cephalosporinen** liegt bei ca. **100 t**
 - Entsprechend würde die **Wirkstoffproduktion** von **500 t Cephalosporinen** den **europäischen Markt** zu einem soliden Teil **abdecken**

Eine lokale Antibiotikawirkstoffproduktion für den europäischen Markt ist nicht wirtschaftlich – EBIT von ca. EUR -78 mio im Mittel

Approximierte GuV¹⁾ lokaler Wirkstoffproduktion für europäischen Markt, 500 t [EUR mio]



Kommentar

- > Eine Produktion von 500 t Cephalosporin-wirkstoffen in Deutschland für den europäischen Markt würde Umsätze von EUR 105 bis 151 mio erzielen
- > Geschäftsergebnis bereits nach Abzug der Herstellungskosten im Mittel negativ
 - Vertriebs- und Verwaltungskosten sowie Abschreibungen mit weiterem negativen Effekt auf das Geschäftsergebnis

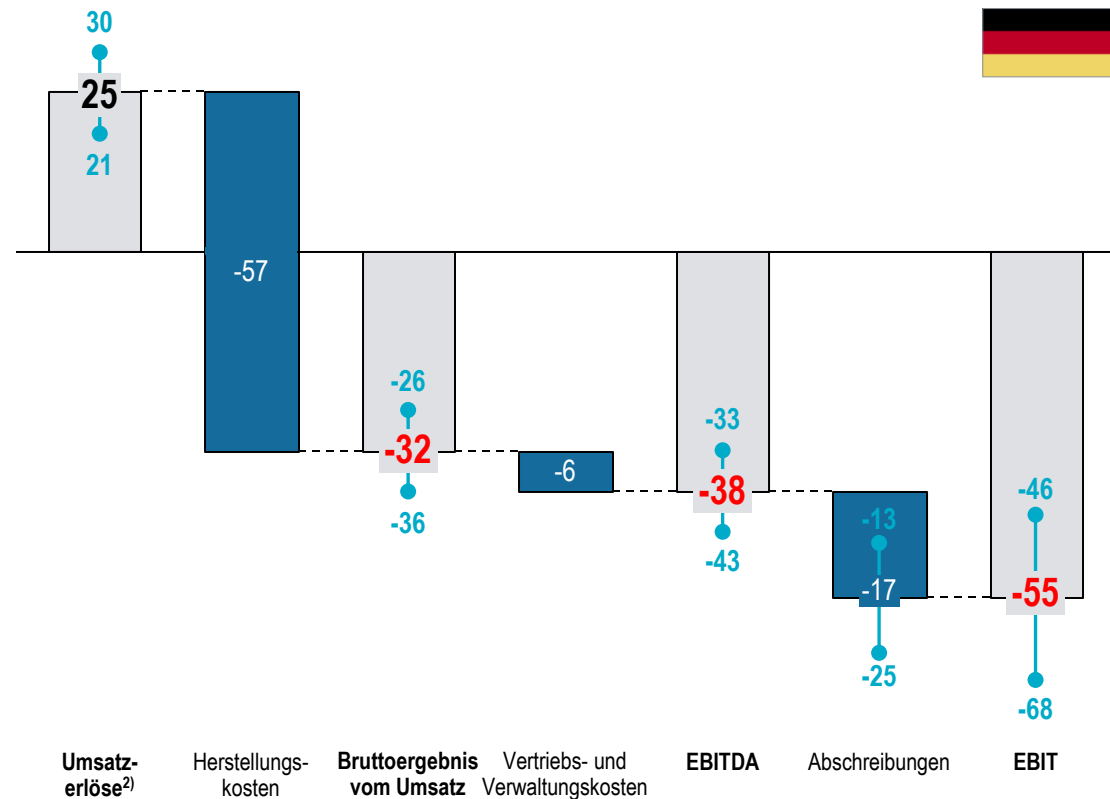
Spanne abhängig von modellierter Preis- und Kostenentwicklung für Wirkstoffe/Fertigprodukte sowie Abschreibungszeiträume

1) Gewinn- und Verlustrechnung

2) Umsatz zu Herstellerabgabepreis

Auch die Produktion für den deutschen Markt ist unwirtschaftlich – Absolute Unterdeckung geringer als bei Produktion für Europa

Approximierte GuV¹⁾ lokaler Wirkstoffproduktion für deutschen Markt, 100 t [EUR mio]



Kommentar

- > Die Produktion von 100 t Cephalosporinwirkstoffen zur Abdeckung des innerdeutschen Verbrauchs erzielt lediglich einen Umsatz von ca. EUR 21 bis 30 mio
- > Hohe Herstellungskosten (v.a. getrieben durch niedrige Skaleneffekte) sowie die Notwendigkeit hoher Investitionen mit einhergehenden Abschreibungen lassen das operative Geschäftsergebnis negativ werden

Negatives EBIT absolut gesehen geringer als bei Produktion für europäischen Markt

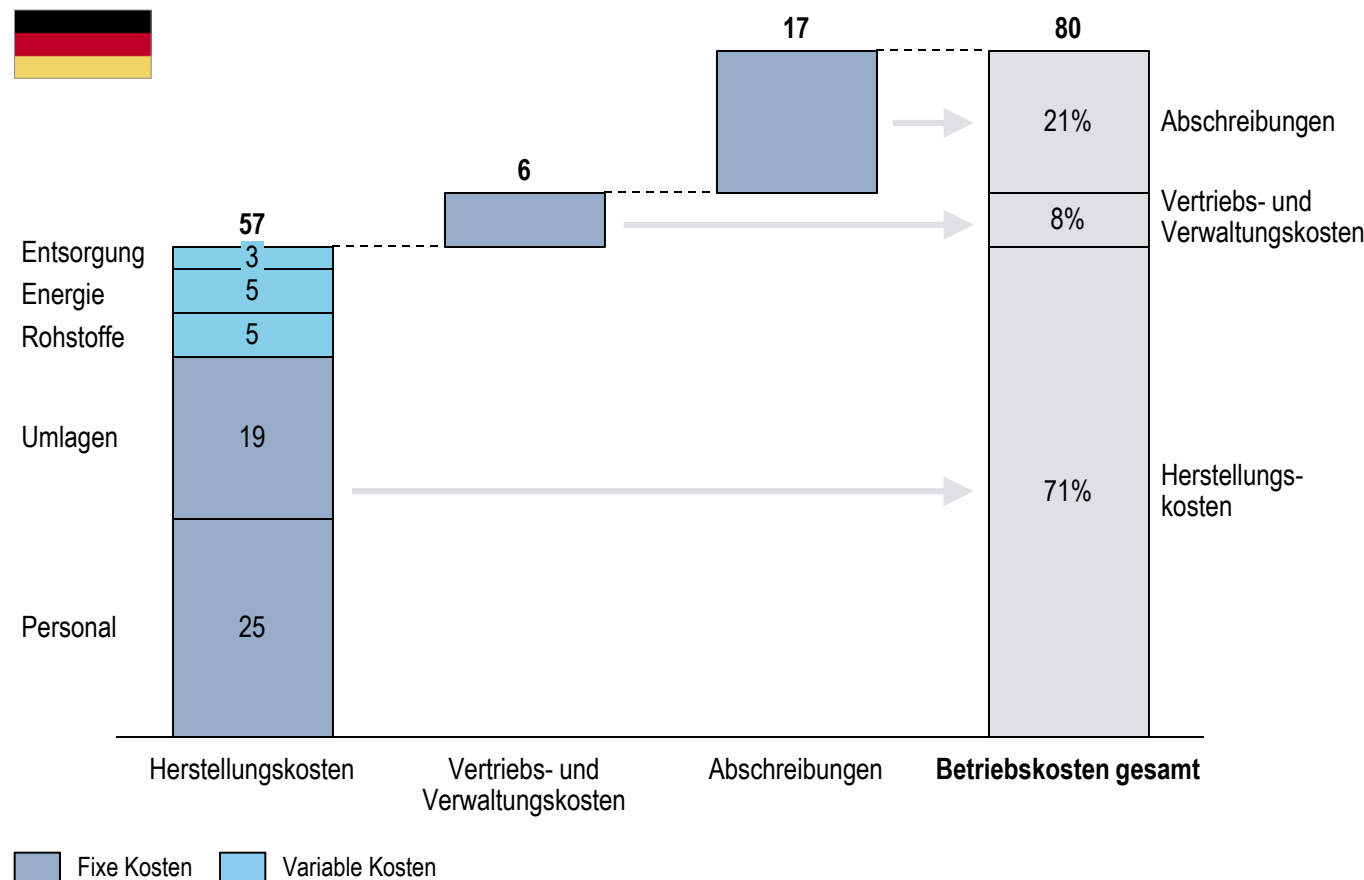
Spanne abhängig von modellierter Preis- und Kostenentwicklung für Wirkstoffe/Fertigprodukte sowie Abschreibungszeiträume

1) Gewinn- und Verlustrechnung

2) Umsatz zu Herstellerabgabepreis

Die Hauptgründe für die Unwirtschaftlichkeit einer Produktion in Deutschland/der EU sind hohe Betriebs- und Investitionskosten

Betriebskosten lokaler Wirkstoffproduktion für den deutschen Markt, 100 t [EUR mio]

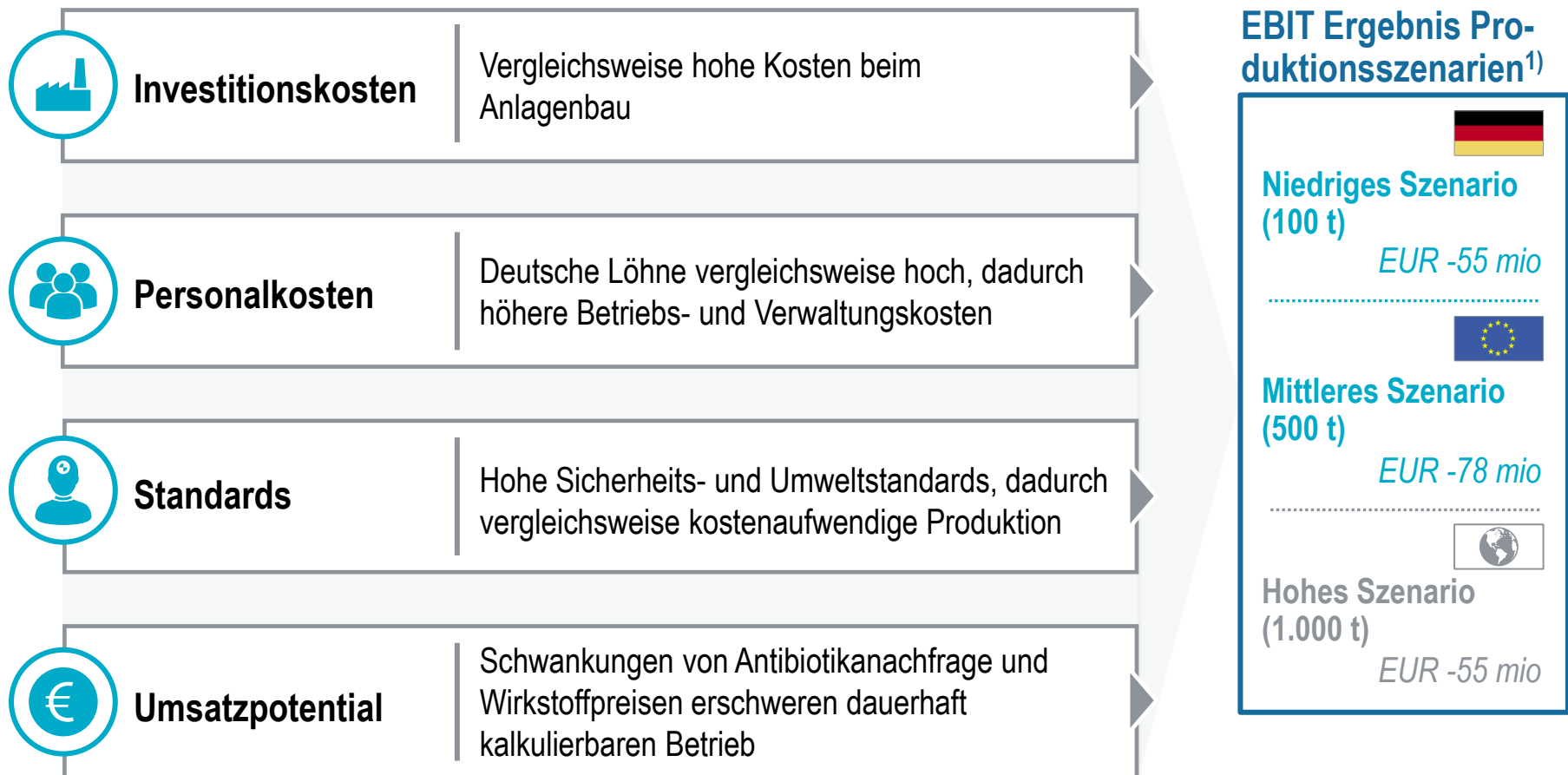


Warum sind die Kosten derart hoch?

- > Im Vergleich zur Konkurrenz in Asien sind die Herstellungskosten in Deutschland signifikant höher – Gründe sind
 - Geringe Skaleneffekte (Produktion nur für Deutschland)
 - Hohe Kosten für Personal und Umlagen (z.B. Qualitätskontrolle, Logistik, Produktionsverwaltung)
- > Selbst die Investitionen und damit die Abschreibungen sind in Deutschland deutlich höher als im asiatischen Raum – Höhere Personalkosten notwendig für den Anlagenbau

Die Produktion von Antibiotikawirkstoffen in Deutschland ist in allen drei Szenarien nicht wirtschaftlich

Gründe und Ergebnis der Unwirtschaftlichkeit einer lokalen Antibiotikaproduktion



1) Mittelwerte der Gewinn- und Verlustrechnung

Zum Ausgleich des negativen EBIT der Produktion für Deutschland müssten EUR 55 mio Mehrkosten vom System getragen werden

Theoretische Mehrkosten bei einer lokalen Wirkstoffproduktion für den deutschen Markt

Mehrkosten durch eine lokale Produktion
(am Beispiel von generischen Cephalosporinen)



Mehrkosten für das System

EUR 55 mio

Arzneimittelausgaben GKV 2017

EUR 22,0 mrd¹⁾

ca. 0,25%



Mehrkosten pro Tagesdosis

EUR 55 mio



120 mio



46 Cent

Mehrkosten für das System

Anzahl der Tagesdosen

- > Die **Mehrkosten** beziehen sich ausschließlich auf die **lokale Produktion von Cephalosporinen**, der zweithäufigst verordneten Gruppe aller Antibiotika (nach den Aminopenicillinen)
- > Der Anteil an den Gesamtausgaben der GKV für Arzneimittel anfallend auf die pharmazeutische Industrie (inkl. Rohstoffen) beträgt rund EUR 22,0 mrd in 2017 in Deutschland
- > Die **gesamten Mehrkosten von EUR 55 mio** entsprechen
 - Mehrkosten pro **Tagesdosis** von **46 Cent**
 - **ca. 0,25% der Arzneimittel-**
ausgaben¹⁾ von 2017

1) Anteil der GKV-Arzneimittelausgaben anfallend auf die pharmazeutische Industrie (inkl. Rohstoffen) zu Herstellerabgabepreisen – PKV nicht inkludiert

Um durch lokale Produktion die Versorgungssicherheit in Deutschland zu erhöhen, ist staatliche Unterstützung notwendig

Verschiedene Möglichkeiten staatlicher Unterstützung

Um die lokale Produktion von Cephalosporinwirkstoffen für private Unternehmen attraktiv zu machen, müssen Wege gefunden werden, das negative EBIT durch staatliche Eingriffe auszugleichen



Möglichkeiten staatlicher Unterstützung

1

Staatliche Eingriffe in die Marktmechanismen zur Erhöhung der Endpreise

- > Umsatzsteigerung durch Sicherstellung höherer Endpreise im Markt, z.B. durch Eingriffe am Tendermarkt

2

Staatliche Bezuschussung der Herstellungskosten

- > Staatliche Bezuschussung der Fix- und/oder variablen Kosten, welche bei der Herstellung auftreten, z.B. Personal- und Energiekosten

2

Investitionsbezuschussung zur Reduktion der Abschreibungshöhe

- > Staatliche Bezuschussung des Produktionsanlagenbaus und/oder eines Grundstückserwerbs

3

Staatliche Vergütung von Kapazitätsbereitstellung zur Minimierung eines Versorgungsrisikos

- > Staatliche Zahlungen für die Vorhaltung der Herstellungskapazität von generischen Antibiotika zur Gewährleistung der Versorgungssicherheit


Vor- und Nachteile der verschiedenen staatlichen Unterstützungsoptionen


Bewertung staatlicher Unterstützungsoptionen

1 Preisregulierung durch Eingriffe am Tendermarkt

Bedingte Erhöhung der Endpreise im Tendermarkt für Produkte auf Basis von lokal produzierten Wirkstoffen


Bewertung


 Keine direkten Mehrkosten oder Verwaltungsaufwände für den Staat

 Erhöhung der Kosten für Gesundheitssystem durch erhöhte Endpreise für in der EU produzierte Wirkstoffe

2 Preisregulierung durch Subventionen des Betriebs oder der Investition

Staatliche Bezuschussung, um die Gesamtkosten der lokalen Produktion wettbewerbsfähig zu gestalten


 Möglichkeit der gezielten Förderung einzelner Standorte zur Steigerung der volkswirtschaftlichen Gesamterträge


 Sicherheit für Betreiber ggü. regulatorischen/politischen Schwankungen


 Relativ höhere Einmalkosten für den Staat zur Initialisierung des Betriebs

3 Absicherung des Versorgungsrisikos

Staatliche Zahlungen für die Bereitstellung von Produktionskapazitäten als Risikoabsicherung gegen Versorgungsengpässe

 Staat gewährleistet Versorgungssicherheit durch Bereithaltung von Produktionskapazitäten – Direkte Gegenleistung für staatliche Zahlungen

 Ausschreibung der Risikoabsicherung führt zu möglichst hoher Effizienz, d.h. möglichst niedrigen Kosten für das System

 Notwendige Bereitschaft zur Verantwortungs- und Kostenübernahme durch ein Ressort (z.B. BMF, BMG, BMWi)

Umsetzungsmöglichkeiten für alle Modelle – Stakeholder-übergreifende Abstimmung notwendig

Umsetzungsmöglichkeiten staatlicher Unterstützungsoptionen

1 Preisregulierung durch Eingriffe am Tendermarkt

Bedingte Erhöhung der Endpreise im Tendermarkt für Produkte auf Basis von lokal produzierten Wirkstoffen

Umsetzungsmöglichkeiten

- > **Änderung** bestehender nationaler **Gesetzgebung** für die **Ausschreibungen von Antibiotika** hinsichtlich **"Made in EU"**
- > Gesetzlich verankerte Bevorzugung von europäischer Produktion als Beitrag zur Steigerung der Versorgungssicherheit in Deutschland

2 Preisregulierung durch Subventionen des Betriebs oder der Investition

Staatliche Bezuschussung, um die Gesamtkosten der lokalen Produktion wettbewerbsfähig zu gestalten

- > **Investitionsbezuschussung** eines lokalen Standorts für die Wirkstoffproduktion mit dem Effekt der Reduktion der Abschreibungen zur EBIT-Verbesserung
- > Beitrag zur Versorgungssicherheit und Förderung der volkswirtschaftlichen Gesamterträge

3 Absicherung des Versorgungsrisikos


Staatliche Zahlungen für die Bereitstellung von Produktionskapazitäten als Risikoabsicherung gegen Versorgungsengpässe

- > (EU-weite) **Ausschreibung** für die **Vorhaltung von Produktionskapazitäten zur Risikoabsicherung**
- > Vertraglich gesicherte Versorgungsfähigkeit für längere Perioden durch Gewährung einer regelmäßigen Grundgebühr

Alle Betreibermodelle sind grundsätzlich **umsetzbar und kombinierbar** – **Gemeinschaftliche Initiative und Diskussion** zwischen den betroffenen **Stakeholdergruppen** (u.a. Industrie, stationäre/ambulante Versorger, Politik, Krankenkassen) auf nationaler bzw. europäischer Ebene notwendig zur **Einigung über ein Lösungsmodell**

Wiederaufbau von Produktionskapazitäten mithilfe staatlicher Unterstützung zur nachhaltigen Reduktion der Abhängigkeit anzustreben

Vorschlag und erwartete Effekte für Versorgungssicherheit bei (generischen) Antibiotika

Situation	Vorschlag	Erwarteter Effekt
 <ul style="list-style-type: none"> > Abhängigkeit von ausländischen Antibiotika-Intermediate- und Wirkstoff-Produzenten, vorwiegend aus Non-EU Low-Cost-Ländern, z.B. China > Produktion in Deutschland aufgrund Konkurrenz aus Low-Cost-Ländern bei gegebenem niedrigen Preisniveau nicht wirtschaftlich > Rückführung lokaler Produktion erstrebenswert für die langfristige Versorgungssicherheit 	 <ul style="list-style-type: none"> > Weitere Eruierung und Umsetzung konkreter Möglichkeiten zur Förderung lokaler Antibiotikawirkstoffproduktion gemeinschaftlich, z.B. im Rahmen des Pharmadialogs > Drei mögliche Betreibermodelle/ Komponenten <ul style="list-style-type: none"> – Preisregulierung durch Eingriffe am Tendermarkt – Preisregulierung durch Subventionen der Betriebs- und Investitionskosten – Absicherung des Versorgungsrisikos durch staatliche Zahlungen 	 <ul style="list-style-type: none"> > Sicherstellung der kontinuierlichen Versorgung durch lebenswichtige Antibiotika in Deutschland > Attraktivität für Betreiber zu lokaler Wirkstoffproduktion durch dauerhafte Sicherung ihrer Geschäftsgrundlage > Stärkung/Erhaltung des Know-Hows in der lokalen Antibiotikaproduktion sowie des hiesigen Produktionsstandorts (Wertschöpfung/Arbeitsplätze) > Reduktion der (politischen) Abhängigkeit von Produktion in Non-EU-Ländern

Roland
Berger



Position paper on best procurement practices

Summary

Across Europe, the current procurement practices have generated a number of undesired effects, namely reduced competition and consequently medicine shortages, which in the long term also lead to originator monopolies and unwanted price increases. Developing optimal procurement practices is an opportunity to create healthy competition and guarantee patient access to medicines, by increasing the number of manufacturers in the market and thereby reducing the risk of medicine shortages.

Medicines for Europe believes that the procurement process design can be optimised by:

- Adjusting the number of procurement winners according to the market, product and country characteristics
- Preventing disproportionate penalties to encourage a sustainable supply of medicines to patients
- Guaranteeing that the procurement processes open after the entry of the first multisource medicine to ensure a competitive and predictable supply to patients
- Using selection criteria that consider other factors than price and ensure fair competition
- Using extended lead times that guarantee a predictable supply of medicines to patients

Procurement specialists should take a holistic view when designing procurement processes to safeguard that competition is guaranteed in the long run. A well-functioning system would ultimately lead to a competitive market environment that benefits patients, healthcare professionals and payers, in both the short and long-term.

The objective of this position paper is to recommend the best procurement practices, where procurement is already in place, in order to address the increased challenges for sustainable healthcare systems.

Background on procurement/tendering

The sustainability of healthcare systems is a challenge for many European governments. Multiple factors, such as a growing and ageing population, increased disease burden, the introduction and increased cost of new innovative medicines and cuts to pharmaceutical expenditure have intensely affected access to medicines in Europe^{1,2,3}. In particular, the generic, biosimilar and value added medicines industry continues to be heavily

¹ The Parliament Magazine. 2015. Available at: <https://www.theparliamentmagazine.eu/articles/opinion/many-patients-europe-have-limited-or-no-access-treatment>

² Eurostat Population Statistics

³ OECD, Fiscal Sustainability of Health Systems: Bridging Health and Finance Perspectives. 2015.

affected by cost-containment measures that do not take into account the merits of these medicines in expanding the availability of pharmaceutical treatments to a larger number of patients and in reducing overall public spending. In particular, some authorities are applying cost-containment measures such as procurement/tendering on generic and biosimilar medicines, which in the long-term can prevent competition and will not provide the expected additional efficiency for healthcare budgets that a timely access to these medicines would bring.

Experience has shown that these practices can result in the continuation of monopolies that will have little positive impact on the pharmaceutical budgets and increase the risk of medicine shortages. In some countries, the number of multisource competitors in some disease areas has already decreased to a critical level for sufficient market competition, due to unsustainable market conditions. For instance in Germany, a study that regularly analyses generic medicines competition has recently demonstrated that the number of generic medicines manufacturers has halved from the period of 2006-2009 to 2013-2014, mainly due to the tendering system in place⁴. In Italy, the rate of participation from generic medicines manufacturers at hospital level has also progressively decreased, mainly due to the current tendering practices⁵. This has also been acknowledged by WHO⁶. As shown in Figure 1, the application of short-term cost-containment measures such as centralised procurement/tendering by authorities, have been demonstrated to reduce the number of suppliers for essential life-saving medicines in both the hospital and ambulatory sectors, ultimately putting patients' health at risk by increasing the potential for shortages^{7,8,9, 10,11,12,13,14,15,16,17,18,19,20,21,22,23,24}.

⁴ IGES analysis on generic medicines competition. 2017. Available at: <http://www.progenerika.de/presse/zahl-des-monats-juni-2017/>

⁵ Nomisma study. The generic medicines system in Italy. Hospital spending, tenders impact and sustainability. 2016. Available at: <http://www.assogenerici.it/it/download/rapporto-nomisma-2016-assogenerici.pdf>

⁶ WHO report. Challenges and opportunities in improving access to medicines through efficient public procurement in the WHO European Region. 2016.

⁷ OECD, Fiscal Sustainability of Health Systems: Bridging Health and Finance Perspectives. 2015.

⁸ SFK (Foundation for Pharmaceutical Statistics). Pharmaceutisch Weekblad. 2014.

⁹ QuintilesIMS Health. An International Comparison of Best Practice Approaches to Drug Shortages. 2015.

¹⁰ Alevizakos M, Detsis M, Grigoras CA, et al. The Impact of Shortages on Medication Prices: Implications for Shortage Prevention. *Drugs*. 2016;76(16):1551-8.

¹¹ Barlas S. FDA strategies to prevent and respond to drug shortages: finding a better way to predict and prevent company closures. *P & T: a peer-reviewed journal for formulary management*. 2013;38(5):261-3;

¹² Birgli. An Evaluation of Medicines Shortages in Europe with a more in-depth review of these in France, Greece, Poland, Spain, and the United Kingdom. Zug: Birgli, 2013. Available from: <http://static.correofarmaceutico.com/docs/2013/10/21/evaluation.pdf>.

¹³ Bogaert P, Prokop A, Bochenek T. Prevention and Management of Medicine Shortages in Belgium, France and from The Perspective of the European Union. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2014;17(7):A412.

¹⁴ De Weerd E, Simoens S, Casteels M, et al. Toward a European definition for a drug shortage: a qualitative study. *Frontiers in pharmacology*. 2015;6:253.

¹⁵ Holtorf AP, Rinde H, Maniadakis N. Drug shortages in Europe and the USA: The underlying reasons and consequences. ISPOR 15th Annual European Congress; 10th February 2017; Berlin. Germany: Presented at the ISPOR 15th Annual European Congress (Berlin, 5 November 2012); 2012

¹⁶ Kaposy C. Drugs, money, and power: the Canadian drug shortage. *Journal of bioethical inquiry*. 2014;11(1):85-9

¹⁷ Kweder SL, Dill S. Drug shortages: the cycle of quantity and quality. *Clinical pharmacology and therapeutics*. 2013;93(3):245-51.

¹⁸ Markowski ME. Drug Shortages: The Problem of Inadequate Profits. Cambridge, MA: Harvard Law School, 2012. Available from: <https://dash.harvard.edu/handle/1/11940215>.

¹⁹ McKee AE, Bloch JR, Bratic A. Drug shortages and the burden of access to care: a critical issue affecting patients with cancer. *Clinical journal of oncology nursing*. 2013;17(5):490-5.

²⁰ Pauwels K, Huys I, Casteels M, et al. Drug shortages in European countries: a trade-off between market attractiveness and cost containment? *BMC health services research*. 2014;14:438.

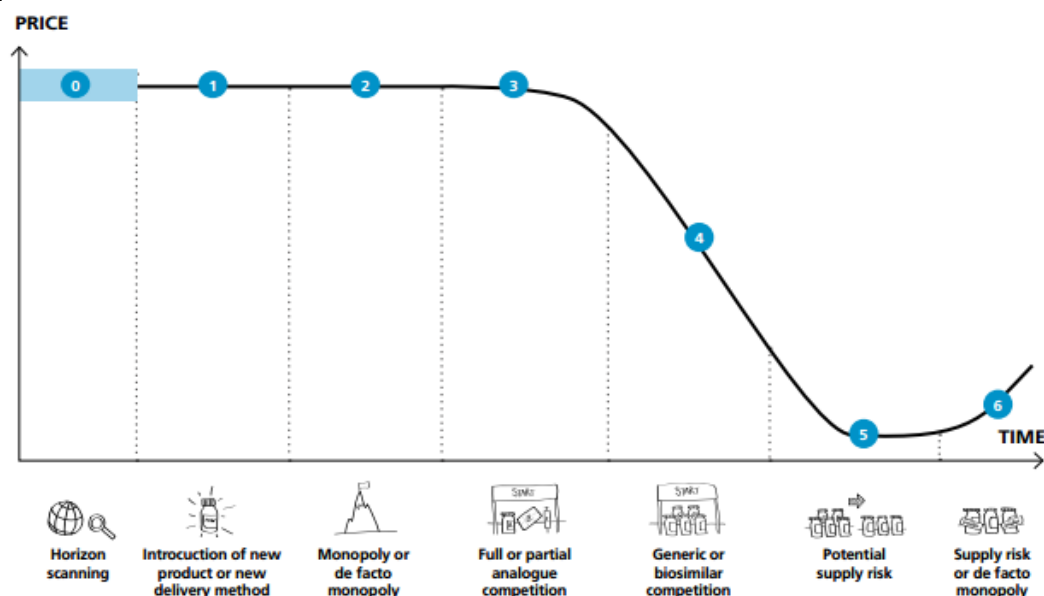
²¹ Pauwels K, Simoens S, Casteels M, et al. Insights into European drug shortages: a survey of hospital pharmacists. *PloS one*. 2015;10(3):e0119322.

²² Reed BN, Fox ER, Konig M, et al. The impact of drug shortages on patients with cardiovascular disease: causes, consequences, and a call to action. *American heart journal*. 2016;175:130-41.

²³ Woodcock J, Wosinska M. Economic and technological drivers of generic sterile injectable drug shortages. *Clinical pharmacology and therapeutics*. 2013;93(2):170-6.

²⁴ Yurukoglu AL, E. Ridley D.B. The Role of Government Reimbursement in Drug Shortages. US: Stanford University, 2016. Available from: <https://web.stanford.edu/~ayurukog/shortages.pdf>.

Figure 1. Pharmaceutical lifecycle stages and generalised price development for a specific disease area or condition.



Source: WHO report 2016⁶.

To avoid this risk of market consolidation, which might endanger patients' health in case of medicines shortages, it is necessary to achieve a healthy market which considers long term objectives for achieving sustainability. Therefore, governments must review the long-term consequences of applying procurement/tendering mechanisms to this sector and, whenever this mechanisms are in place, develop optimal procurement practices that guarantee competition and patient access to generic, biosimilar and value added medicines.

The objective of this position paper is to recommend the best procurement practices, where procurement is already in place, in order to address the increased challenges for sustainable healthcare systems. Designing a well-performing procurement mechanism is crucial to achieve a sustainable and competitive market for medicines and should be a strategic priority for all stakeholders including healthcare policymakers, payers and providers, as well as medicines manufacturers and distributors.

Best procurement practices recommended by Medicines for Europe

Adjust the number of procurement winners according to the market, product and country characteristics

The market environment for medicines can differ considerably between different settings. To guarantee sustainable competition, an analysis of the market should be made and the number of procurement winning

manufacturers should be selected according to the different characteristics of the market. **Multi-winner tenders should be preferential²⁵** to guarantee multiple manufacturers in the market and prevent medicine shortages.

For instance, for the market of pediatric anesthetics, with a very limited number of suppliers, the risk of medicine shortages is very high when a sole winning manufacturer has a supply issue. The remaining manufacturers might not always be able to remedy a potential medicine shortage in a timely manner due to the lack of manufacturing capacity to address unexpected demand. Additionally, the remaining manufacturers might have decided to withdraw the production of the concerned medicines due to not being awarded in the procurement process. This might lead to a delay in patient access to medicines, as re-starting a manufacturing process can be lengthy. If there are only a few players on the market for a given medicine, awarding a single-winner tender might endanger the supply-reliability as there will be limited opportunities to source the product with another supplier.

The objective of procurement models is to avoid having a limited number of suppliers for all medicines and to consider a number of winners according to the market, product and country characteristics (preferentially multi-winner tenders²⁵). This might be achieved, for instance, by dividing the market into lots for the different winners (e.g. first winner gets 50% of market, second winner 30%, etc.).

Prevent disproportionate penalties to encourage competition and a sustainable supply of medicines to patients

Penalties should be proportionate to the contract value to ensure competition in the procurement process

In most procurement contracts, there are clauses that stipulate penalties in case the manufacturer is unable to supply the awarded medicine. In some cases, the penalty for one month of inability to supply might be as high as the value of the entire business per annum. It is clear that this practice puts the manufacturers at considerable financial risk and thereby acts as a disincentive to compete in the procurement process. **Therefore, the value of penalties should be proportionate to the contract value agreed by the manufacturers in order to encourage participation in the tenders and ensure a sustainable supply.**

Before the application of penalties, there should be some flexibility to find solutions for the interruption in supply.

The inability of a manufacturer to supply may sometimes be due to reasons beyond their control (e.g. manufacturing problems with the supplier of the active pharmaceutical ingredient, regulatory related problems, hurricanes, unplanned political issues, etc.). It is also known that some medicine product characteristics might make them more vulnerable to supply disruptions than others (e.g. injectable medicines vs. standard oral tablets). Therefore, **penalties should be adjusted according to the cause of the inability to supply and the medicine product characteristics. Classifying circumstances that are beyond the control of the manufacturer and medicines that are more susceptible to supply disruptions than others in the procurement contract would**

²⁵ Except Belgium where the quantity of medicines tendered is low and consequently the market volume is too small to create a mature and balanced market.

better reflect the complex process of manufacturing and significantly relieve the burden of penalties. Particularly, in the case where a supplier is unable to supply the medicine due to external reasons, there should be an exit clause for the manufacturer and/or a **flexible framework that allows the manufacturer to find a solution for the supply interruption** (e.g. buying the medicine from another supplier) and avoid medicine shortages.

Accurate estimates of volume to be provided should guarantee a continuous supply

The operational business of manufacturers is complex: raw material availability, excipient availability, manufacturing time, manufacturing capacity, packaging time, availability of human resources, etc. These are amongst the many factors that have to be in place before a medicine is manufactured. Therefore, it is essential that the procurement awarding bodies provide accurate estimates of the volumes to be supplied (e.g. minimum and maximum volume caps), as manufacturers cannot increase their manufacturing capacity in a short period of time. In some cases, an unexpected peak in demand (e.g. to avert stock-out caused by the inability of another company to supply) leads to the manufacturer being unable to supply the requested volume. Therefore, **manufacturers should only be liable for volumes that were specified in the procurement contract and no penalty should be imposed in case of inability to supply unexpected volumes.**

Guarantee that the opening of a procurement process ensures a competitive and predictable supply

In some countries, all the procurement processes start in the same period of the year (e.g. January-March). In this case, a manufacturer that wins multiple procurement processes for various medicines in the same period of time can have its ability to supply these medicines compromised. Therefore, it would be recommended that **the procurement processes should be spread throughout the year to accommodate manufacturing capacity to address demand and avoid medicine shortages. Furthermore, procurement/administrative processes should open when the medicines are about to lose their patent protection/loss of exclusivity, so that competition can start immediately after the patent/exclusivity term i.e. a procurement process should not run longer than the patent term of the originator or there should be an option to invite the respective multisource manufacturers to participate in a procurement process. Finally, the procurement process/administrative procedures should be predictable, harmonised and transparent to ensure participation of multiple manufacturers and reduce the risk of medicine shortages.**

Use of selection criteria that consider other factors than price and ensure fair competition

In many procurement processes, the lowest price is the only or major factor determining the winner. Solely focusing on price does not take into consideration the rising costs associated with manufacturing these medicines (e.g. regulatory costs). In the long-run, manufacturers will have to be more selective when choosing which procurement processes they would like to participate in, leading to a concentration of suppliers (less

manufacturers' participation). Through less competition the supply of medicines is threatened, especially if there are medicines with only one player left alone in the market.

A further key issue that arises from focusing only on the lowest price is that such a system fails to take into account value components which may be beneficial for patients and the wider healthcare system. This means that the best value for money may not be achieved. The recent Public Procurement Directive (PPD), Directive 2014/24/EU, adopted by the Council of the EU on 11 February 2014, highlights that contracting authorities should base their decision on the basis of the most economically advantageous tender (MEAT). The MEAT shall use a cost-effectiveness approach taking into account criteria such as qualitative, environmental and/or social aspects (patients, healthcare professionals, etc.). This shows that focusing on the reduction of price levels does not always mean the best value for money. The Directive provides examples of criteria to possibly be considered: quality, organisation, qualification and expertise; after-sales service and technical assistance, or delivery conditions. It is important to highlight that **these criteria should not put in place any access barriers for generic, biosimilar and value added medicines.**

Procurement criteria should be designed to ensure a secure and continuous supply of medicines to patients. For this reason, the focus should not only be on the lowest price of the medicine, but a holistic view should be adopted and additional relevant criteria considered that do not undermine access to generic, biosimilar and value added medicines. These criteria should ensure the best value for money for the benefit of patients and healthcare systems.

- **Procurement criteria should consider product-specific characteristics**

Criteria within the MEAT could also consider product-specific characteristics. This is especially important for value added medicines, medicines based on known molecules that address healthcare needs and deliver relevant improvements for patients, healthcare professionals and/or payers²⁶. An example of a value added medicine are pre-filled syringes (PFS), which are especially beneficial for healthcare professionals (HCPs) in a hospital setting. Medicines delivered through PFS are convenient to use for HCPs as they require a reduction of re-constitution steps when compared to glass or COC²⁷ vials, leading to decreased medication errors and increased safety for patients²⁸. On top of this, these products are not only safer to use for HCPs as they decrease the risk of needle-stick injuries, but also more efficient for payers as they reduce wastage of the medicine²⁹. The stakeholder benefits and long-term efficiency gains generated by value added medicines are one of the multiple criteria that should be considered by hospital systems when procuring medicines.

- **Procurement criteria that consider other factors than the lowest price should ensure fair competition**

While procurement systems should expand their design to focus on other criteria than the lowest price, this should be performed without raising barriers for competition. For example, if a supplier has just started manufacturing a product, it will not have a 'proven track record of supply' for the specific product, which may be

²⁶ Please see more info on value added medicines [here](#).

²⁷ Cyclic Olefin Copolymer

²⁸ <http://www.pharmtech.com/node/222093?rel=canonical>

²⁹ <http://www.bioprocessonline.com/doc/prefilled-syringes-the-next-big-thing-0001>

included in the procurement criteria. In such cases, context-specific exceptions should be made to allow fair competition and guarantee supply of medicines to patients. Furthermore, allowing more flexibility in the acceptance criteria for specific characteristics such as different strengths³⁰, ensures multiple opportunities and more suppliers interested in the market.

Use of extended lead times that guarantee a predictable supply of medicines to patients

The manufacturing lead time, i.e. the time from the award of the procurement process to the start of the contract when the manufacturer is required to supply, is frequently too short to enable the production of the requested volume of medicine within the estimated time. This inability to supply the medicines in time consequently results in supply disruption that affects both healthcare professionals and patients.

Aiming to comply with the current short lead times in case of award, manufacturers often hold stock in anticipation. However, if the procurement application fails, the manufacturer is left with an excess of stock which generally has a shelf life of only 10-12 months. As a consequence, the manufacturer has to destroy his stock, which is very costly, or faces increased pressure to win the next procurement process, which might disrupt competition and lead to market dumping at unsustainable low prices (sale price or sometimes even below the level of the cost of goods).

Lead times can vary across countries. On average, the minimum lead time needed for a manufacturer to supply a generic medicine is around six months, whereas this might be even longer for biosimilar, complex generic or value added medicines due to the more sophisticated manufacturing processes. **Therefore, lead times should be adapted to the product characteristics (e.g. complexity in manufacturing, regulatory requirements and additional efforts due to serialization) as well as the requested volumes to be supplied, to guarantee a predictable supply. Furthermore, it is important to highlight that the process of extending lead times is not onerous for authorities, and this measure can significantly reduce waste and improve efficiency.**

Conclusion

Cost-containment measures such as procurement/tendering have been applied to pharmaceuticals, in particular to generic and biosimilar medicines. Experience has shown that these practices can result in the continuation of monopolies that will have little positive impact on the pharmaceutical budgets and increase the risk of medicine shortages. Most of these processes focus mainly on the lowest price and do not consider other criteria (that would not create access barriers to generic, biosimilar and value added medicines). On top of this, most procurement processes do not take into account the unique characteristics of pharmaceutical manufacturing operations (e.g. insufficient lead times, disproportionate penalties, inaccurate volumes, etc.), do not promote an adequate number of participating suppliers in tenders and do not guarantee competition as soon as patent/exclusivity ends. The combination of these factors is preventing competition by threatening the long-

³⁰ As long as the concerned medicines deliver the same outcomes.

term sustainability of the pharmaceutical industry as well as the supply-reliability of medicines which ultimately harm patient health.

Procurement specialists should take a holistic view when designing procurement processes to ensure that competition is guaranteed in the long run. It is therefore crucial that procurement specialists and industry have a dialogue to better understand each other's needs and requirements. A well-functioning system would ultimately lead to a competitive market environment that benefits patients, healthcare professionals and payers, both in the short- and long-term.

Nichtverfügbarkeit von rabattierten Arzneimitteln

Ariane Höer, Lukas Maag, IGES Institut

Ergebnispräsentation
Berlin, 19. November 2019

1. Hintergrund und methodisches Vorgehen (inkl. Überprüfung des ATC-Konzepts)
2. Ergebnisse
3. Übersichtsdarstellung für ausgewählte ATC7-Steller
4. Zusammenfassung

1. Hintergrund und methodisches Vorgehen

- Arzneimittelrabatte, denen individuelle Verträge zwischen einem Hersteller und einer gesetzlichen Krankenkasse zugrunde liegen, beeinflussen seit 2007 maßgeblich das Marktgeschehen, insbesondere bei generischen Arzneimitteln. Die Verträge werden durch § 130a Abs. 8 bzw. § 120c SGB V ermöglicht.
- Im Jahr 2017 betrug der Umsatz von Arzneimitteln, die entsprechend dieser Verträge rabattiert waren, 16,01 Mrd. Euro bzw. 40,4 % des Umsatzes für ambulant abgegebene Arzneimittel. Bezogen auf den Verbrauch von Arzneimitteln (gemessen in DDD), handelte es sich 2017 bei 63,2 % um rabattierte Arzneimittel*.
- Die Individualrabatte beliefen sich laut KJ1-Statistik im Jahr 2017 auf insgesamt 4,03 Mrd. Euro und wachsen in den letzten Jahren stetig.

Quelle: Häussler B, Hörer A (2018) Arzneimittel-Atlas 2018. Medizinisch Wissenschaftliche Verlagsgesellschaft, Berlin

- Beobachtungszeitraum der Studie ist das Jahr 2017
- Datengrundlage bildet die Nationale Versorgungsinformation des Marktforschungsinstitutes INSIGHT Health
- Daten aus Apothekenrechenzentren zur Abrechnung der zu Lasten der GKV verordneten Fertigarzneimittel
- In der NVI ist jedes Fertigarzneimittel durch eine Pharmazentralnummer (PZN) definiert. Je PZN standen die folgenden Angaben zur Verfügung:
 - Monat der Verordnung
 - Kostenträger
 - Verordnungsmenge je PZN
 - Verordnungen unter Rabatt
 - Verordnungen mit NV-Kennzeichen 1 und 3

- Wenn Rabattverträge vorhanden sind, ist nach Möglichkeit ein rabattiertes Arzneimittel abzugeben.
- Ist ein verordnetes, rabattiertes Arzneimittel nicht verfügbar, kann die Apotheke ein anderes abgeben, dass den Aut-idem-Kriterien entspricht.
- Mit dem NV-Kennzeichen 1 wird die PZN gekennzeichnet, die anstelle der nicht verfügbaren, rabattierten PZN abgegeben wurde.
- Es ist daher nicht bekannt, welche PZN nicht verfügbar war, sondern nur, dass eine bestimmte PZN für eine andere abgegeben wurde.

Arbeitshypothese der Studie:

Der Anteil von NV-Kennzeichen ist höher, wenn die Kasse für einen Wirkstoff nur bei einem einzigen Hersteller einen Rabattvertrag abgeschlossen hat.

- Ursprünglich war geplant, den Anteil von NV-Kennzeichen auf Ebene von Aut-Idem-Gruppen durchzuführen:
 - Doch nicht einmal die Hälfte aller PZN kann einer Aut-idem-Gruppe zugeordnet werden
 - Die Mehrzahl von NV-gekennzeichneten Verordnungen betraf PZN, die keiner Aut-idem-Gruppe zugeordnet sind.
- Ist ein rabattiertes AM nicht verfügbar, muss der Austausch „Aut-idem-konform“ erfolgen, aber nicht innerhalb einer Aut-idem-Gruppe
- Daher wurden der NV-Anteil auf Wirkstoffebene (ATC-Kode) bestimmt
- Hintergrund für diese Entscheidung ist die Annahme, dass Kassen Rabattverträge nicht für bestimmte PZN oder Aut-idem-Gruppen, sondern für bestimmte Wirkstoffe abschließen.
 - Diese Annahme wird in der Studie methodisch belegt → Prüfung des ATC-Konzepts

1.1 Überprüfung des ATC-Konzepts

- Rabattverträge zu unterschiedlichen Wirkstärken, Darreichungsformen und Packungsgrößen eines Wirkstoffs mit jeweils unterschiedlichen Herstellern → ATC-Konzept wäre nicht valide
- Für die einzelnen Kassen wurde daher je Kasse, Hersteller und rabattierten Wirkstoff ermittelt, wie hoch der nicht rabattierte Anteil des Wirkstoffs an den Verordnungen ist.
- Hypothese: Je Kasse, Hersteller und rabattierten Wirkstoff ist der Anteil nicht rabattierter Verordnungen bei den meisten Wirkstoffen zu vernachlässigen
- Detaillierte Betrachtung am Beispiel BARMER
- Aggregierte Ergebnisse werden für 10 Kassen dargestellt
- Auswahlkriterium der Kassen:
 - Jede Kassenart (AOK, BKK, EKK, IKK und LBS) wird abgebildet
 - Es wurden jeweils die zwei Kassen mit der größten Verordnungsmenge 2017 ausgewählt
 - Da die LBS nur aus einer Kasse besteht wurde noch die DAK (drittgrößte Kasse gemessen an den Verordnungen) berücksichtigt
 - Die 10 Kassen umfassen 55% der 2017 abgerechneten Verordnungen (insgesamt 113 Kassen)

Rabattierte PZN mit Basics, Betapharm und ratiopharm

- 7156314
- 7156320
- 7156337
- 7156343
- 7156372
- 7156389
- 7280190
- 7280209
- 7280215
- 7280221
- 7280238
- 7280244
- 7567974
- 7567980
- 7567997
- 7568005
- 7568011
- 7568028

Nicht rabattierte PZN mit Basics, Betapharm und ratiopharm

- 2029462 (keine Normpackung; auslaufende PZN)
- 2160759 (auslaufende PZN)
- 2160788 (auslaufende PZN)
- 3688362 (Klinikpackung)
- 5499783 (keine Normpackung)
- 7430749 (Injektionslösung)

BARMER: 166 Wirkstoffe wurden 2017 komplett rabattiert abgegeben

Wirkstoffe	Anzahl	Anteil* an VO insgesamt (60.697.788)	Anteil VO nicht rabattiert
für die 2017 prinzipiell ein Rabattvertrag bestand	427	100,0	3,3
für die 2017 alle Verordnungen unter Rabatt abgegeben wurden	166	11,2	0,0
für die 2017 auch VO ohne Rabatt abgegeben wurden	261	88,8	3,8

* Anteil umfasst alle Verordnungen der prinzipiell rabattierten Wirkstoffe (ATC)

IGES Berechnungen nach Daten von Insight Health

BARMER: Gros rabattierter Wirkstoffe wird zu sehr hohem Anteil rabattiert abgegeben

Prinzipiell rabattierte Wirkstoffe nach Anteil nicht rabattierter Verordnungen je Wirkstoff (ATC)	Anzahl	Anteil* an VO insgesamt (60.697.78)
0%	166	11,2
über 0 bis 0,5%	88	29,2
über 0,5 bis 10%	128	51,5
über 10%	45	8,1

* Anteil umfasst alle Verordnungen der prinzipiell rabattierten Wirkstoffe (ATC)

BARMER: Wirkstoffe mit den höchsten Anteilen nicht rabattierter VO

Wirkstoff	Summe VO Wirkstoff	Anteil VO NR (%)	Hintergrund
Colecalciferol	209.207	82,5	Nicht rabattiert: Überwiegend 20.000 IE Wirkstärke zur Einmalanwendung
Estradiol	129.293	77,1	Nicht rabattiert: Überwiegend Gel-Zubereitung (keine Entsprechung bei rabattiert)
Macrogol; Kombi	46.677	71,2	Unter Rabatt waren auslaufende PZN-> RV nicht verlängert?
Glyceroltrinitrat	85.147	69,8	Unklar; nur eine PZN rabattiert; in der Vergangenheit Rückrufaktionen in Zusammenhang mit rabattiertem Produkt
Haloperidol	36.532	64,2	Unter Rabatt nur 4 PZN (nur ein Bruchteil der verfügbaren Varianten)
Testosteron	40.745	59,9	Nicht rabattiert: Höhere Wirkstärke (Injektion alle 10 bis 14 Wochen statt alle 4)
Fentanyl	135.123	53,8	Siehe Details übernächste Folie
Propiverin	50.878	53,7	Rabattiert nur Wirkstärken bis 15mg, nicht rabattierte überwiegend höhere Dosierung
Somatropin	867	48,3	15mg-Wirkstärke (nur 1 Hersteller) nicht rabattiert, alle übrigen WS rabattiert
Valproinsäure	84.616	44,1	Hersteller Sanofi: rabattiert nur Generika von Sanofi nicht das Original; bei Valproinsäure keine Austauschpflicht

IGES Berechnungen nach Daten von Insight Health

BARMER Colecalciferol: nur ein AWG bei einem Hersteller rabattiert

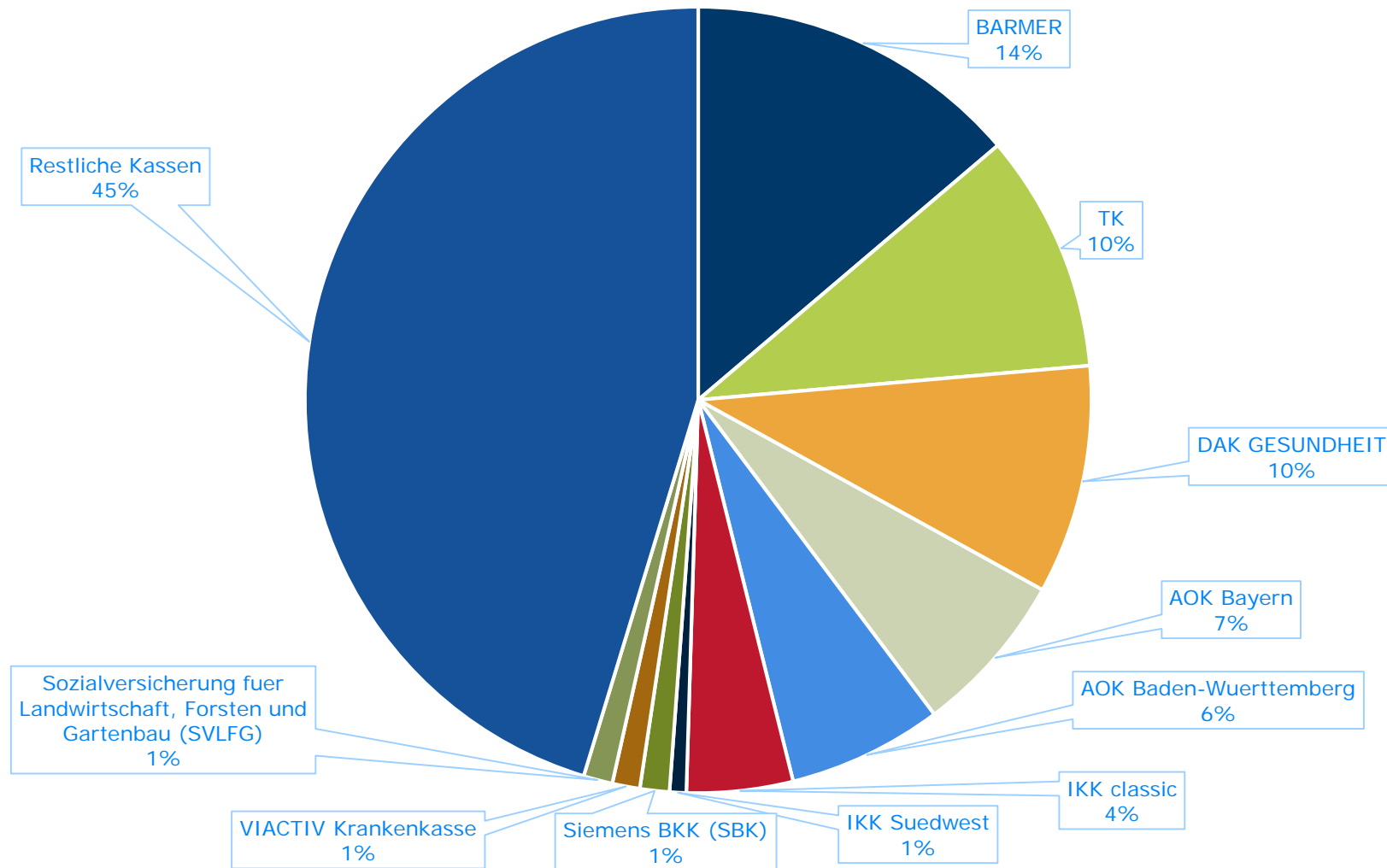
Wirkstärke	DAR	Hersteller	Konzern	VO	VO rabattiert	VO mit NV-Kennz.	Anwendungsgebiet
1000IE	oral fest	Mibe	Dermapharm	21.201	6.713	2	Prophylaxe Vit.-D-Mangel Kinder/Erwachsene und supportiv bei Osteoporose
500IE				15.469	2.867	2	
4000IE		Mibe	Dermapharm	6.354	0	0	Nahrungsergänzungsmittel
4000IE				61	0	0	Nahrungsergänzungsmittel
20000IE				166.183	0	3	einmalig bei Anfangsbehandlung Vitamin-D-Mangel
2000IE		Huebner	402	0	0	Nahrungsergänzungsmittel	
1000IE	oral fest	Hevert	Hevert	13.267	0	2	Prophylaxe Vit.-D-Mangel Kinder/Erwachsene und supportiv bei Osteoporose
500IE				82	0	0	
1000IE				218	0	0	
100000IE	parenteral	Heyl	Heyl	1.147	0	0	wenn orale Therapie nicht möglich
25000IE	oral flüssig	Infecto- pharm	Infectopharm	66	0	0	Anfangsbehandlung von Vitamin D Mangelerscheinungen
100000IE				198	0	0	
20K	oral flüssig	Merck Selbstm.	Merck KGaA	35.844	0	4	Prophylaxe Vit.-D-Mangel Kinder/Erwachsene und supportiv bei Osteoporose; Behandlung von Rachitis, Osteomalazie und Hyperparathyreodismus
1000IE	oral fest			85.360	0	23	Prophylaxe Vit.-D-Mangel Kinder/Erwachsene und supportiv bei Osteoporose
500IE				58.273	0	12	
2400IE	oral fest	Paedia 1	Paedia 1	2.880	0	1	Prophylaxe Vit.-D-Mangel Kinder/Erwachsene und supportiv bei Osteoporose
1000IE	oral fest	Woerwag	Woerwag	2.562	0	3	Prophylaxe Vit.-D-Mangel Kinder/Erwachsene und supportiv bei Osteoporose

BARMER Fentanyl: nur Pflaster und von Hexal nur Teilsegment rabattiert

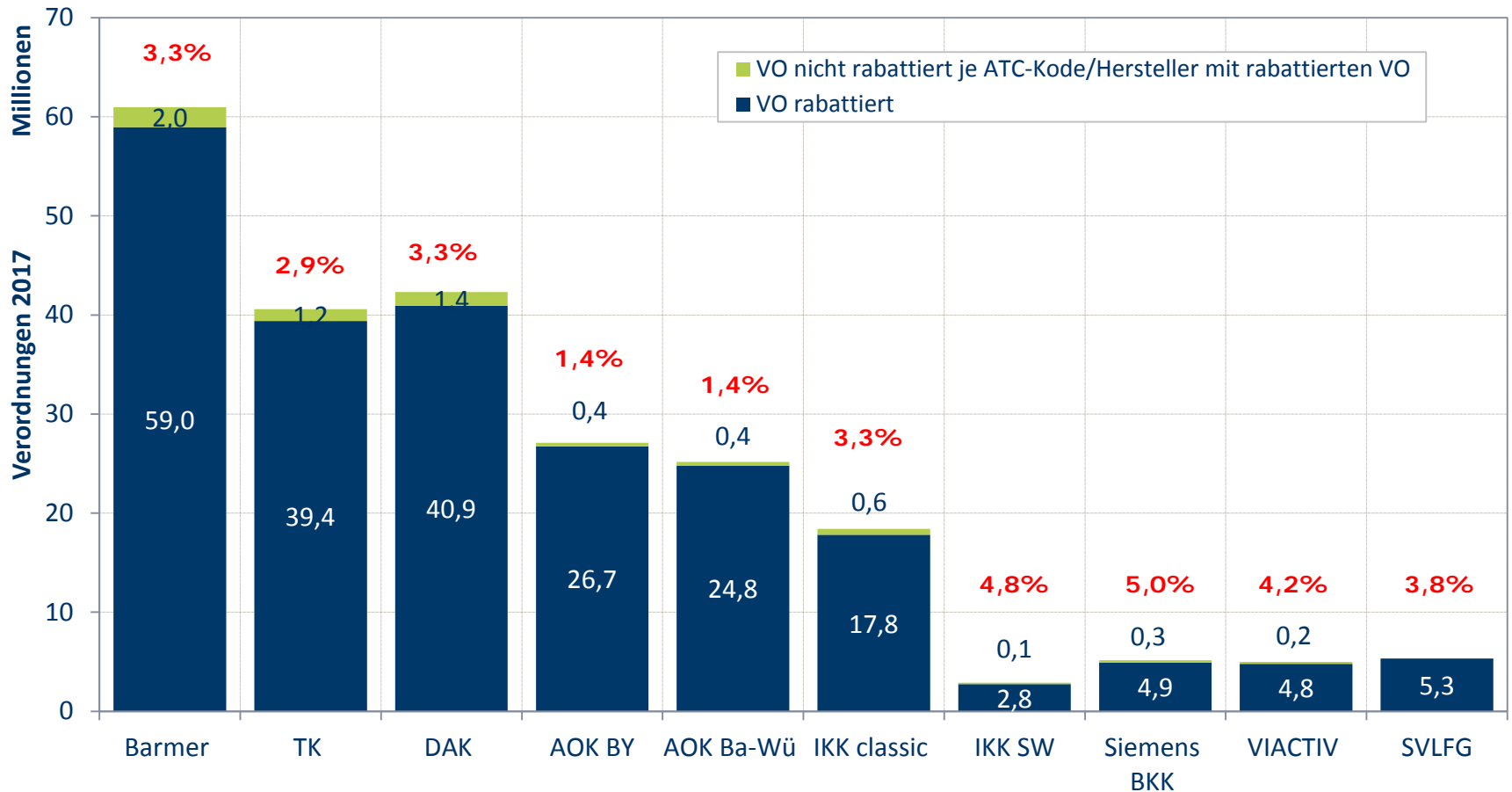
DAR	Hersteller	Konzern	VO	VO rabattiert	VO mit NV-Kennz.	Kommentar
Pflaster	Hexal	Novartis	4.251	4.075	4	nur Fentanyl-Hexal S (Matrixpflaster) -> gleiche Freisetzung wie Durogesic SMAT (Matrixpflaster)
Pflaster	16 weitere	Novartis und 12 weitere	116.298	109.492	121	
oral	Kyowa Kirin	Kyowa Hakko Kirin	7.302	0	5	
oral	Teva	Teva	8.895	0	2	
oral	Hexal	Novartis	513	0	0	
oral	Meda Pharma	Meda AB	3	0	0	
nasal	Takeda	Takeda	1.723	0	2	
nasal	Kyowa Kirin	Kyowa Hakko Kirin	936	0	0	
Pflaster	Hexal	Novartis	29.483	0	18	Fentanyl-Sandoz; Fentanyl-Hexal TTS (Membranpflaster) und Fentanyl-Hexal MAT (Matrixpflaster) -> gleiche Freisetzung wie Durogesic Reservoirpflaster
Pflaster	8 weitere	Novartis und 7 weitere	97.561	0	246	

IGES eigene Recherchen und Berechnungen nach Daten von Insight Health

Anteil der 10 ausgewählten Kassen an der Verordnungsmenge 2017



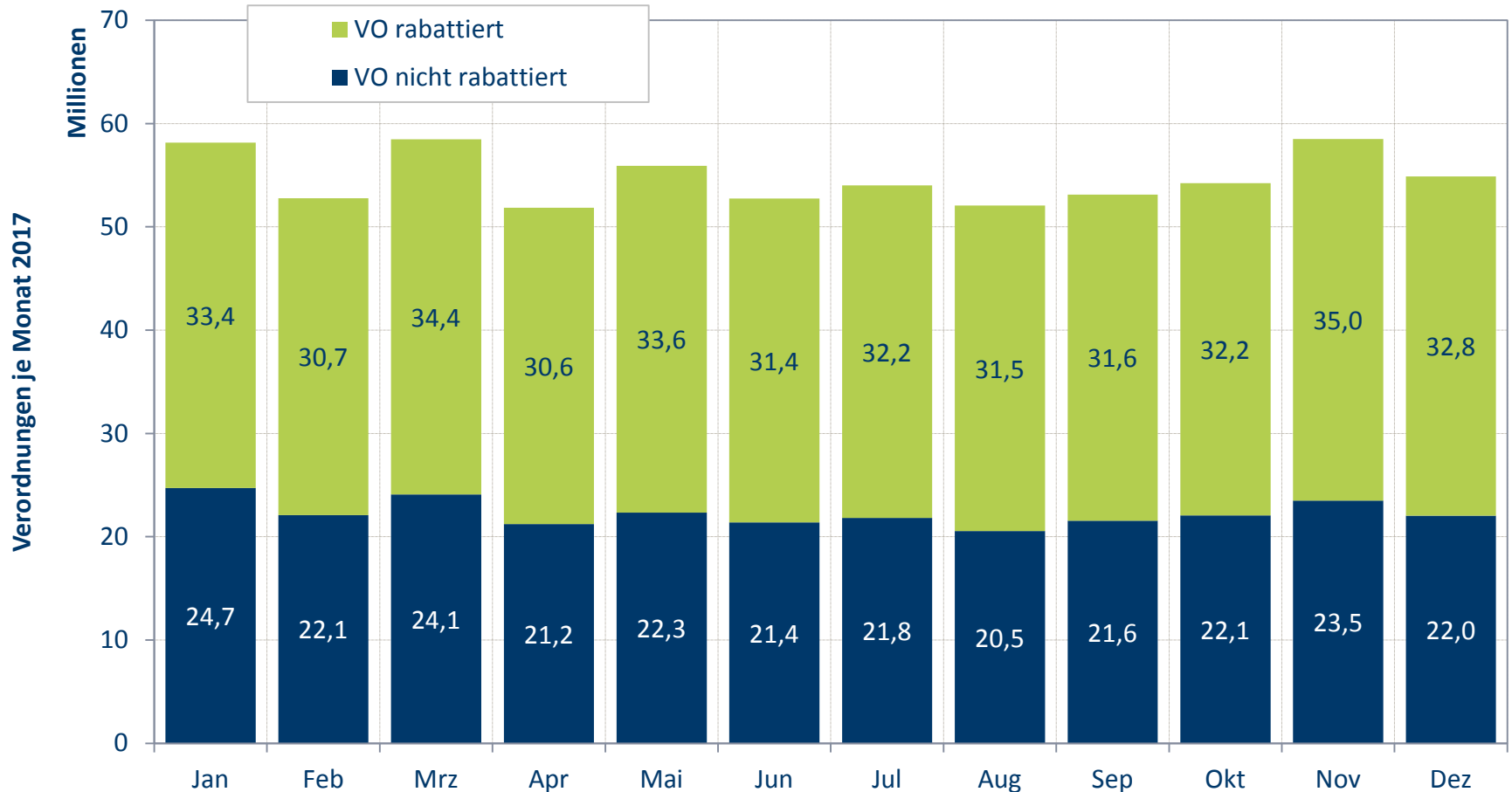
Der Anteil nicht rabattierter VO je ATC/Hersteller ist gering



IGES Berechnungen nach Daten von Insight Health

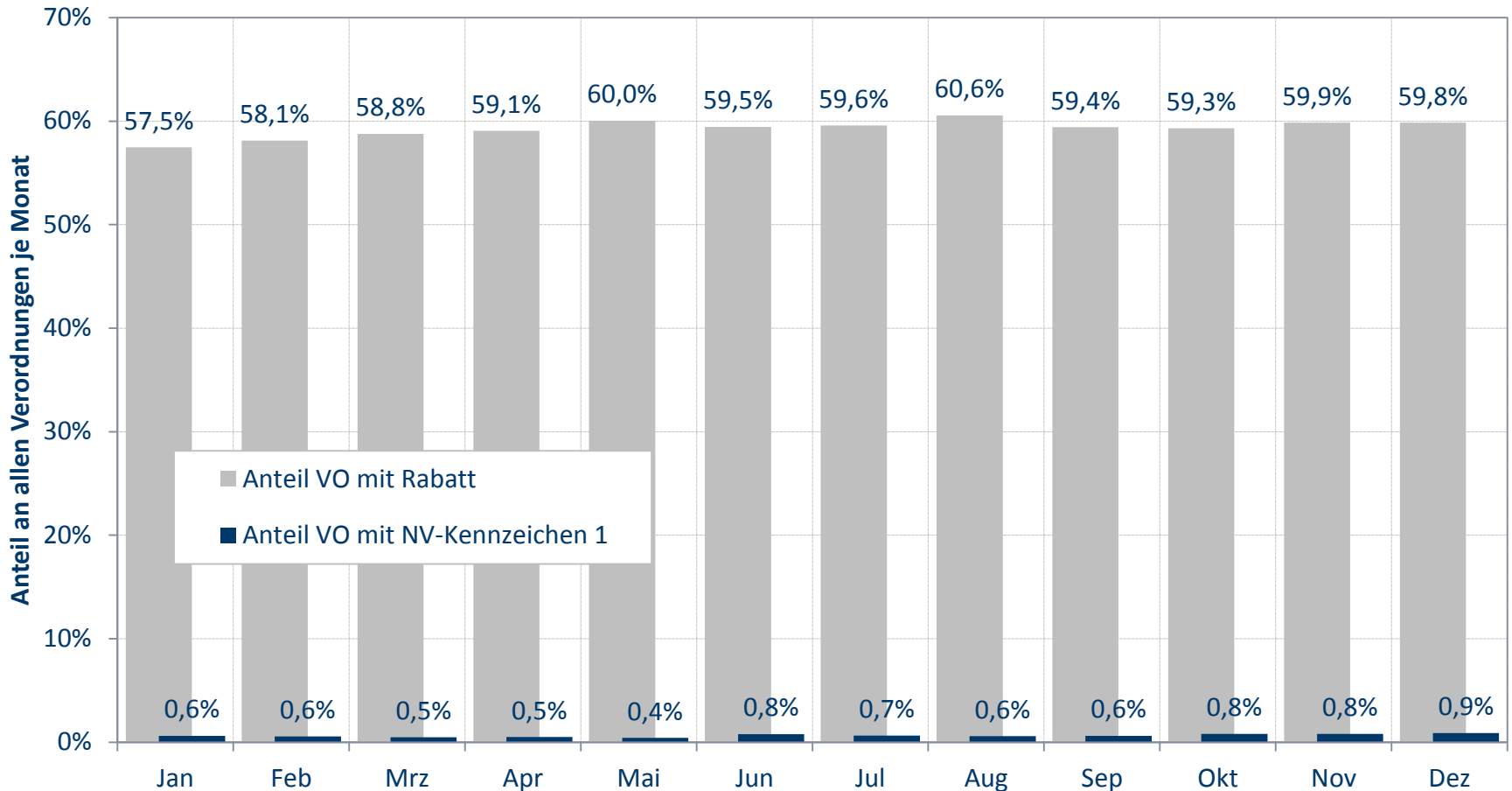
2.1 Ergebnisse: Übersicht

59,3% der betrachteten Verordnungen (656 Mio.) waren unter Rabatt



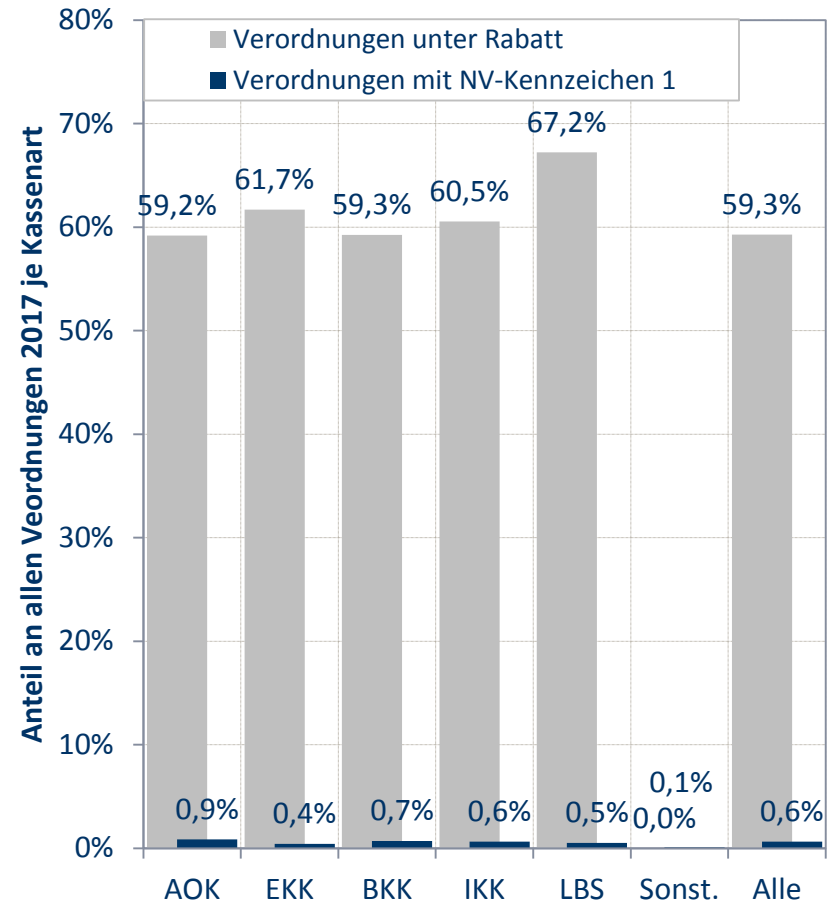
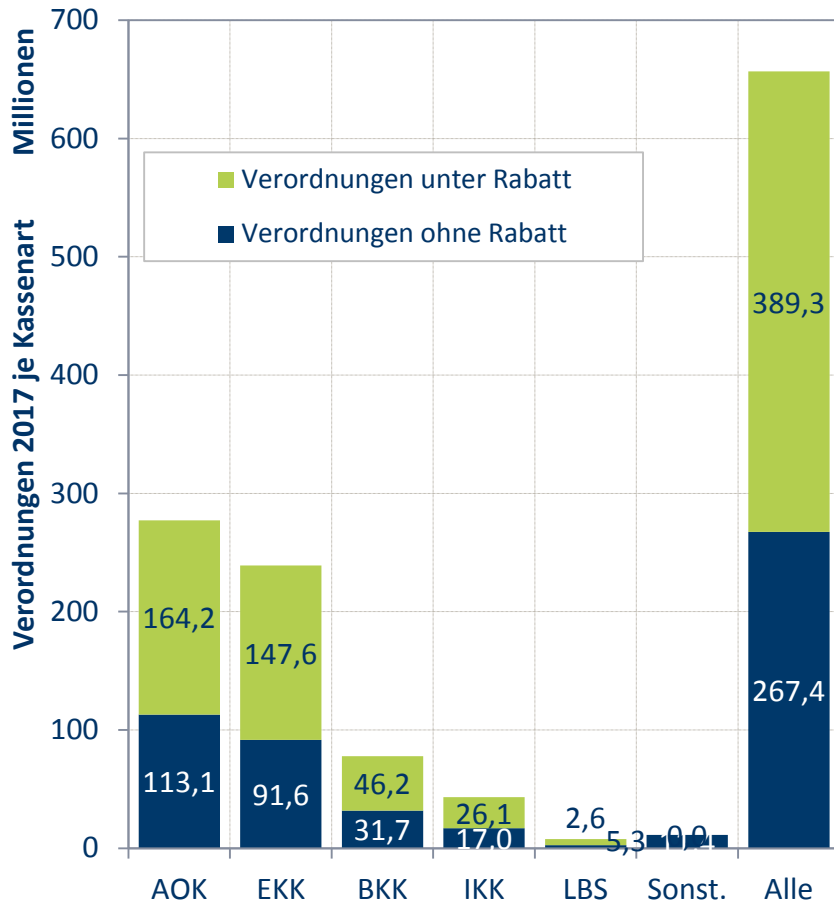
IGES Berechnungen nach Daten von Insight Health

Bei 0,6% aller betrachteten Verordnungen fand sich ein NV-Kennzeichen



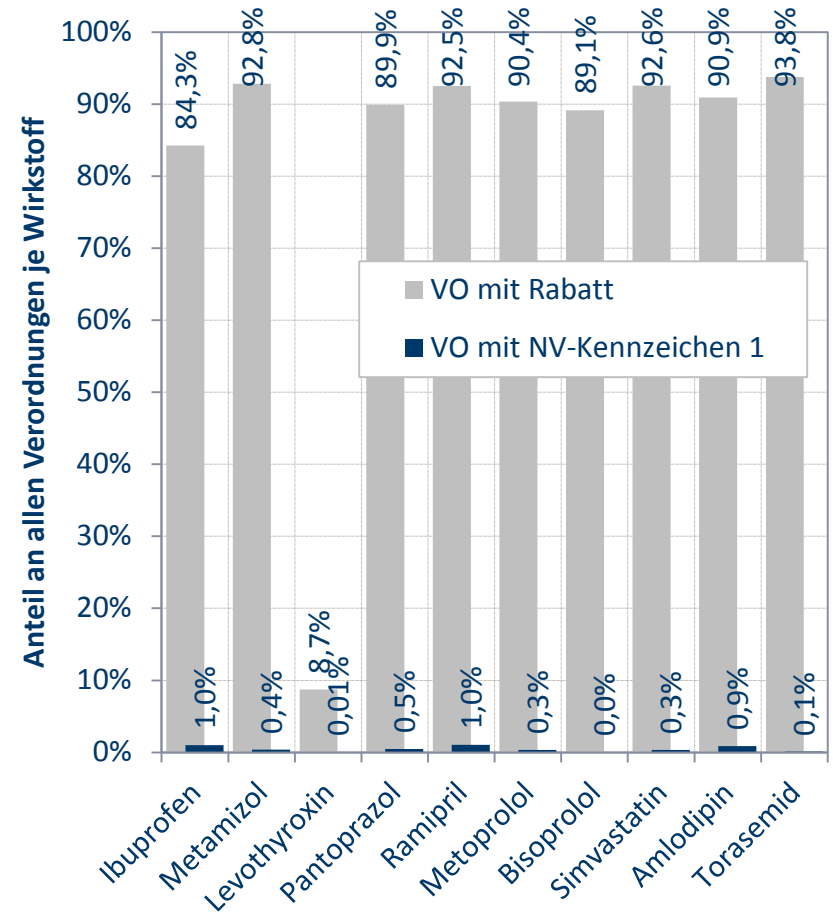
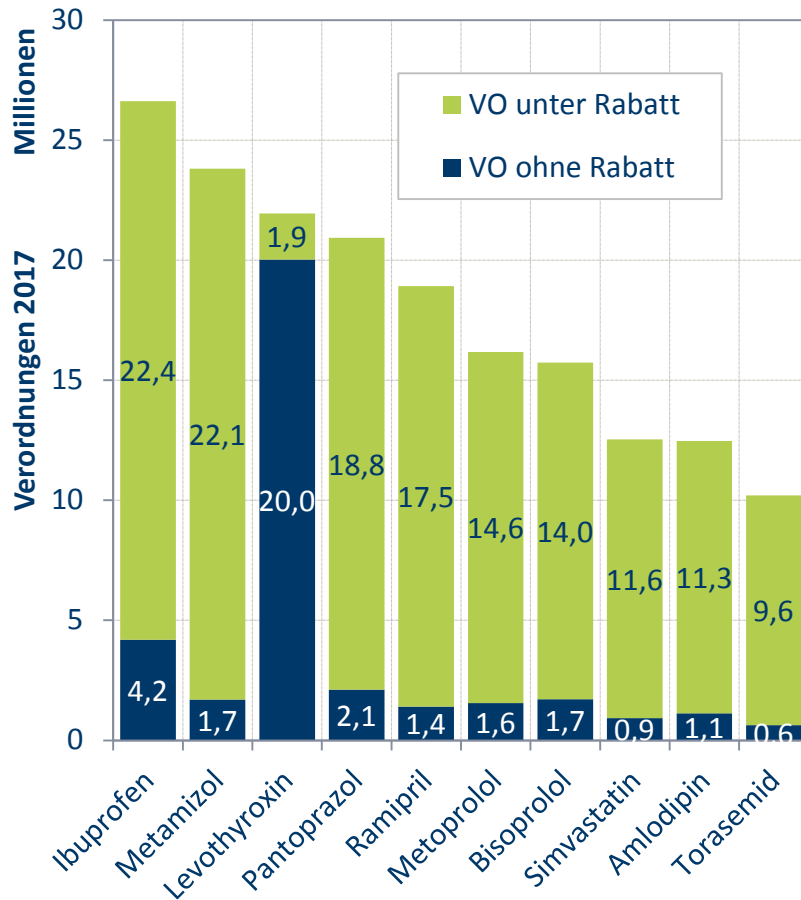
IGES Berechnungen nach Daten von Insight Health

Anteil rabattierter VO bei allen Kassenarten ähnlich



IGES Berechnungen nach Daten von Insight Health

Top 10 Wirkstoffe nach Anzahl Verordnungen (27% aller VO)



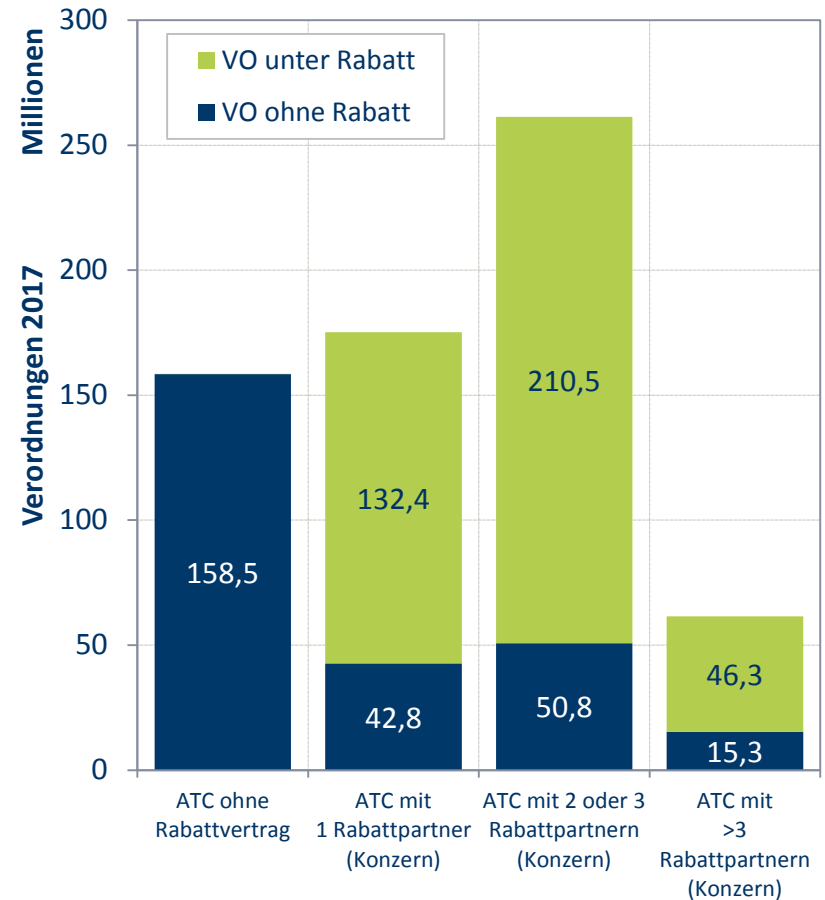
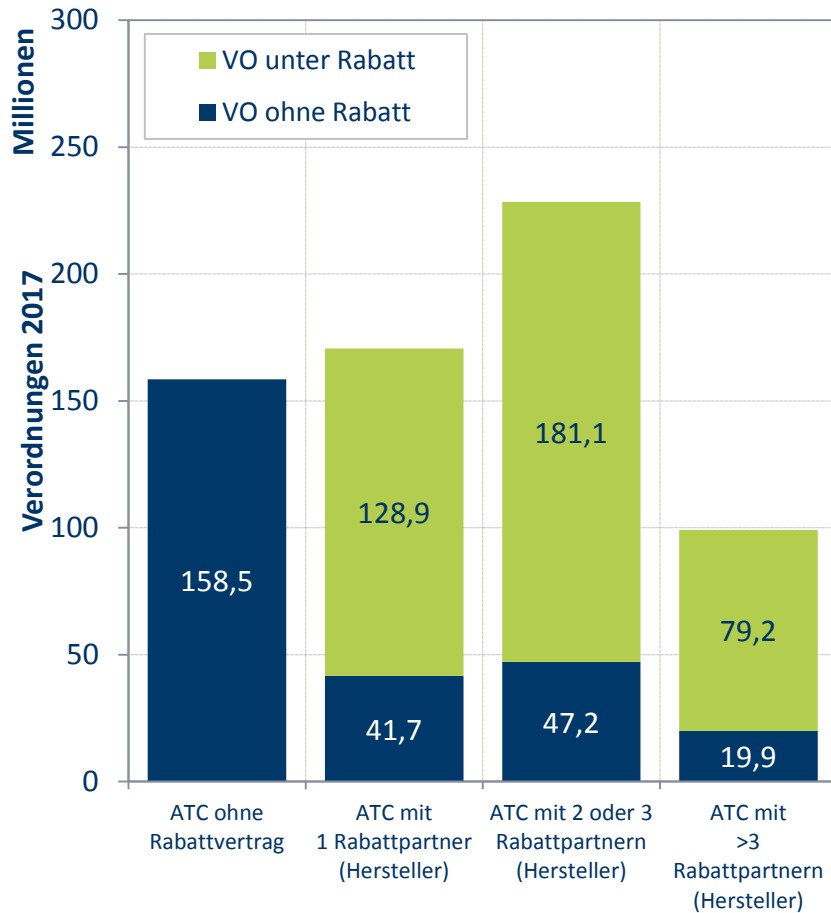
IGES Berechnungen nach Daten von Insight Health

2.2 Ergebnisse: Rabattmodell und NV-Kennzeichen

Zusammenhang zwischen Rabattmodell und Nichtverfügbarkeit - Methodik

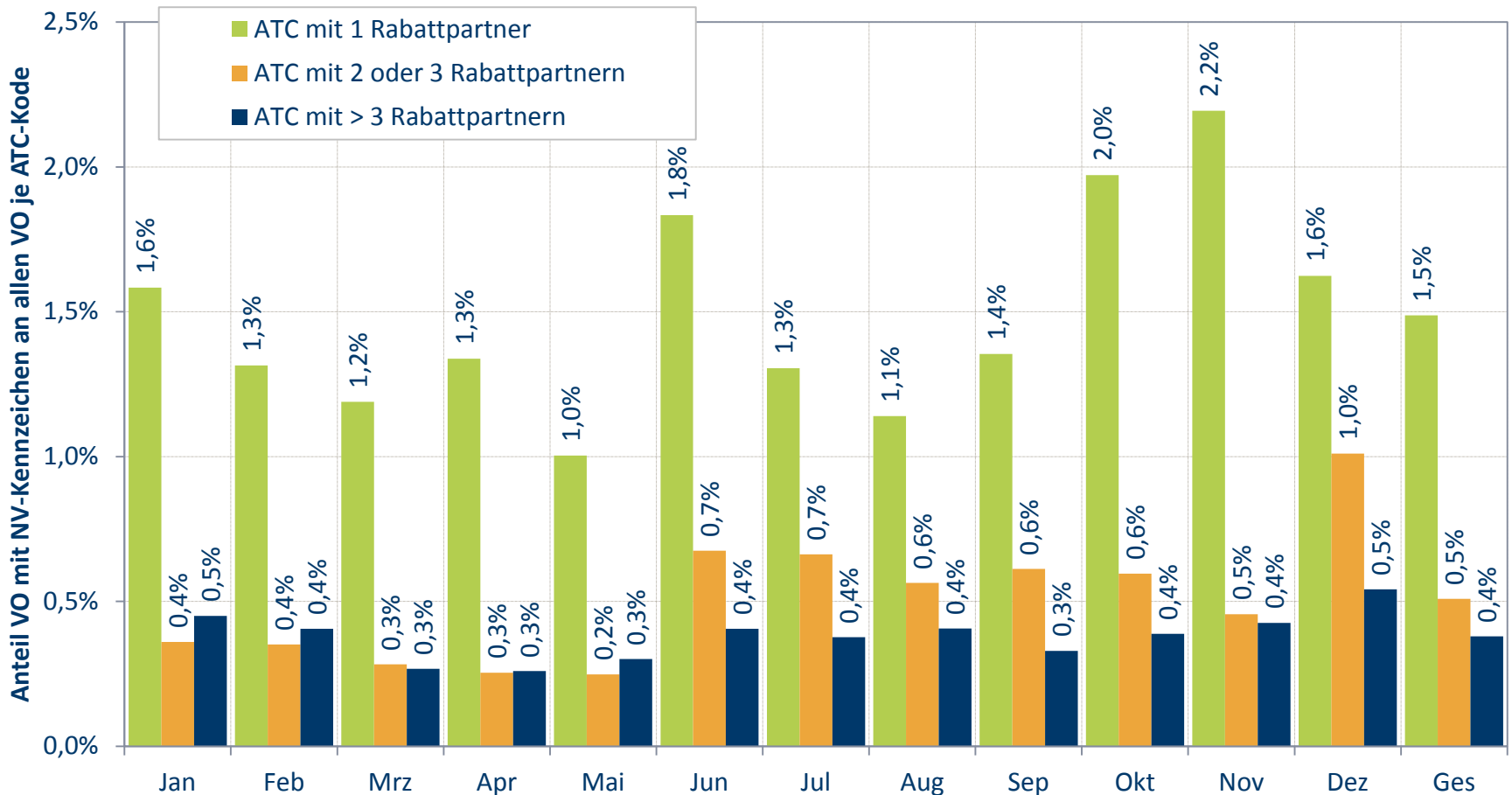
- Die Anzahl der Rabattpartner je Krankenkasse und ATC-Kode wird in drei Kategorien differenziert, um eine systematische Auswertung zu ermöglichen:
 - V1 = Anzahl Hersteller / Konzern = 1
 - V23 = Anzahl Hersteller / Konzern = 2 und 3
 - Vue3 = Anzahl Hersteller / Konzern > 3
- Der Anteil Nichtverfügbarkeit an Verordnungen wird ermittelt indem die Anzahl der NV Kennzeichnungen durch die Anzahl der Verordnungen geteilt wird.

Verordnungen unter Rabatt nach Anzahl Rabattpartner



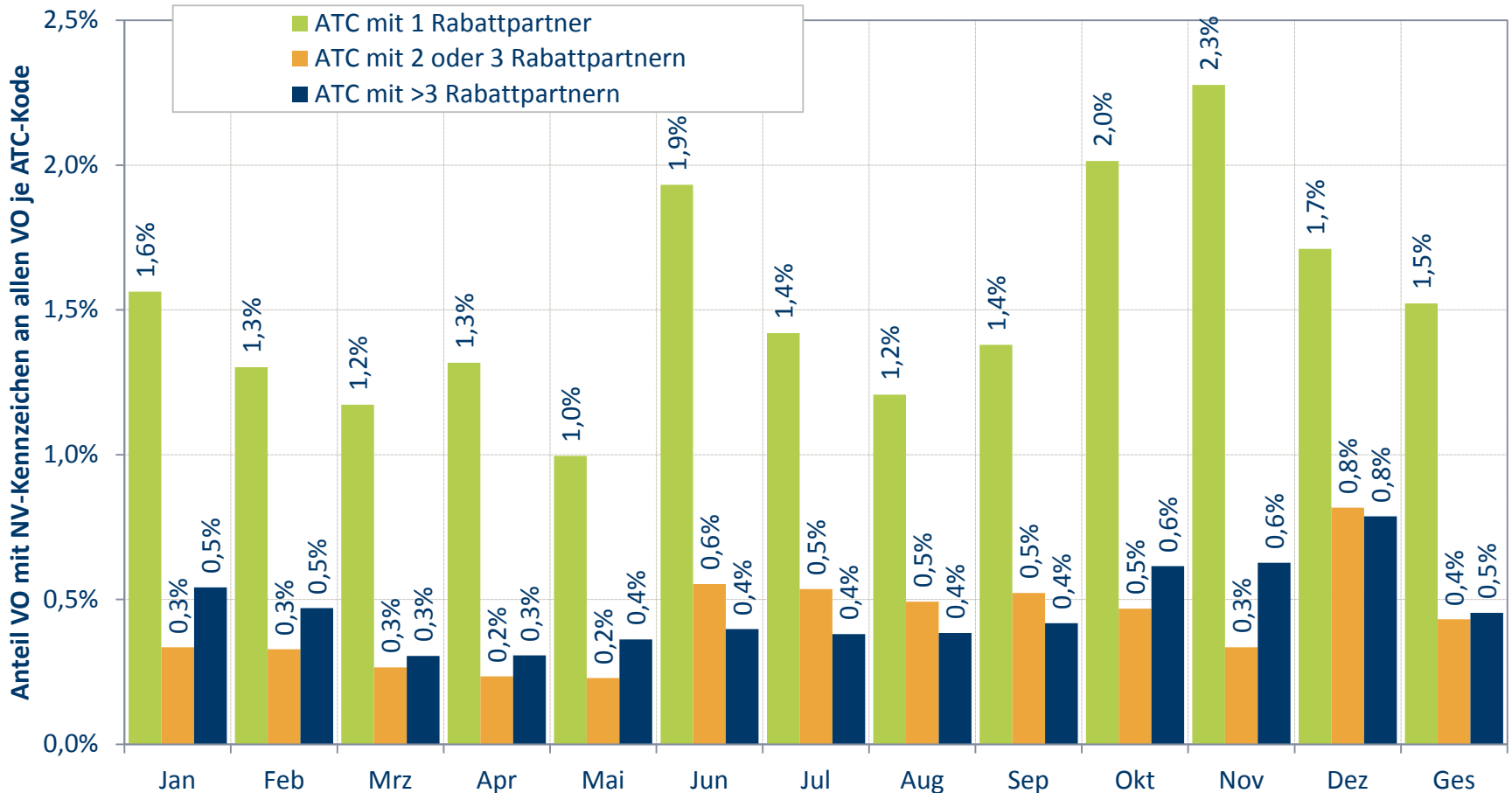
IGES Berechnungen nach Daten von Insight Health

NV-Kennzeichen deutlich häufiger bei nur einem Rabattpartner (Hersteller)



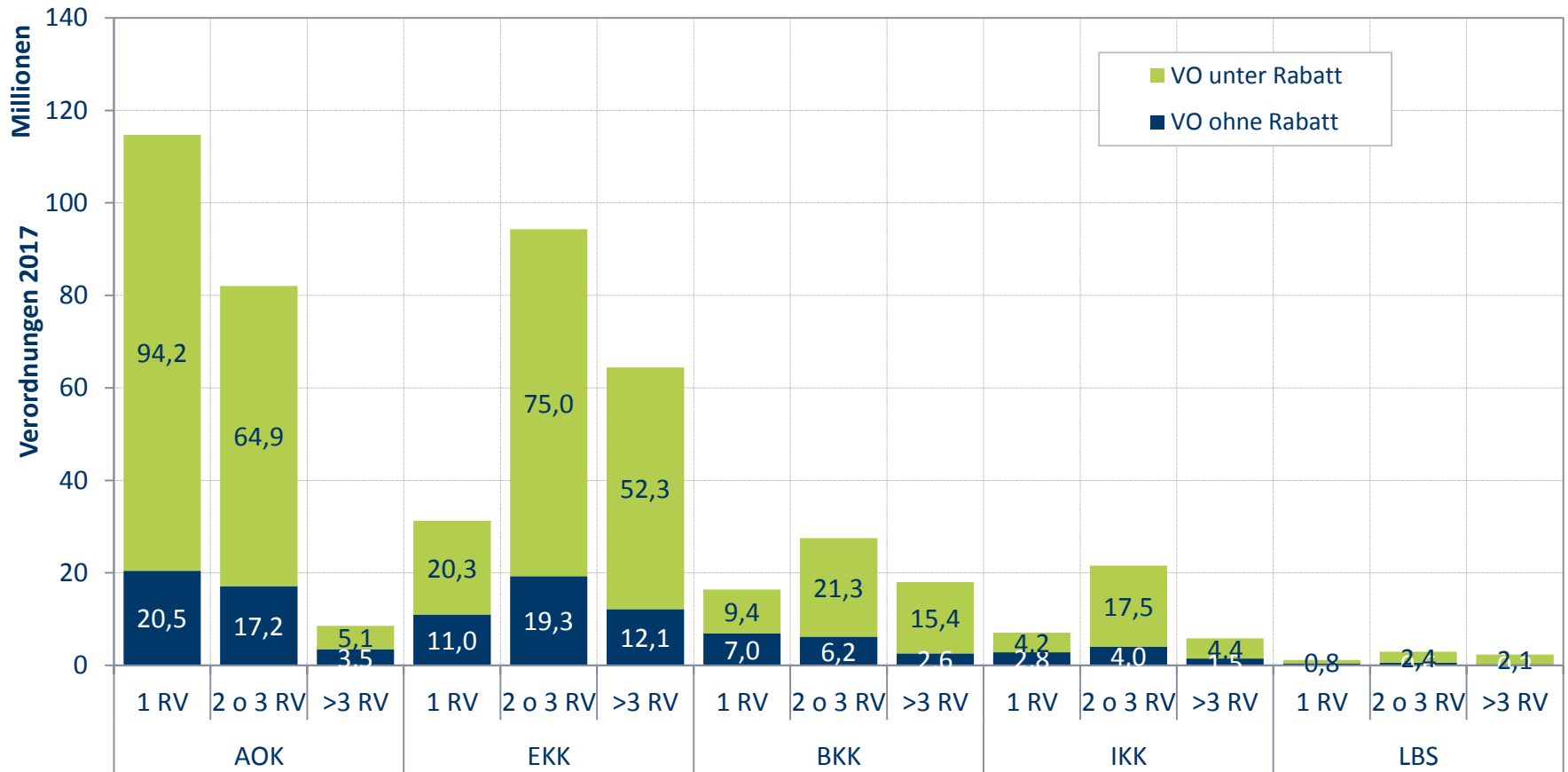
IGES Berechnungen nach Daten von Insight Health

NV-Kennzeichen deutlich häufiger bei nur einem Rabattpartner (Konzern)



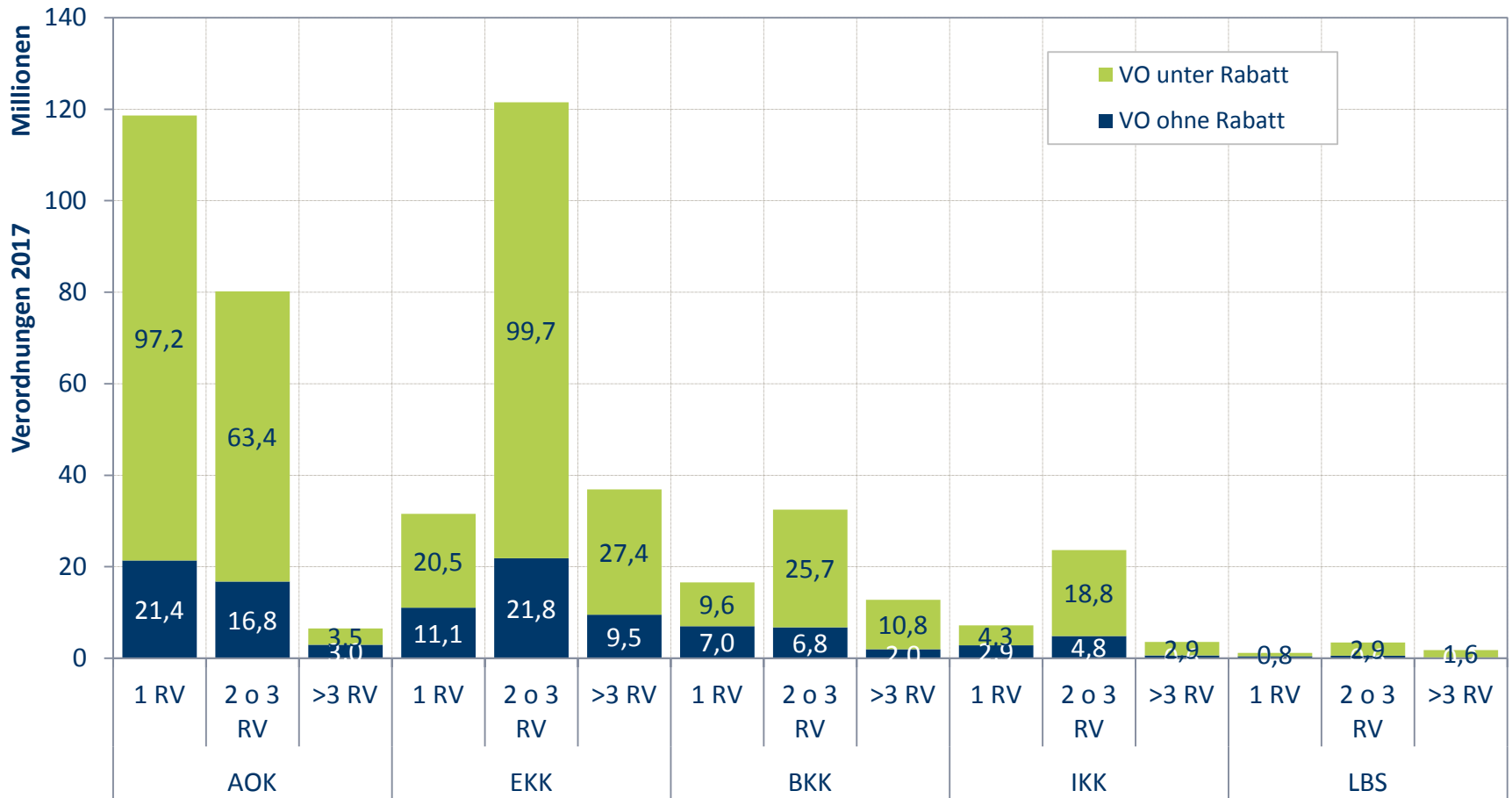
IGES Berechnungen nach Daten von Insight Health

Verordnungen nach Anzahl Rabattpartner und Kassenart (Hersteller)



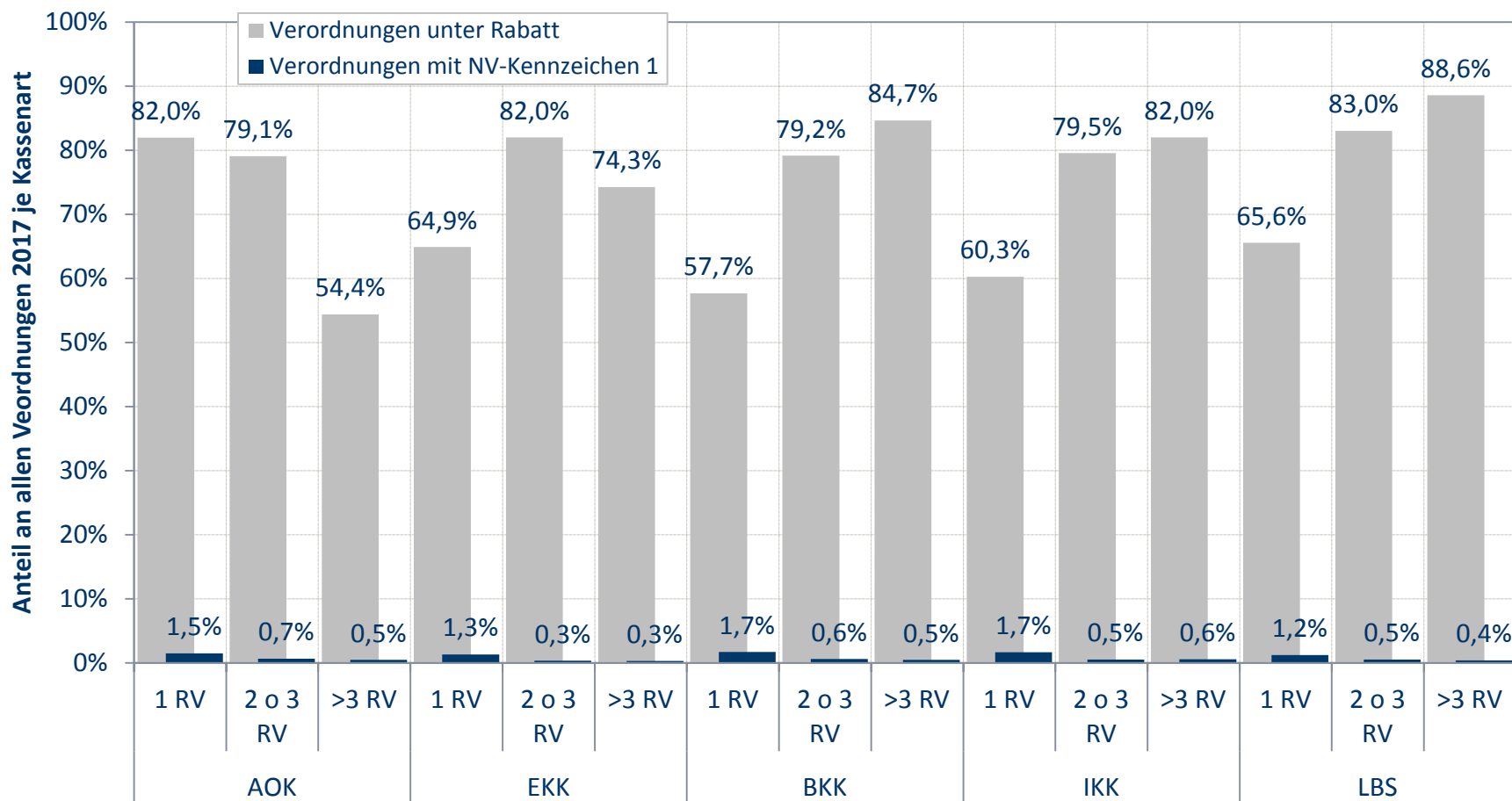
IGES Berechnungen nach Daten von Insight Health

Verordnungen nach Anzahl Rabattpartner und Kassenart (Konzern)



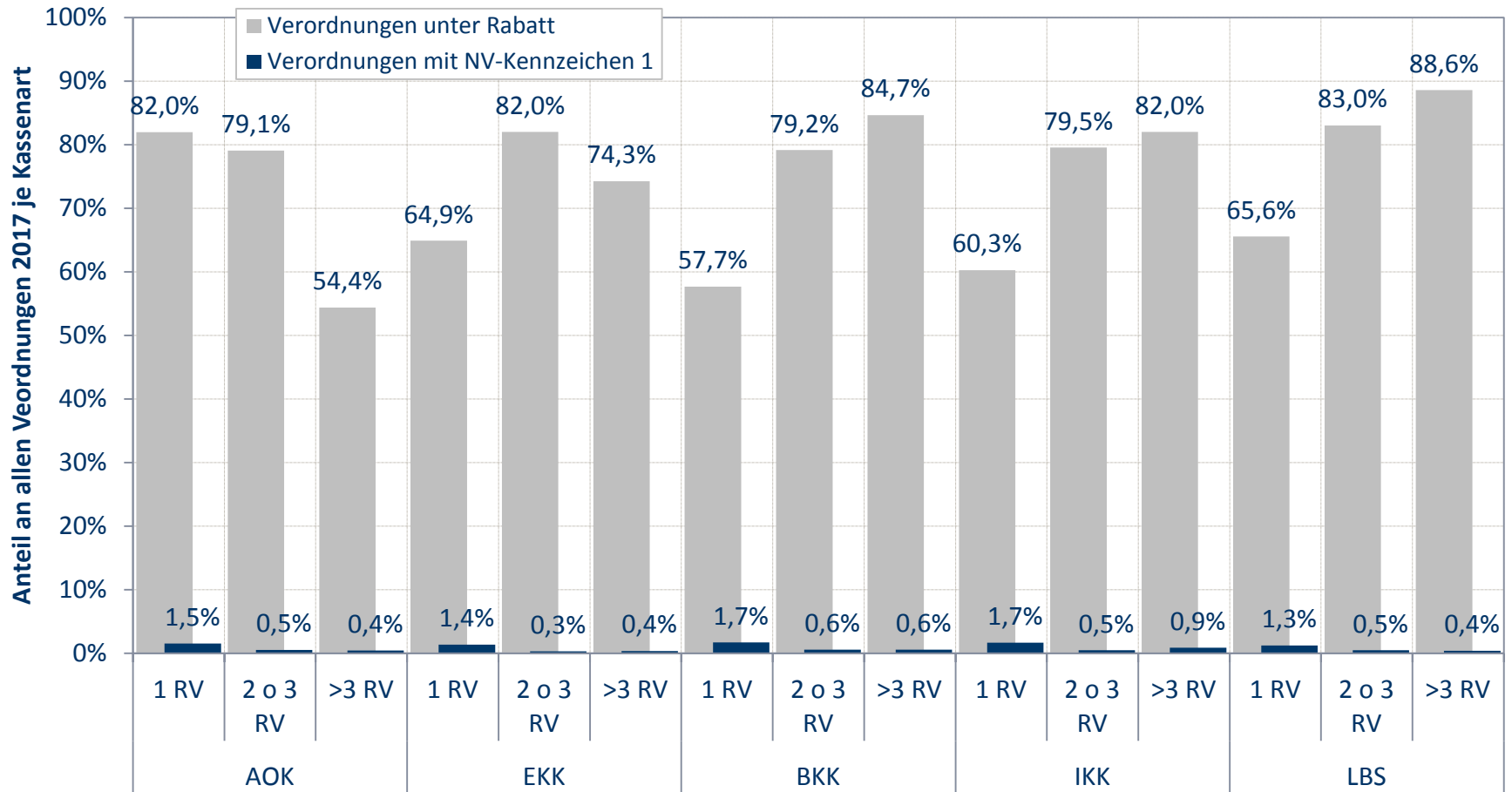
IGES Berechnungen nach Daten von Insight Health

Anteil Verordnungen mit NV-Kennzeichen am höchsten bei einem Rabattpartner (H)



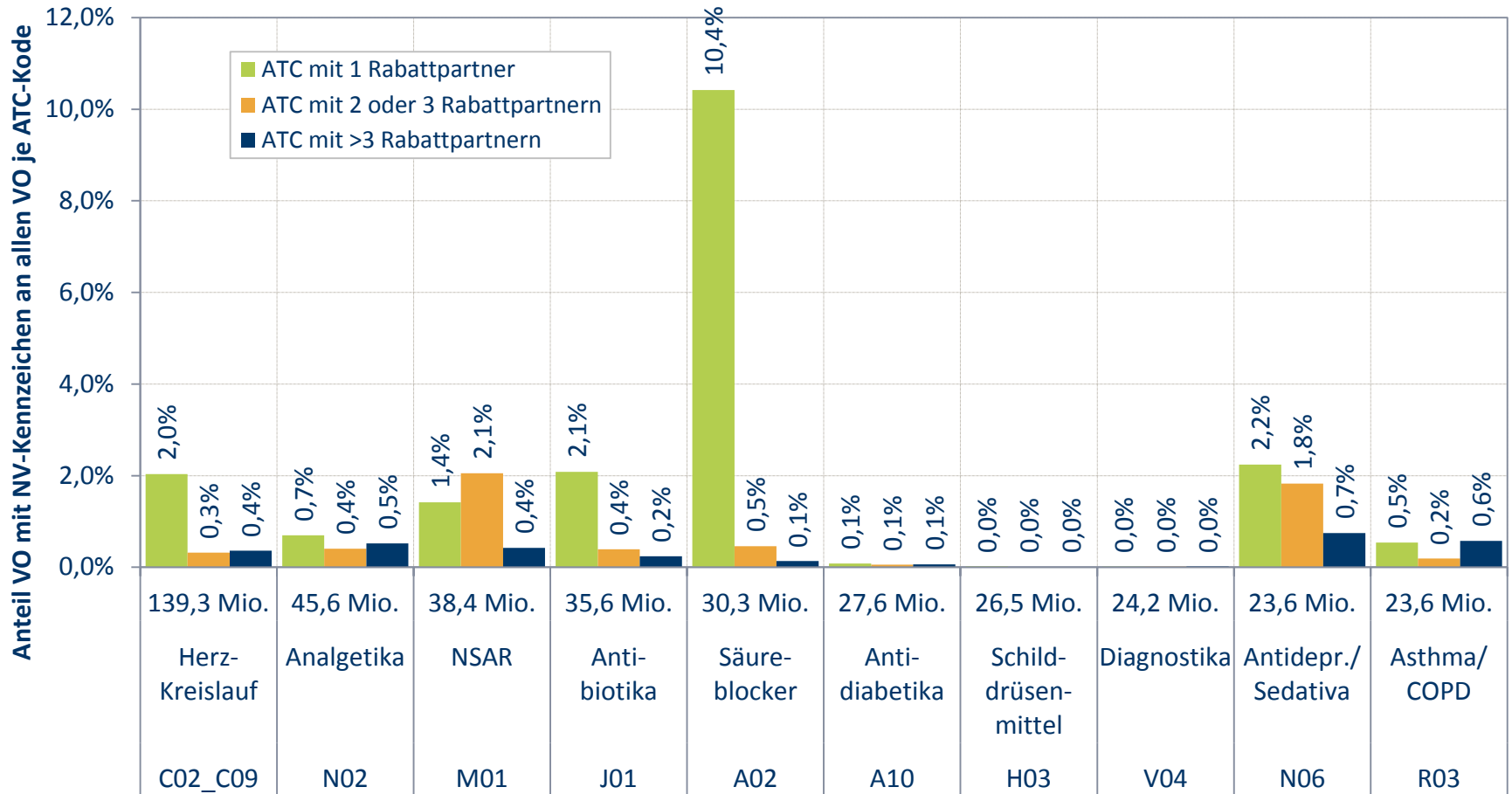
IGES Berechnungen nach Daten von Insight Health

Anteil Verordnungen mit NV-Kennzeichen am höchsten bei einem Rabattpartner (K)



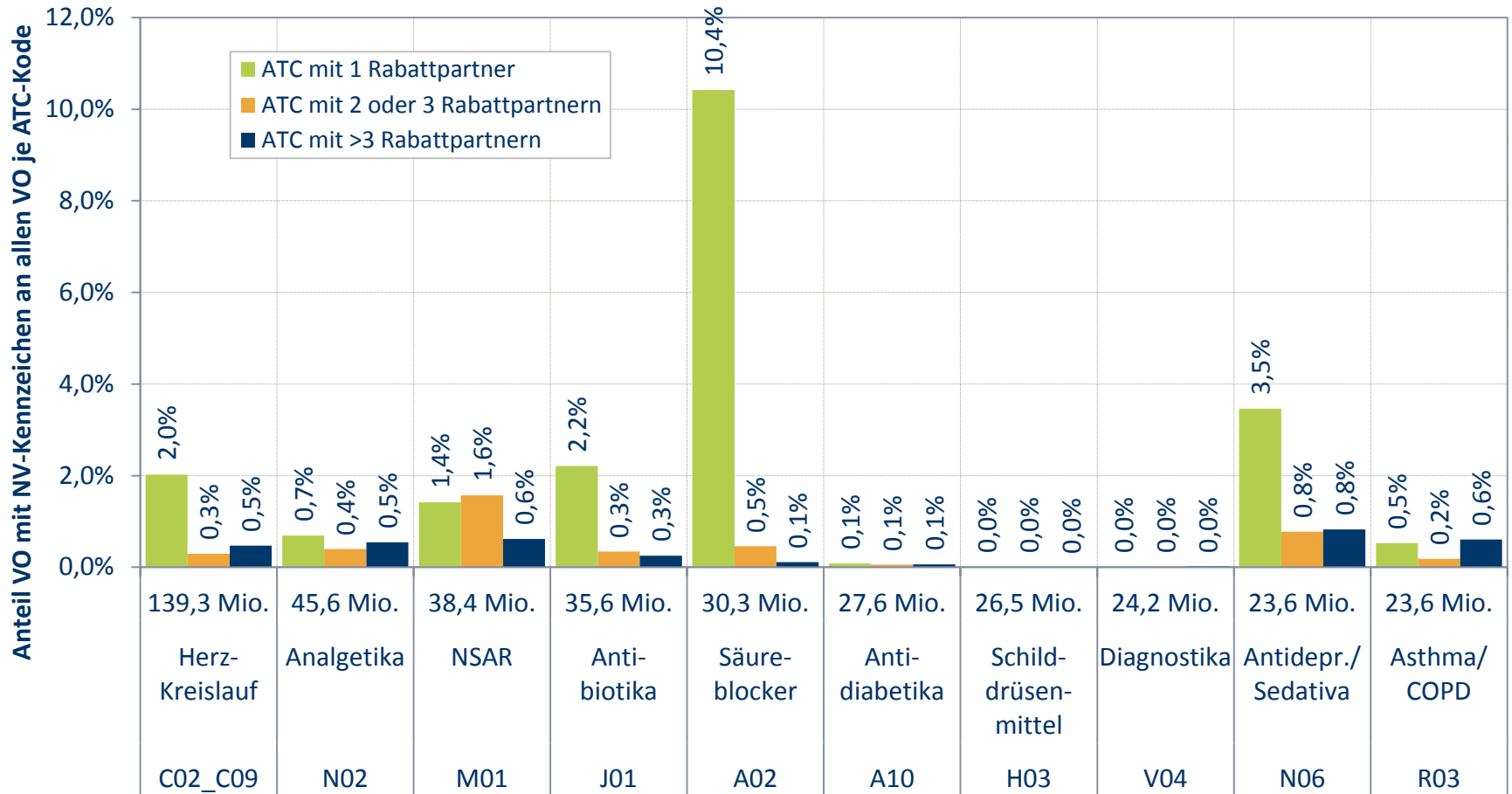
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen ist bei Top-10 ATC3-Stellern oft bei 1 RV am höchsten (Hersteller)



IGES Berechnungen nach Daten von Insight Health

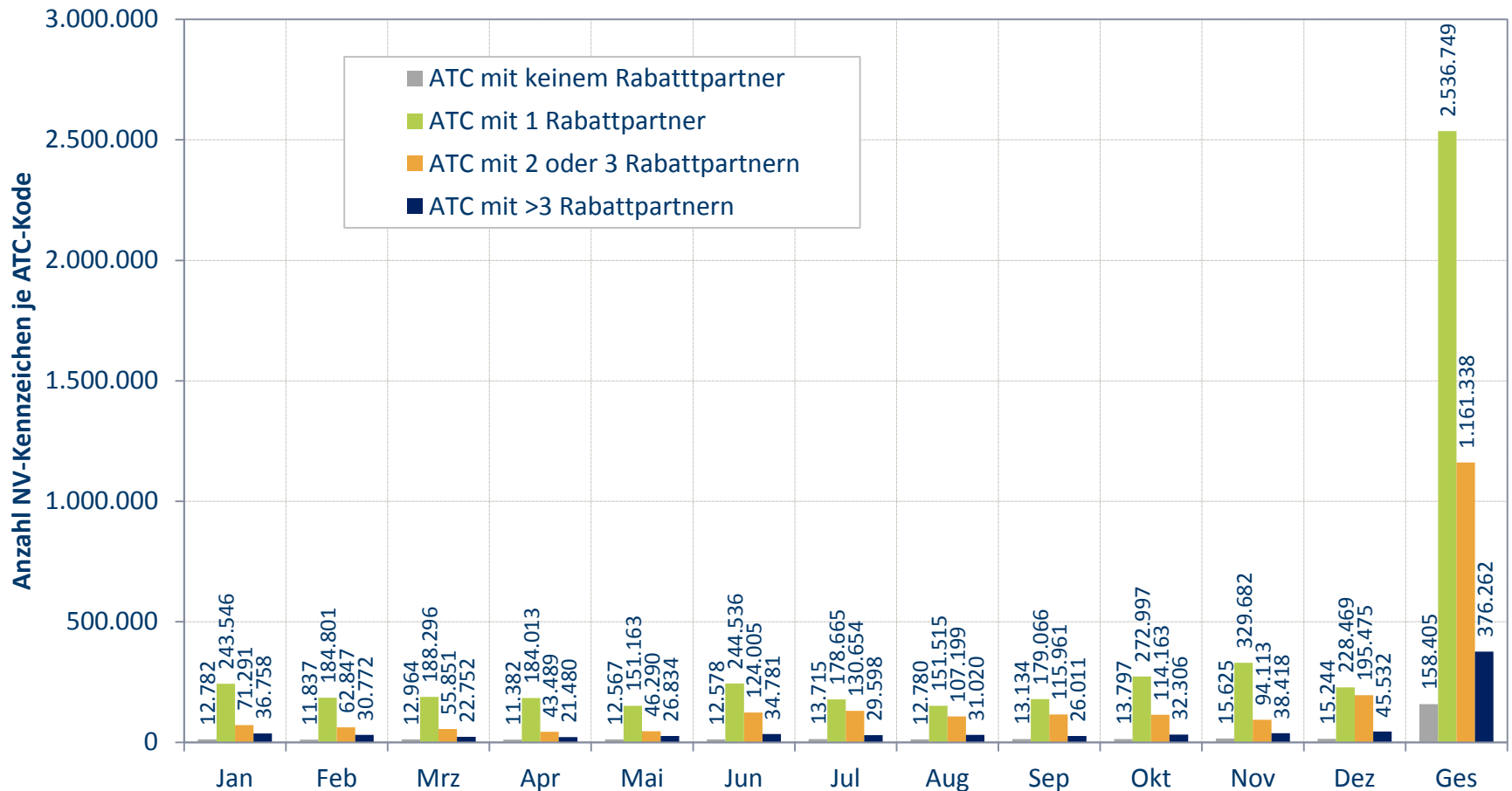
Anteil NV-Kennzeichen ist bei Top-10 ATC3-Stellern oft bei 1 RV am höchsten (Konzern)



IGES Berechnungen nach Daten von Insight Health

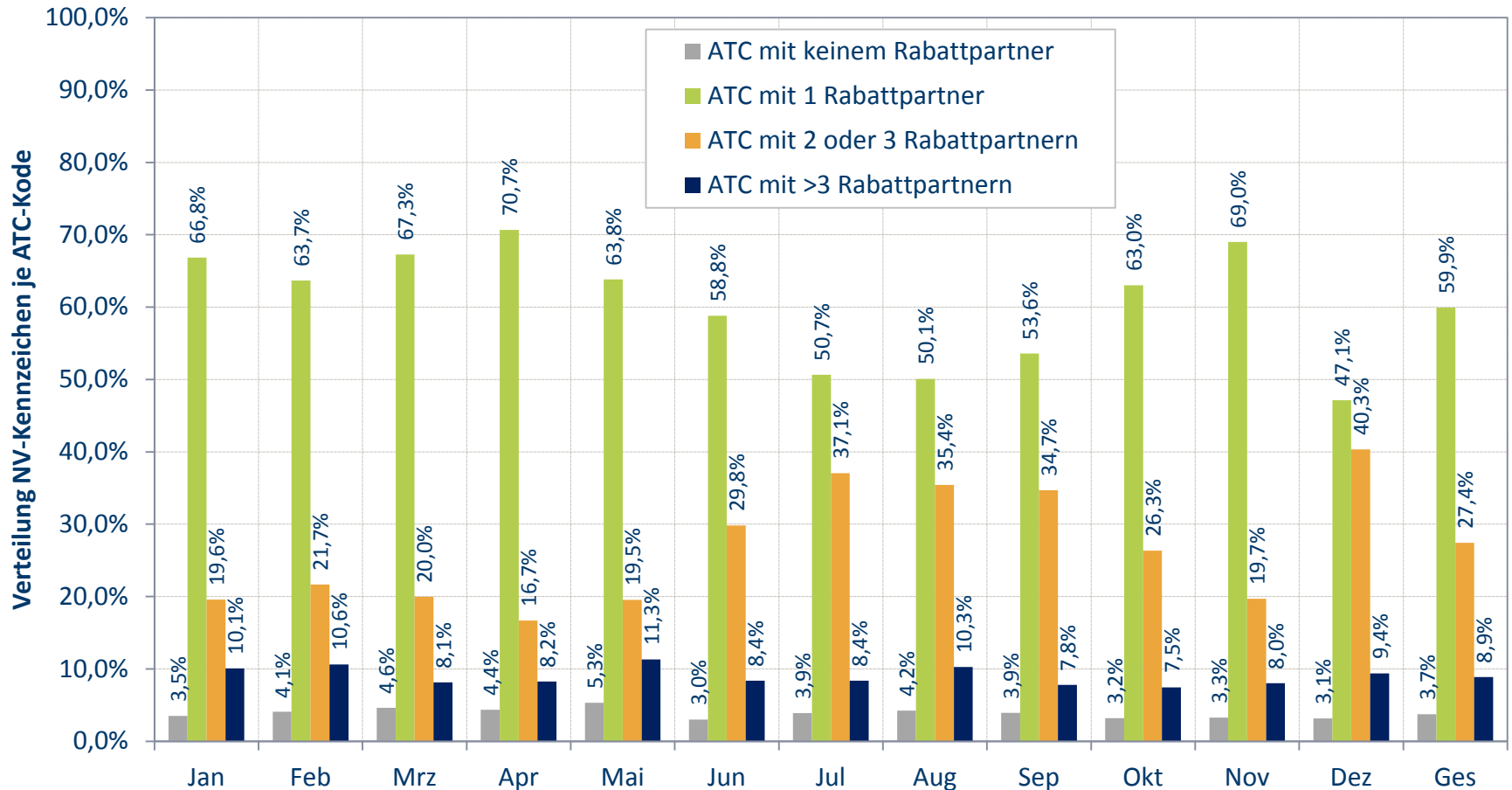
3. Übersichtsdarstellung für ausgewählte ATC7-Steller

Anzahl der NV-Kennzeichen bei nur einem Rabattpartner (Hersteller) im gesamten Zeitverlauf am größten



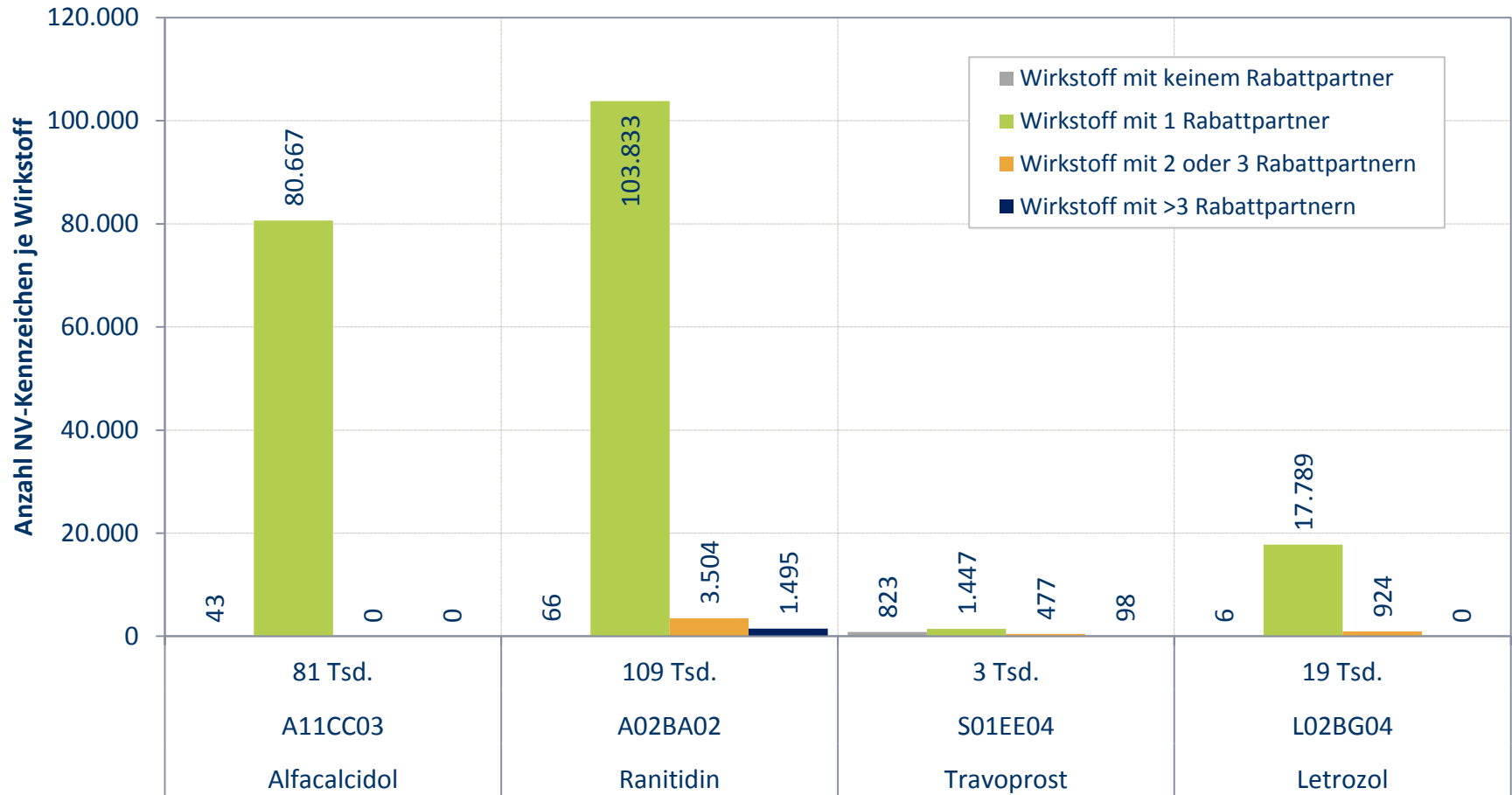
IGES Berechnungen nach Daten von Insight Health

Anteil der NV-Kennzeichen bei nur einem Rabattpartner (Hersteller) im gesamten Zeitverlauf am größten



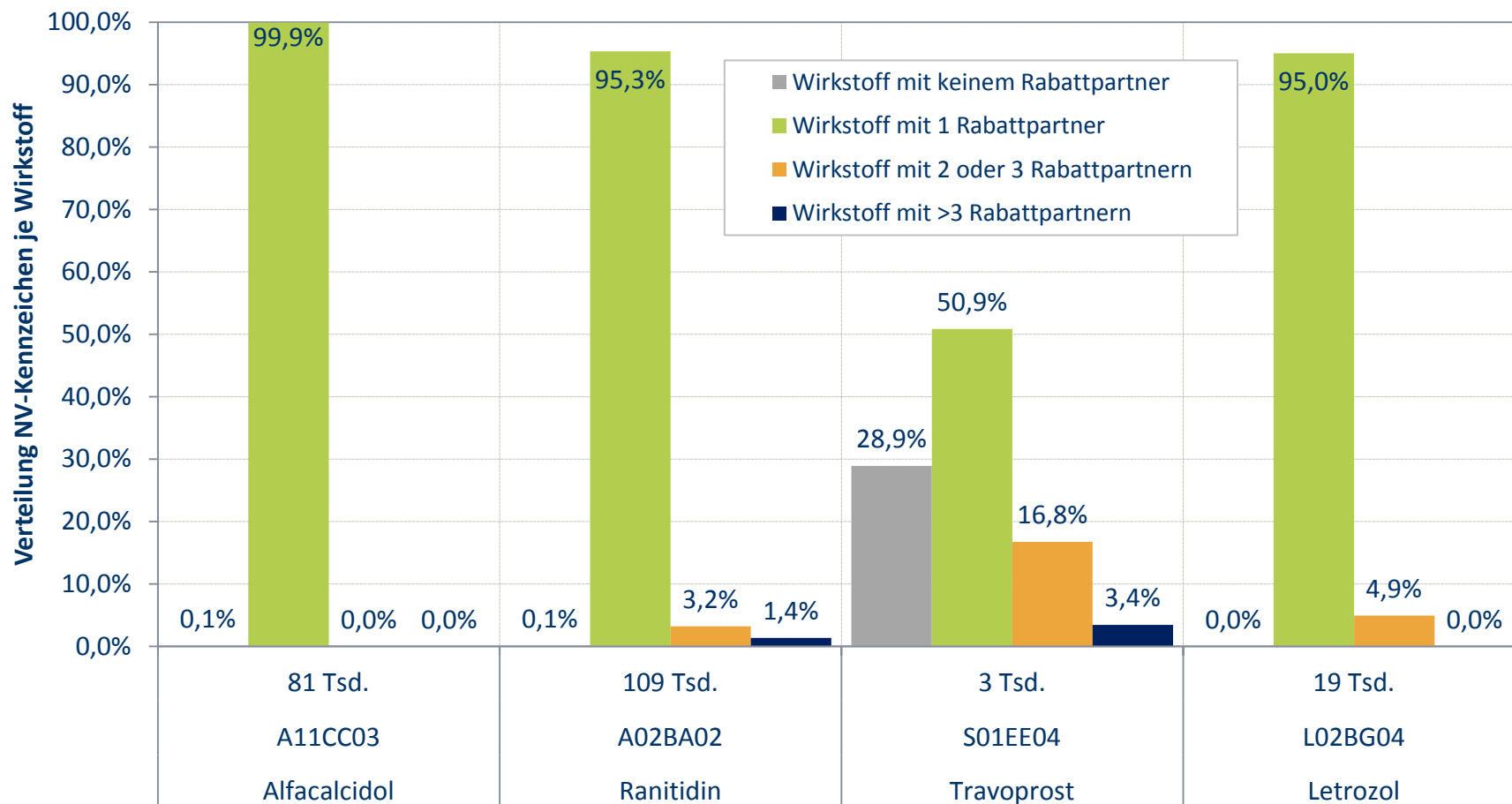
IGES Berechnungen nach Daten von Insight Health

Anzahl NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (1)



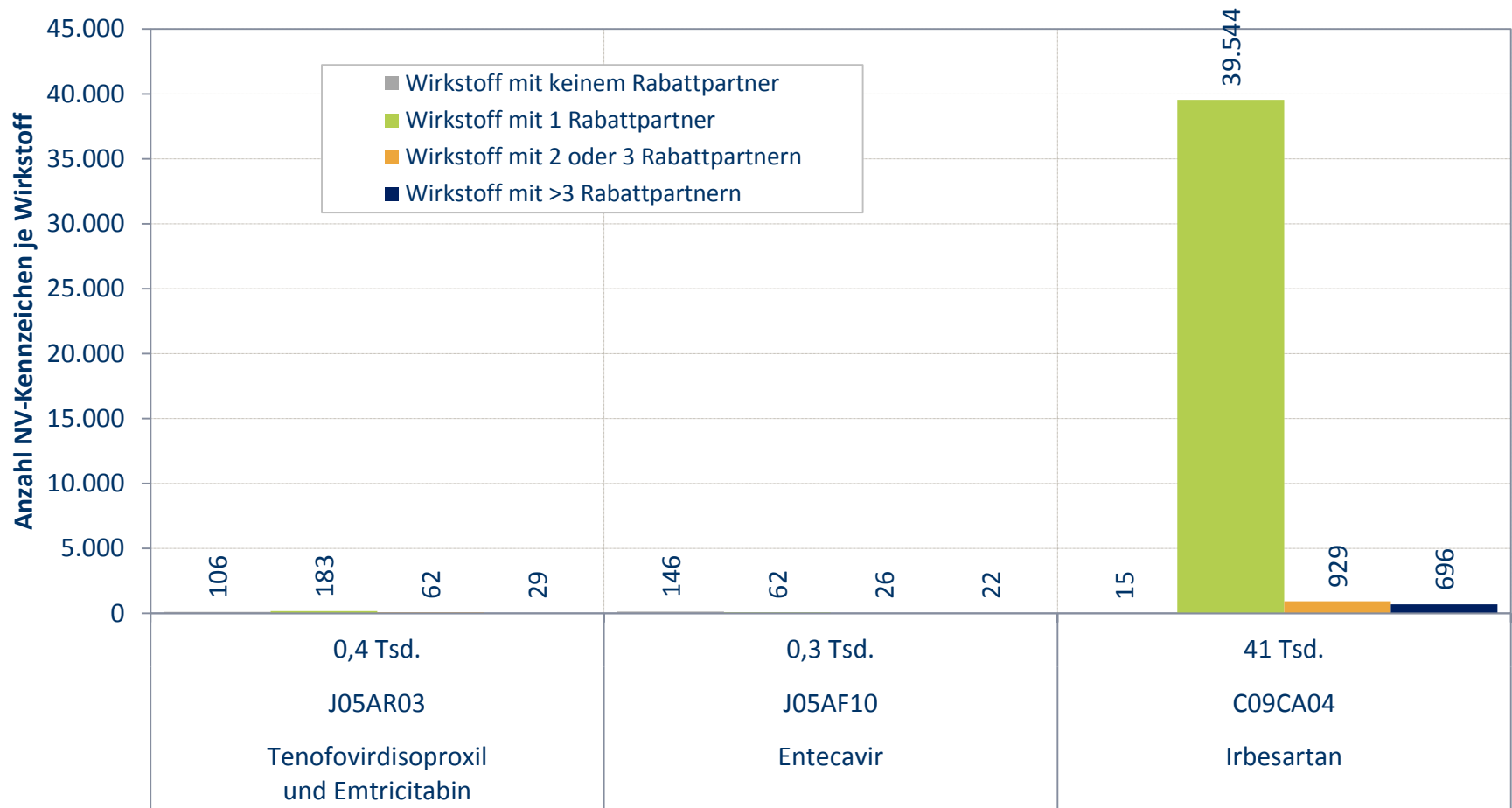
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (1)



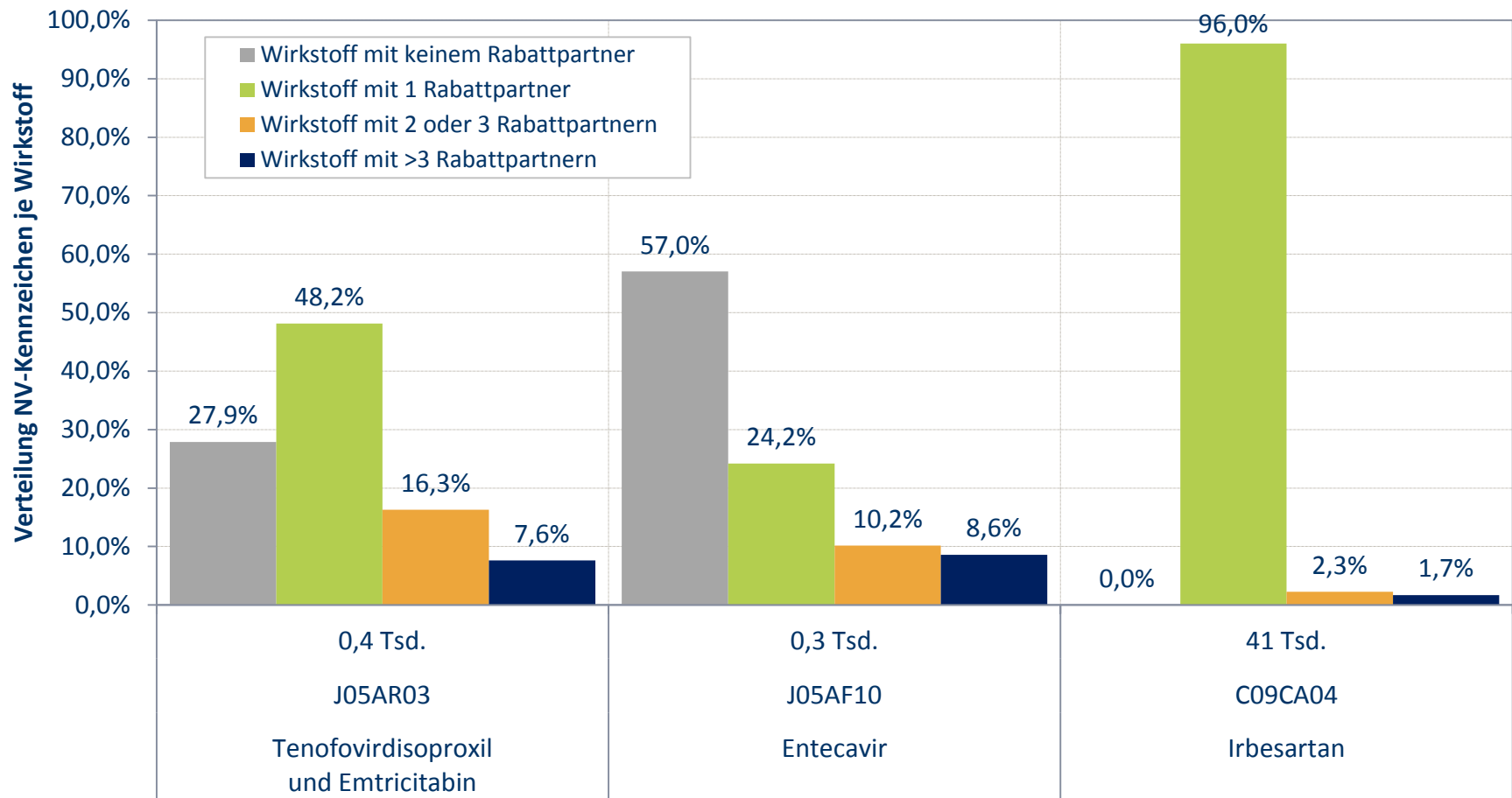
IGES Berechnungen nach Daten von Insight Health

Anzahl NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (2)



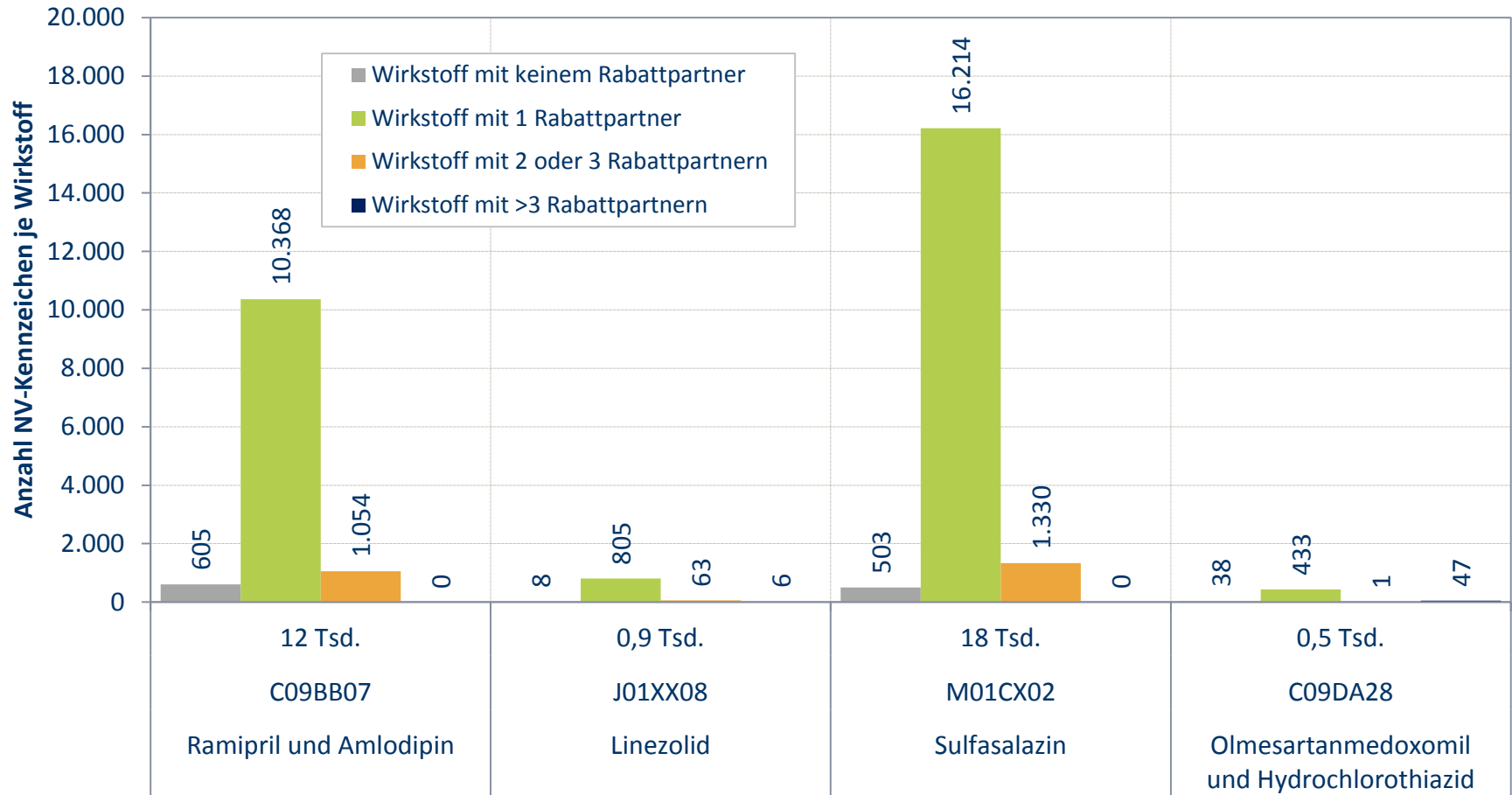
iGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (2)



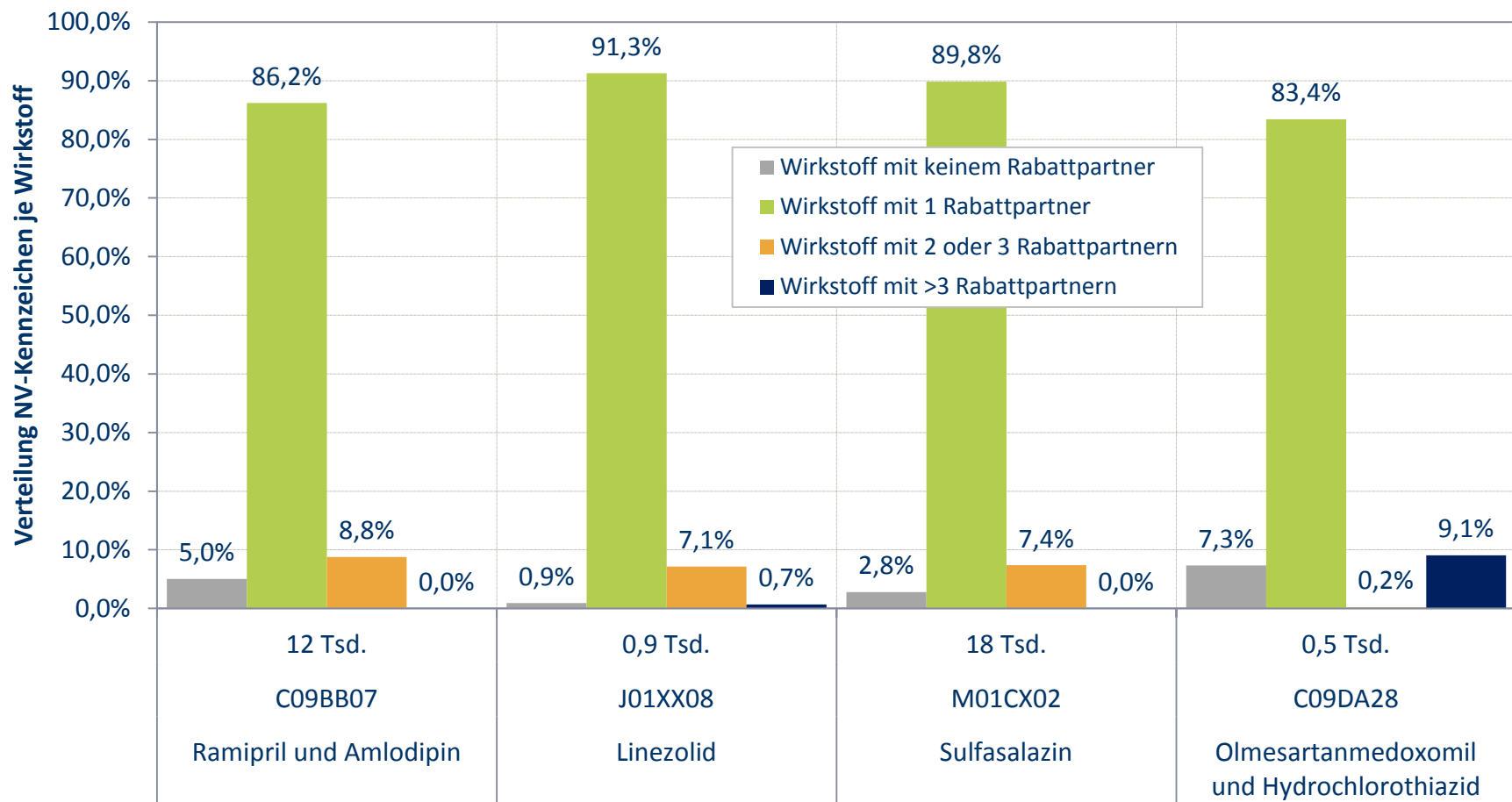
IGES Berechnungen nach Daten von Insight Health

Anzahl NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (3)



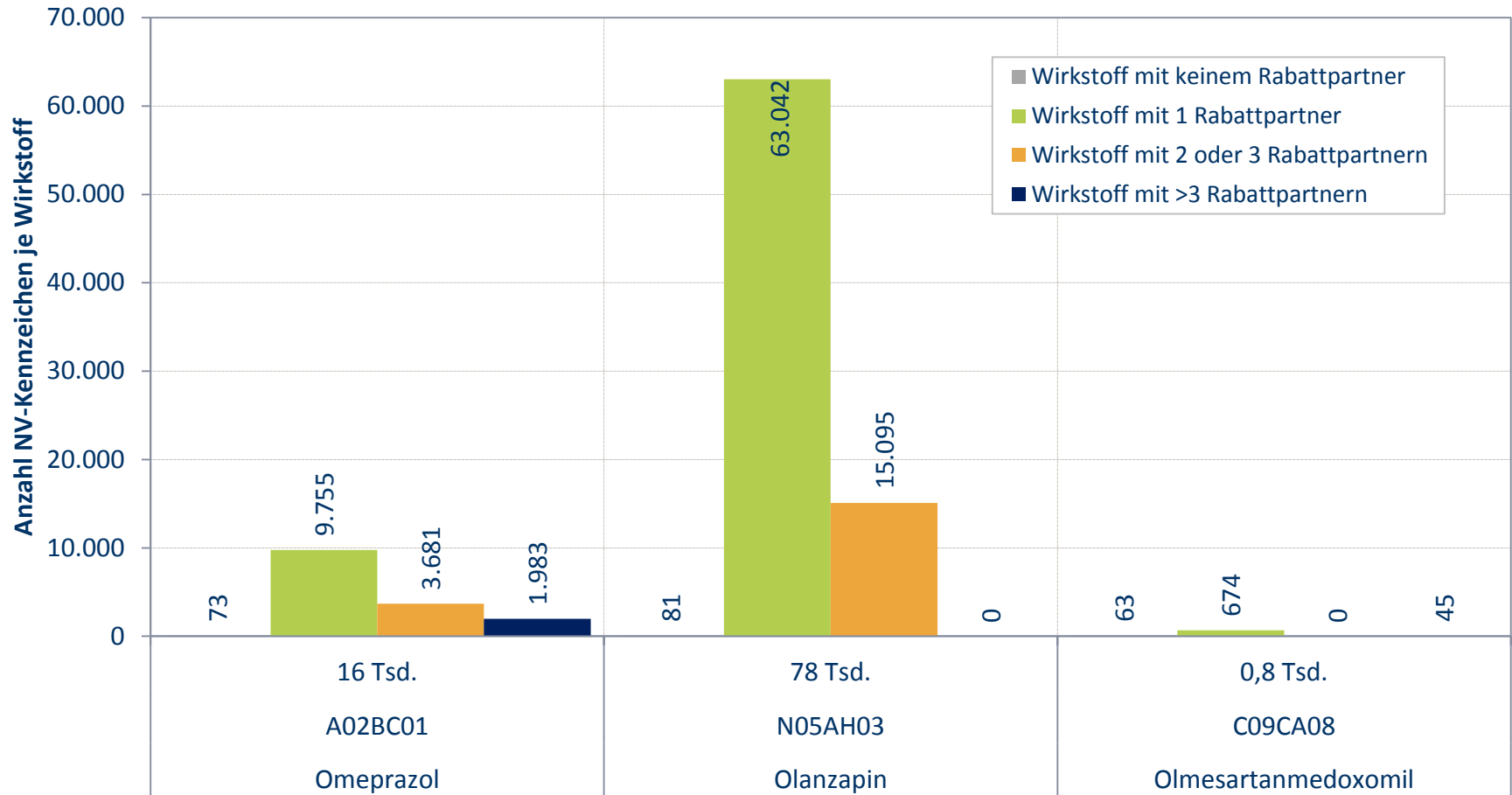
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (3)



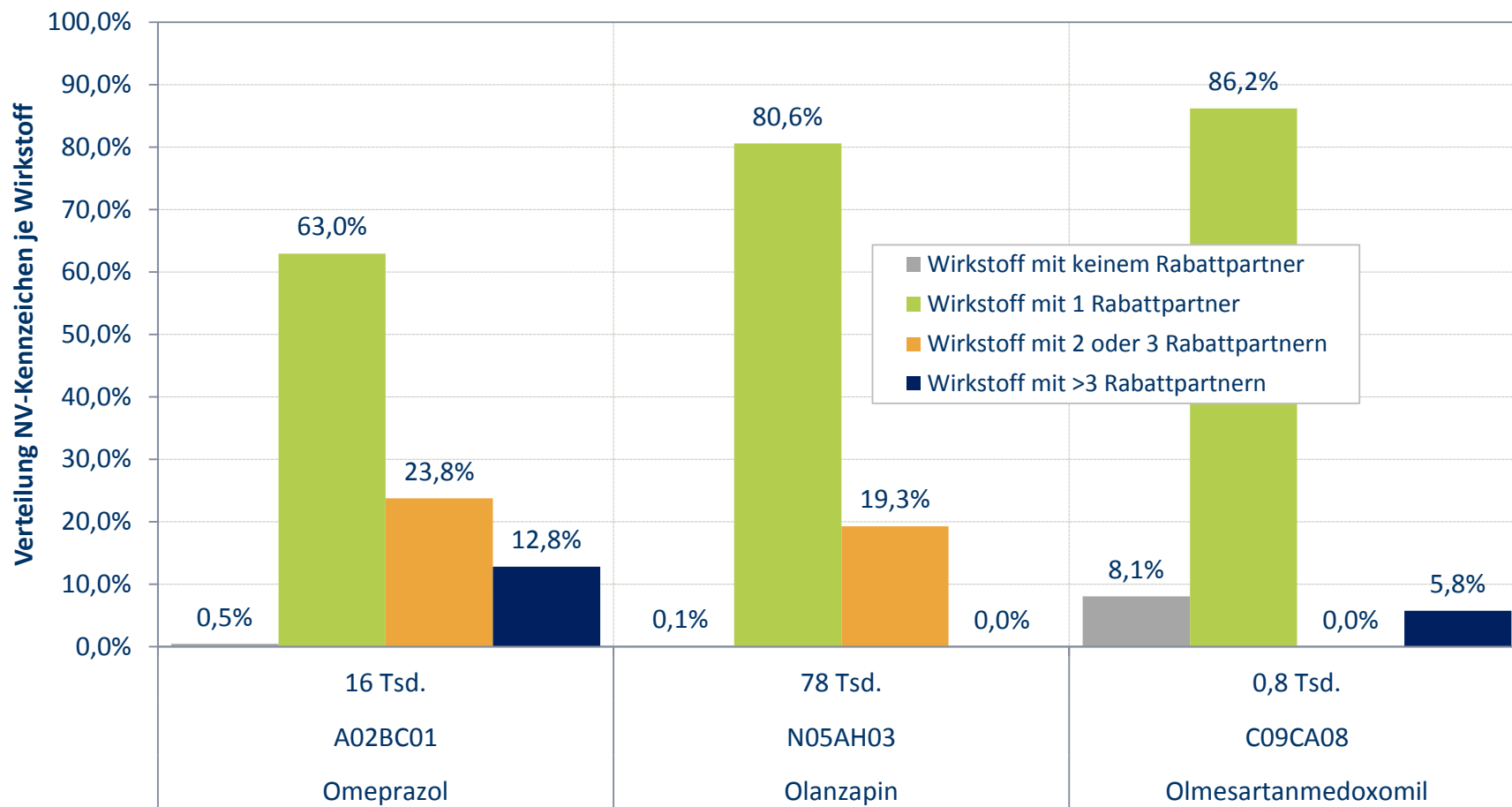
IGES Berechnungen nach Daten von Insight Health

Anzahl NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (4)



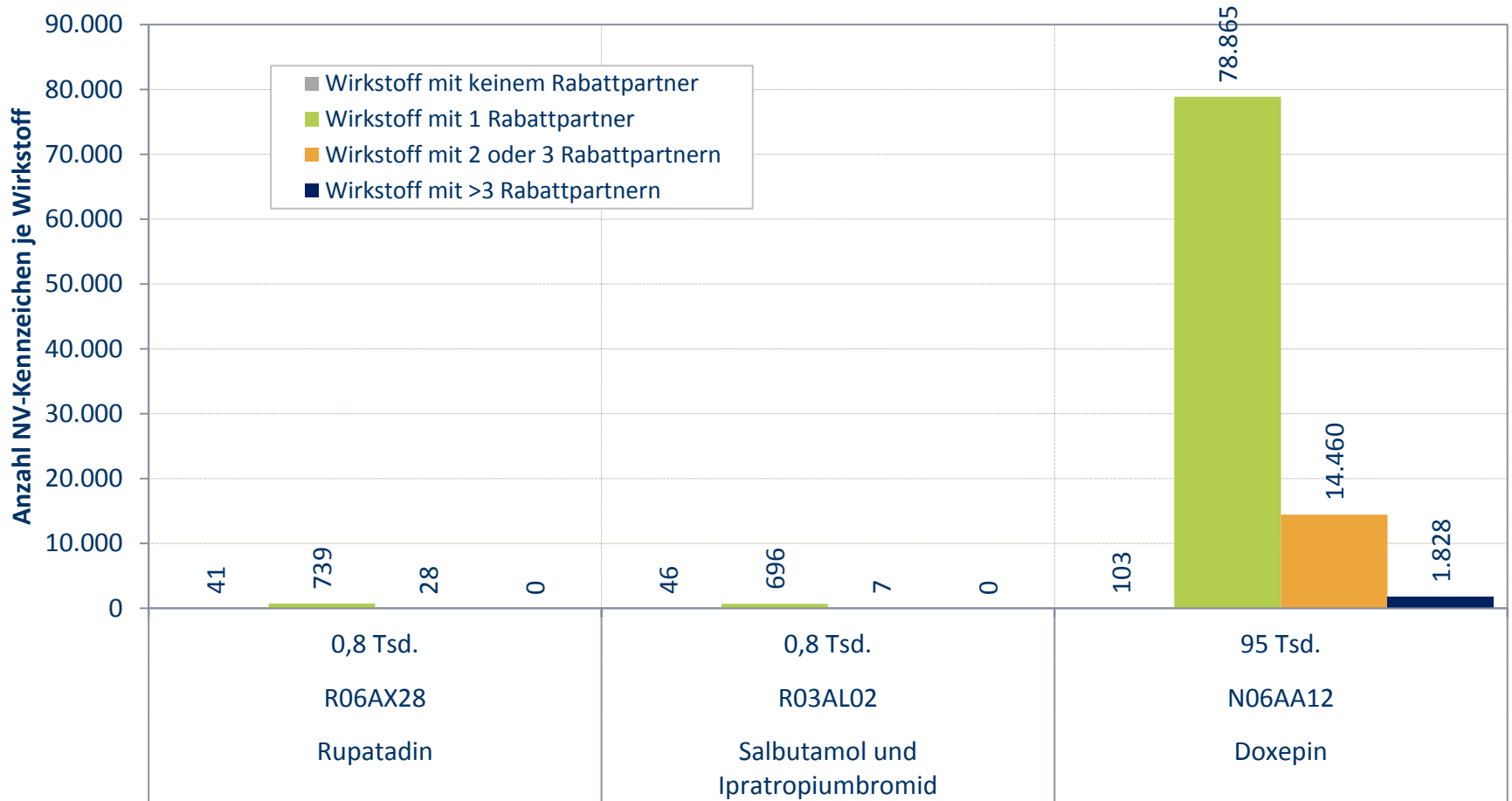
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (4)



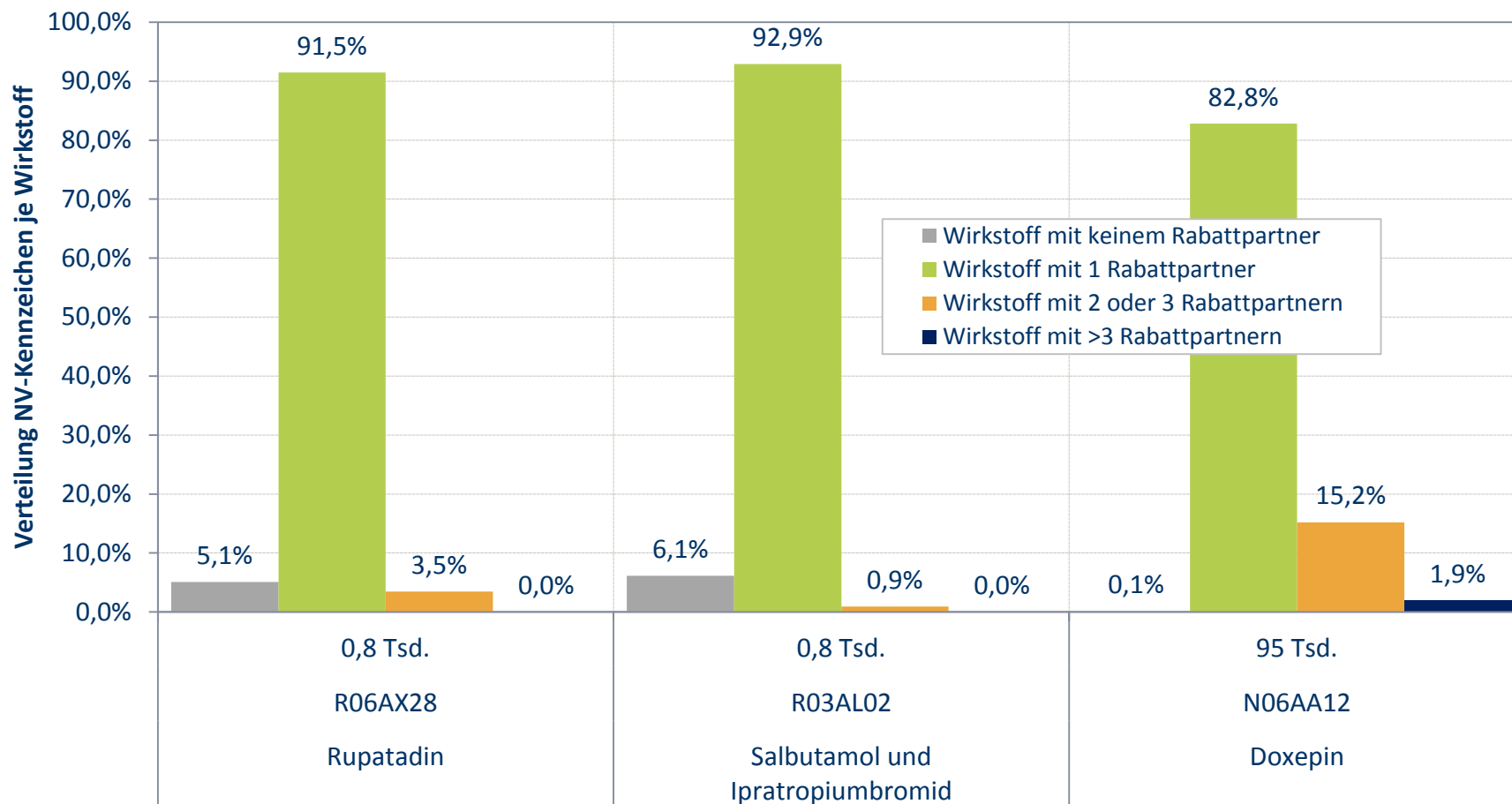
IGES Berechnungen nach Daten von Insight Health

Anzahl NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (5)



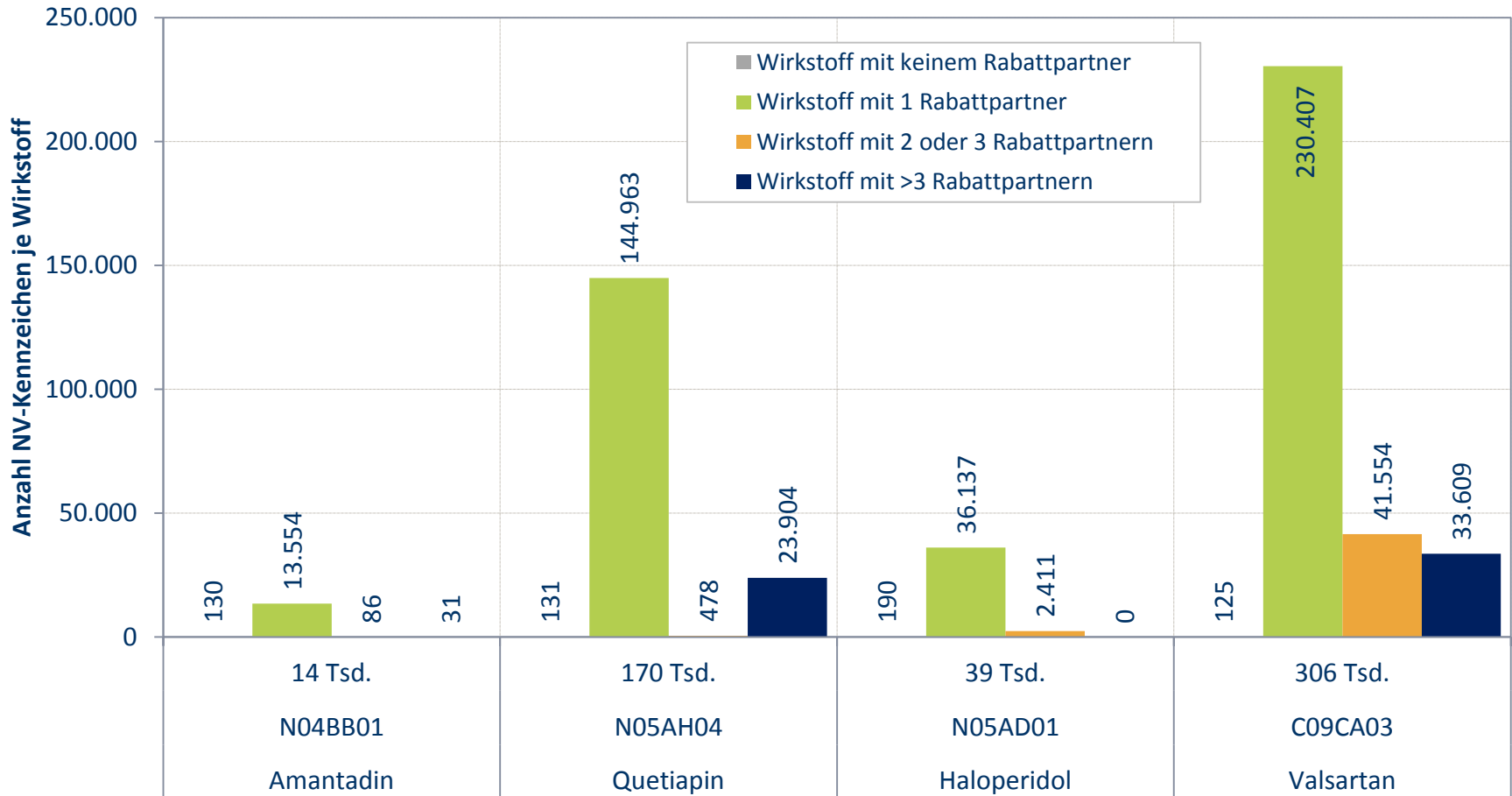
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (5)



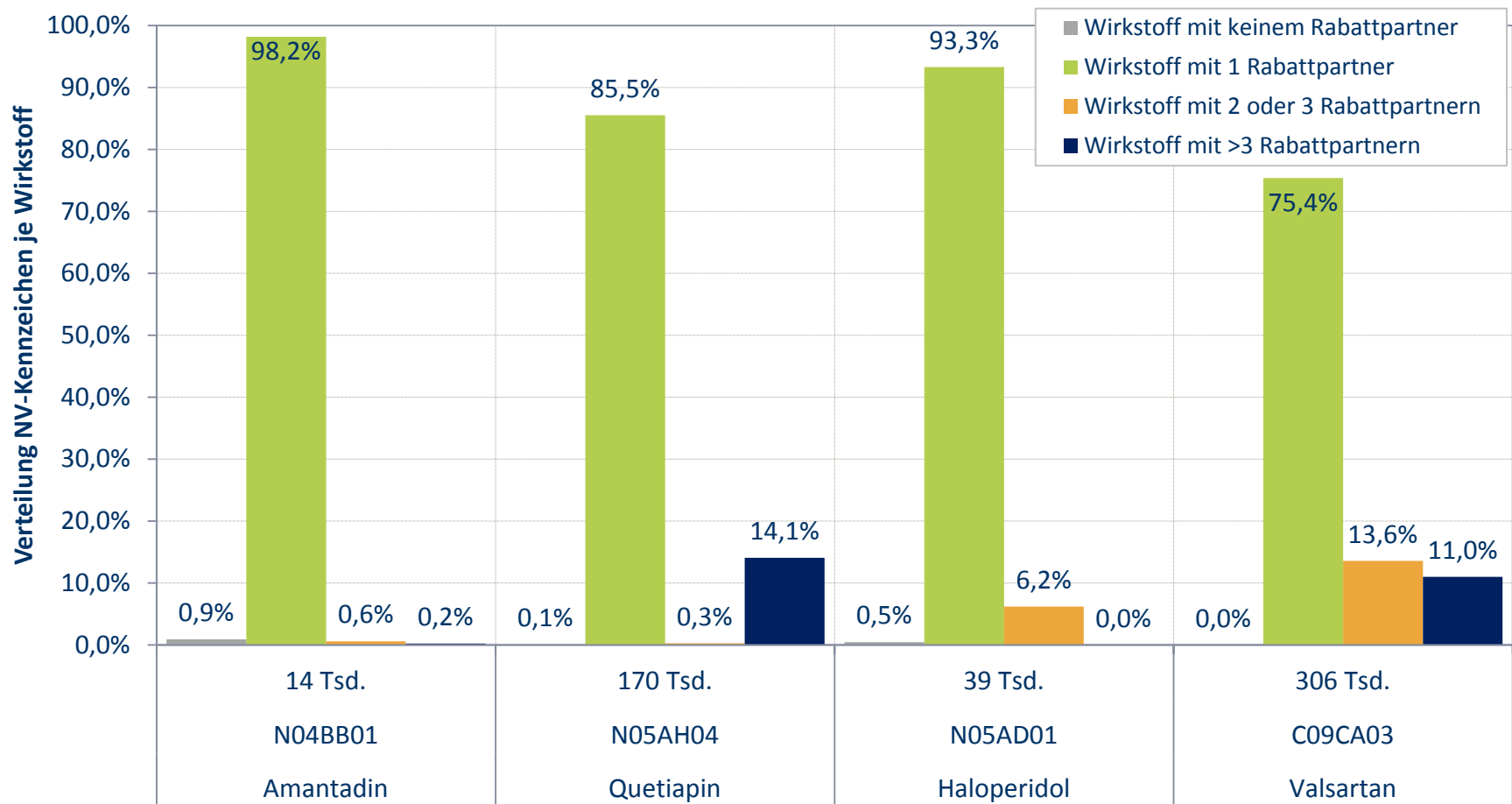
IGES Berechnungen nach Daten von Insight Health

Anzahl NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (6)



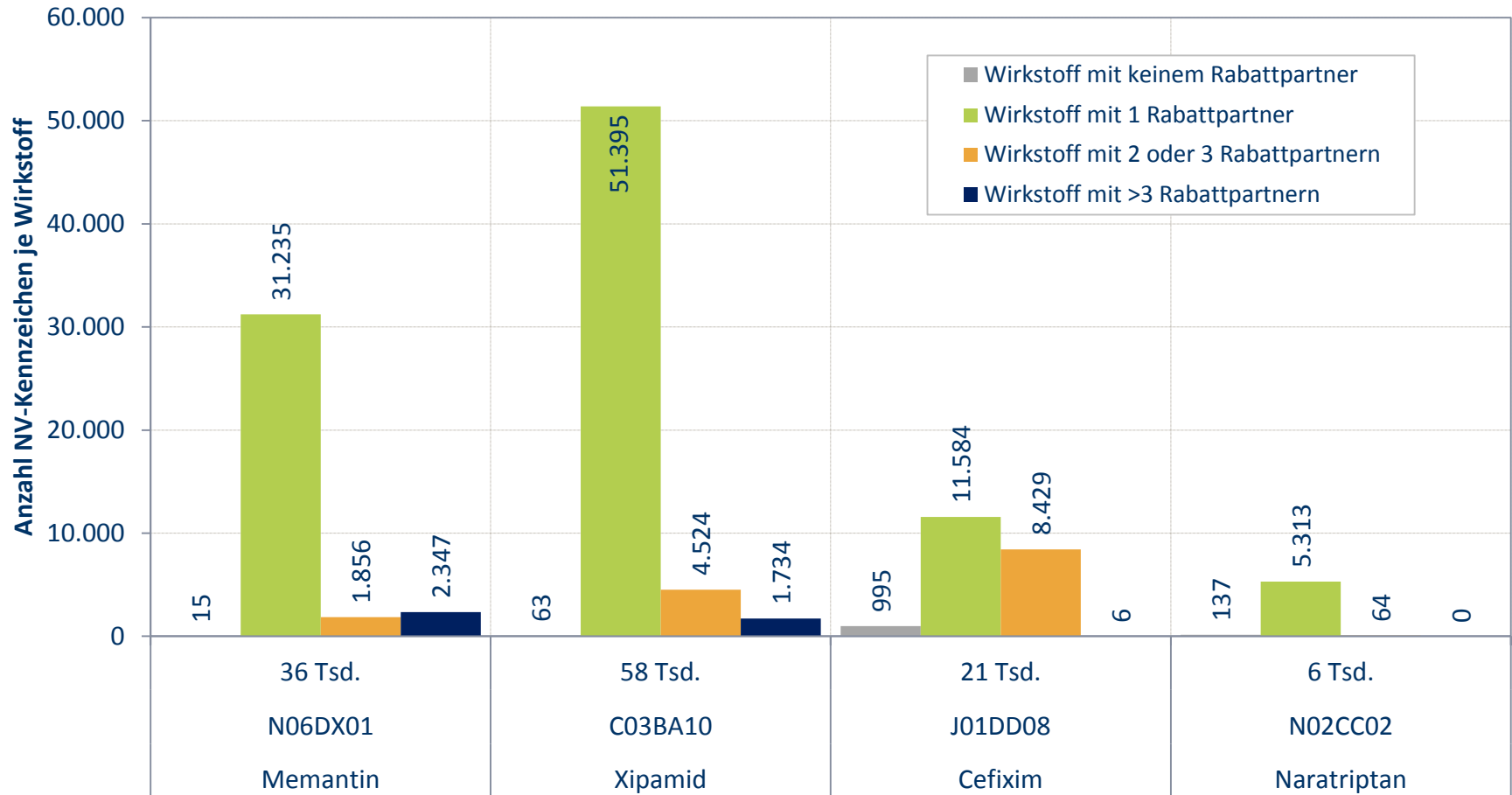
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (6)



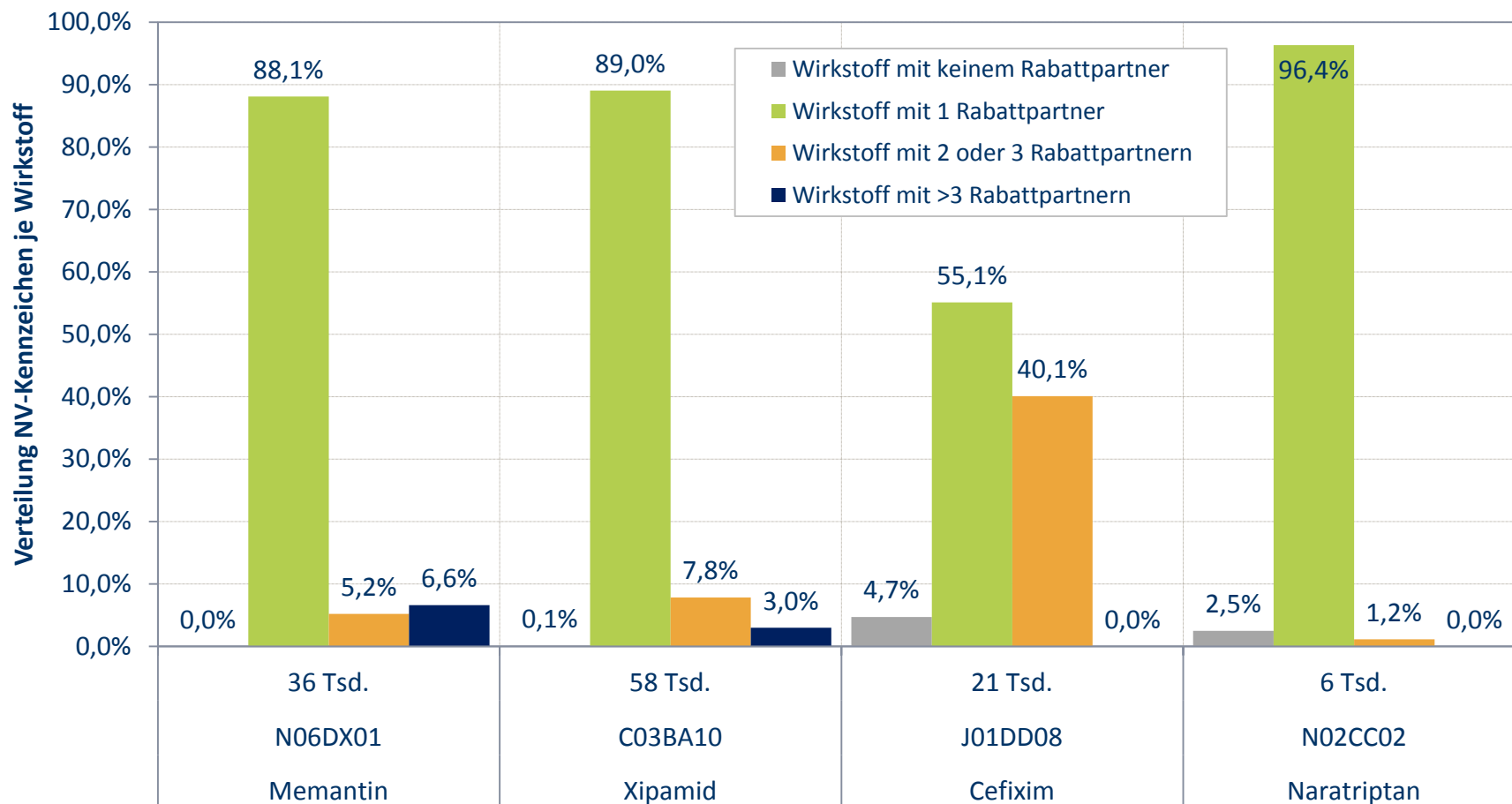
IGES Berechnungen nach Daten von Insight Health

Anzahl NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (7)



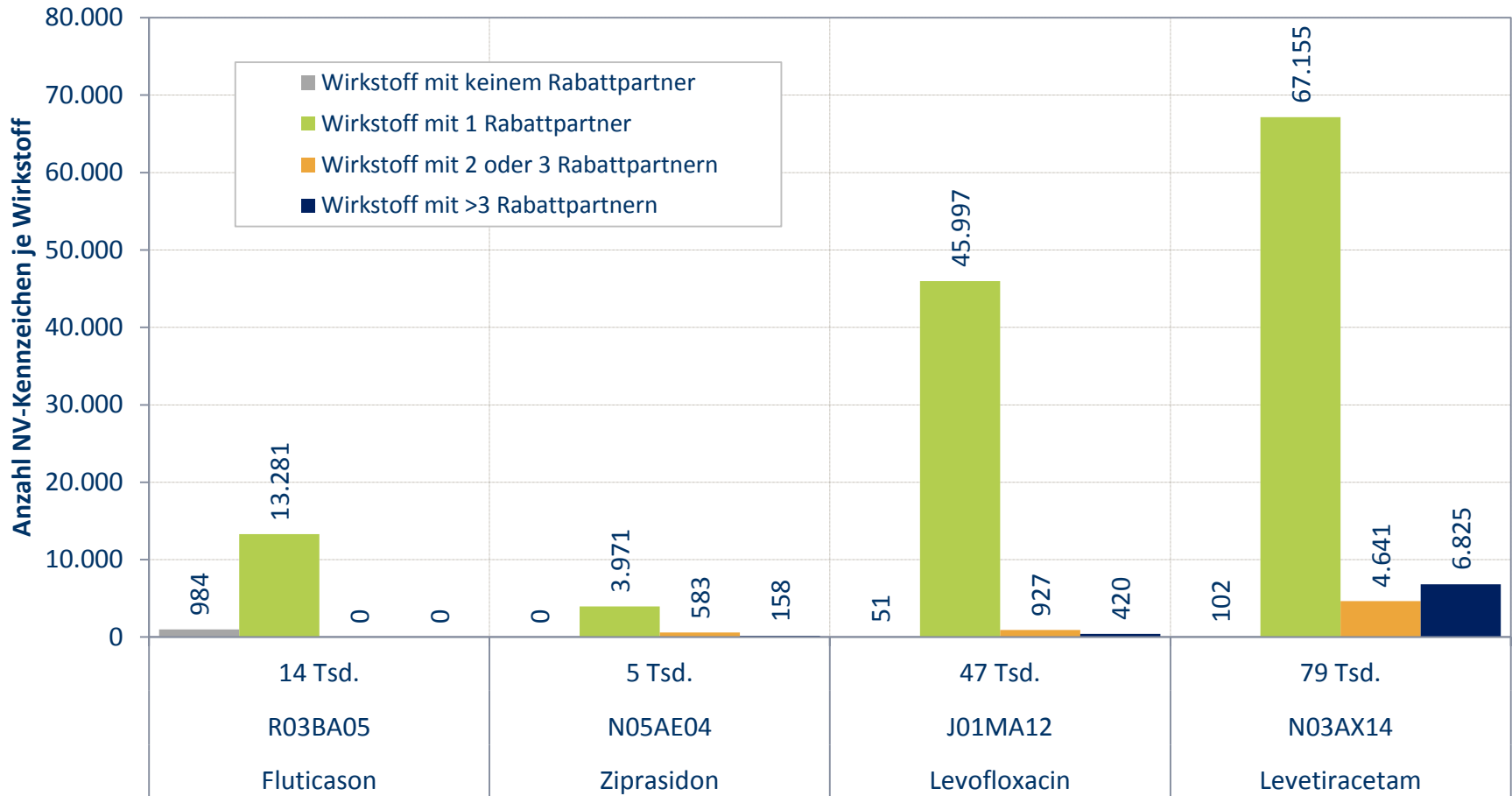
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (7)



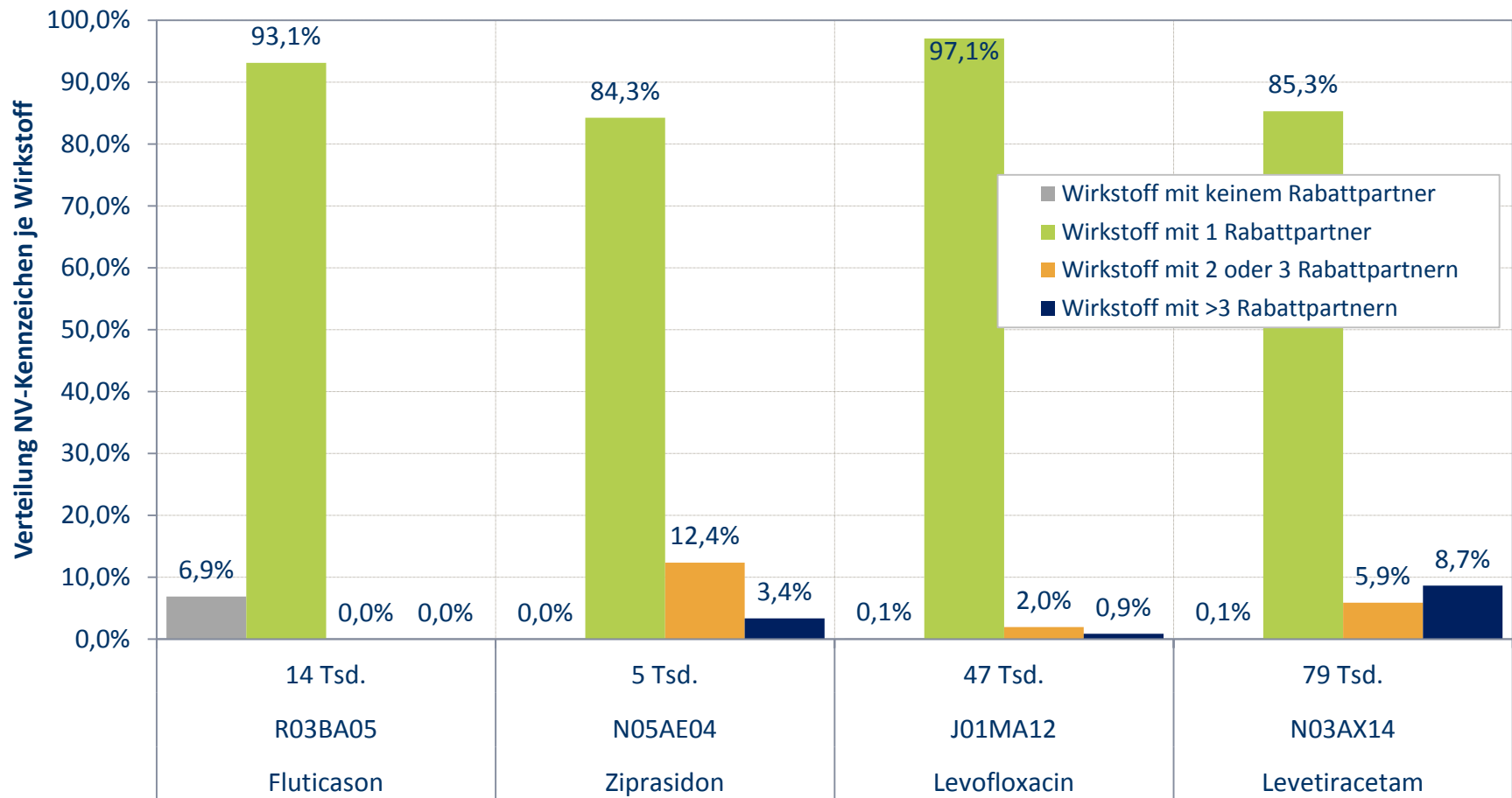
IGES Berechnungen nach Daten von Insight Health

Anzahl NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (8)



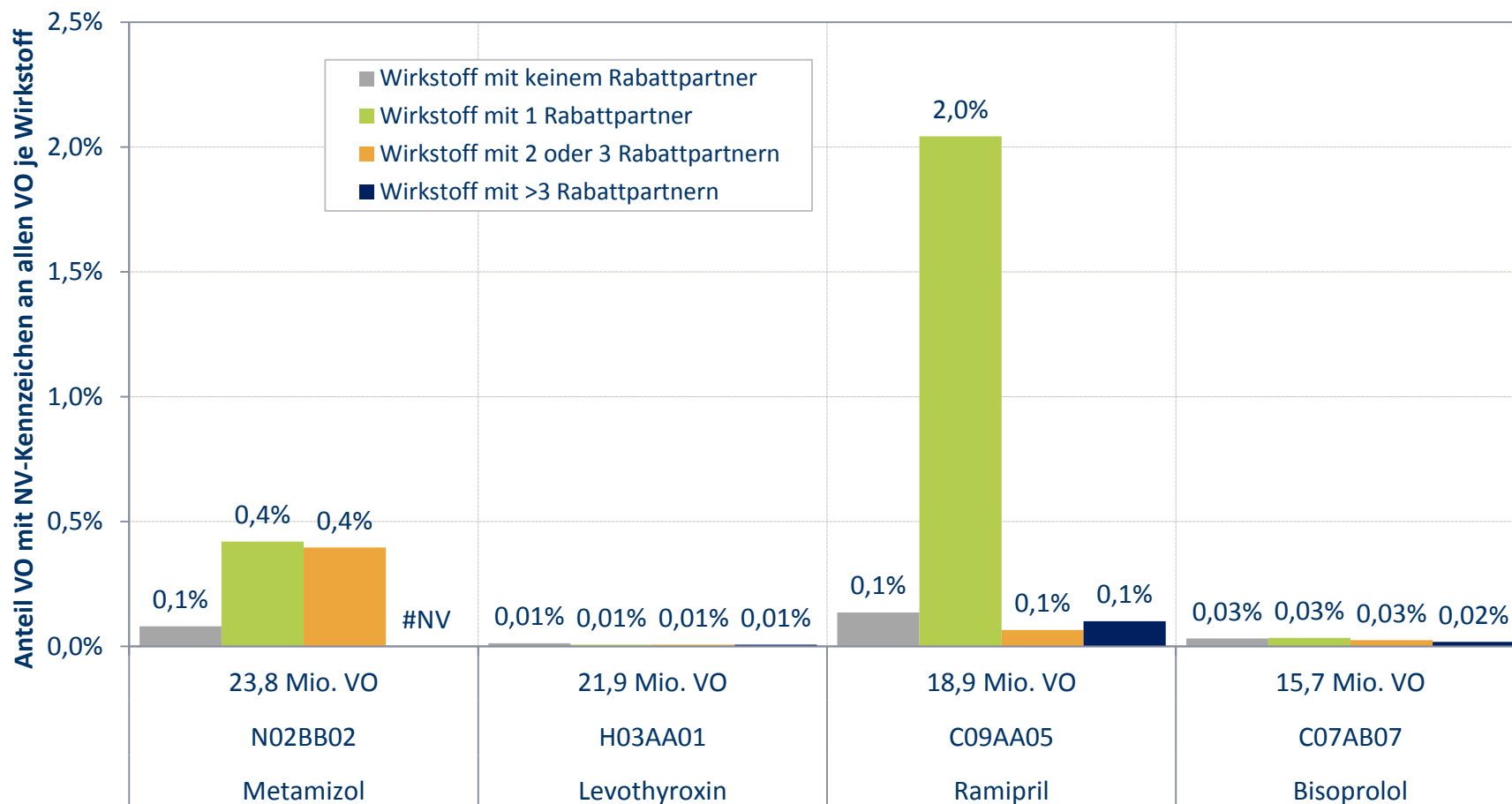
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen innerhalb eines Wirkstoffes: Kategorisierung nach Hersteller und Anzahl der Rabattpartner (8)



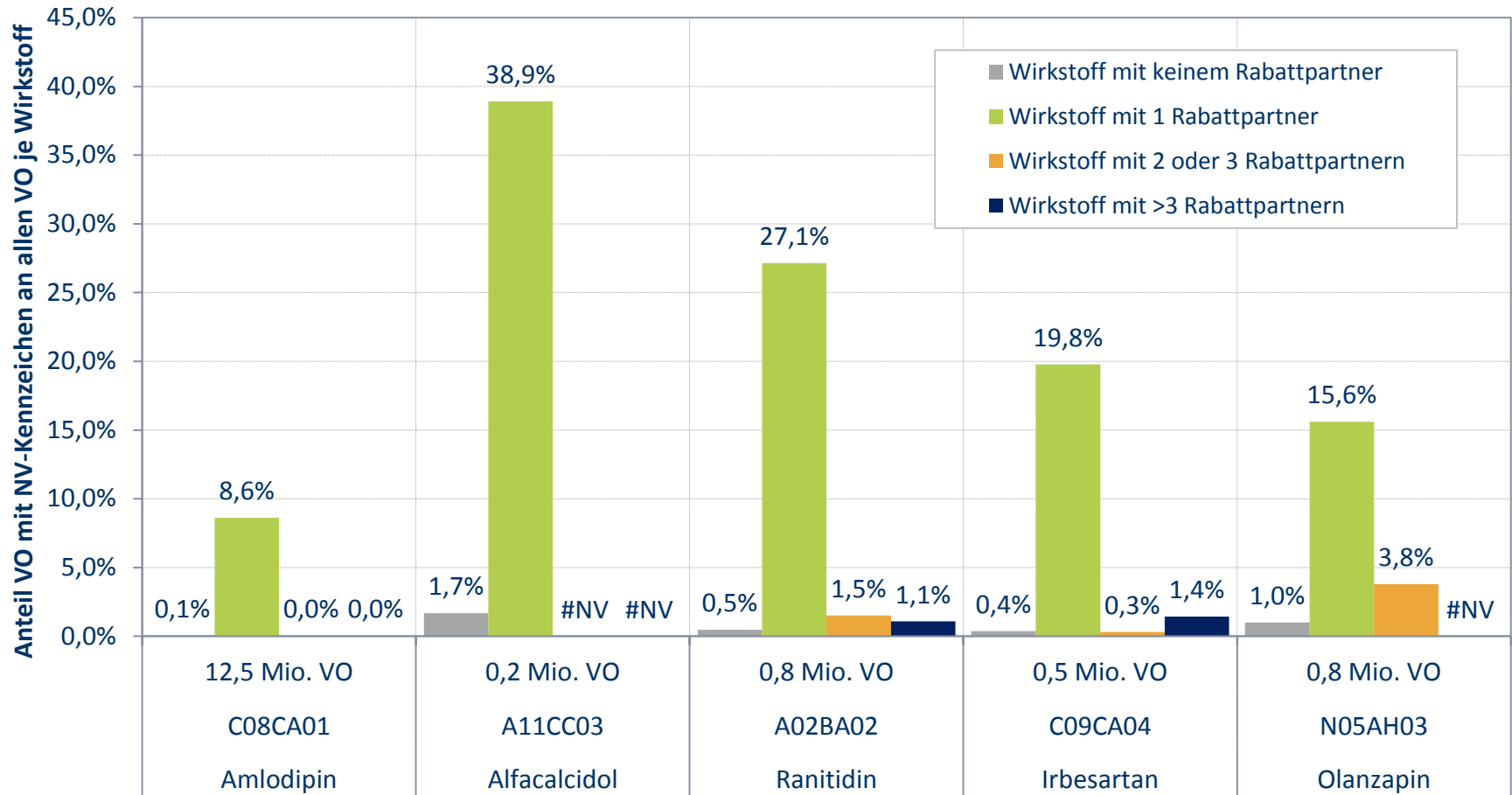
IGES Berechnungen nach Daten von Insight Health

Anteil NV-Kennzeichen an den VO je Wirkstoff – Kategorisierung nach Hersteller und Anzahl der Rabattpartner (1)



IGES Berechnungen nach Daten von Insight Health; #NV = keine NV-Kennzeichnung in der Kategorie

Anteil NV-Kennzeichen an den VO je Wirkstoff – Kategorisierung nach Hersteller und Anzahl der Rabattpartner (2)



IGES Berechnungen nach Daten von Insight Health; #NV = keine NV-Kennzeichnung in der Kategorie

Details zu Alfacalcidol

Wirkstärke	DAR	Hersteller	Konzern	VO	VO rabattiert	VO mit NV-Kennz.	NV- Kennz./all e VO
0,25; 0,5 und 1 µg	oral fest	1 A Pharma	Novartis	549.684	192.912	301.500	54,8%
0,25; 0,5 und 1 µg	oral fest	Aristo Pharma	Aristo	659.232	655.356	2.688	0,4%
0,25; 0,5 und 1 µg	oral fest	Teva	Teva	504.336	179.748	133.824	26,5%
0,25; 0,5 und 1 µg	oral fest	Hexal	Novartis	469.692	0	386.220	82,2%
0,25; 0,5 und 1 µg	oral fest	Leo	Leo	107.304	0	38.256	35,7%
2 µg	oral flüssig	Leo	Leo	48.576	0	60	0,1%
1 und 2 µg	parenteral	Leo	Leo	36.936	0	0	0,0%
0,25 und 1 µg	oral fest	Medice Arzn.	Medice	36.420	0	27.000	74,1%
0,25 und 1 µg	oral fest	ratiopharm	Teva	106.140	0	78.972	74,4%

IGES Berechnungen nach Daten von Insight Health

Details zu Olanzapin: Rabattverträge nur mit 7 von 24 Herstellern

Hersteller	Konzern	VO	VO rabattiert	VO mit NV- Kennz.
Basics	Sun Pharmaceutical Industries	3447012	3413508	8448
Heunet	Torrent	2156052	1477104	208620
Aurobindo	Aurobindo	741036	701820	21156
Glenmark	Glenmark	537279	465975	25671
TAD Pharma	Krka	287424	180828	6984
axcount	Bristol Laboratories	166044	152376	6084
Heumann	Torrent	319452	63408	33528
1 A Pharma	Novartis	596112	0	198588
biomo	Mothes	364804	0	174876
Hormosan	Hormosan	285732	0	131016
Neuraxpharm	Neuraxpharm	195072	0	24600
ABZ Pharma	Teva	182931	0	57324
ratiopharm	Teva	163152	0	19980
Hexal	Novartis	89124	0	10032
Lilly	Lilly	73440	0	132
Hennig	Hennig	49140	0	5232
PUREN Pharma	Aurobindo	39708	0	4344
betapharm	Reddy's, Dr.	14652	0	1428
Zentiva Pharma	Sanofi-Aventis	5976	0	108
Aliud	Stada AG	1440	0	204
Aristo Pharma	Aristo	492	0	72
AAA Pharma	Woerwag	12	0	0
Sun Pharmac.G.	Sun Pharmac.G.	0	0	0
Stadapharm	Stada AG	0	0	0

7.654.299 VO

2.061.787 VO

IGES Berechnungen nach Daten von Insight Health

4. Zusammenfassung

ATC-Konzept für die Auswertung ist valide **IGES**

- Analyse ist auf Basis von Aut-Idem-Gruppen nicht möglich
 - Information zu Aut-Idem-Konformität für weniger als die Hälfte aller Verordnungen
 - Mehrheit der Verordnungen mit NV-Kennzeichen ohne Information zu Aut-Idem-Konformität
- Analyse basiert daher auf ATC-Konzept: Anzahl Rabattpartner je Kasse wurde je Wirkstoff (definiert durch ATC7-Steller) bestimmt
- ATC-Konzept ist valide
 - Für einen hohen Anteil von Wirkstoffen sind für eine Kasse jeweils alle zugehörigen PZN eines Herstellers rabattiert
 - Nicht rabattierte PZN eines Wirkstoffs bei einem Hersteller betreffen häufig PZN, die für die ambulante Verordnung irrelevant sind (bspw. Klinikpackungen oder spezielle Darreichungsformen)
 - Nur bei wenigen Wirkstoffen führt das ATC-Konzept zur Unschärfe, weil je Wirkstoff und Hersteller ein relevanter Teil von PZN nicht rabattiert ist. Dies betrifft allerdings bei den meisten Kassen weniger als 5% aller Verordnungen.

Hoher Rabattquoten und insgesamt Hinweis auf geringe Nicht-Verfügbarkeit

- Rund 60% aller betrachteten Verordnungen waren rabattiert
- Bezogen auf alle betrachteten Verordnungen hatten 0,6% aller Verordnungen ein NV-Kennzeichen
- Für die ausgewählten ATC7-Steller betrug der Anteil der NV-Kennzeichen, an den Verordnungen des Wirkstoffes, zwischen 38,5% und 0,01%
- Die Unterschiede zwischen den Kassenarten waren gering

Trend: Je mehr Rabattpartner, desto geringer ist die Nichtverfügbarkeit (NV)

- Insgesamt war der NV-Anteil geringer, wenn ein Kostenträger für einen Wirkstoff 2 oder 3 Rabattpartner hatte
- Bei mehr als 3 Rabattpartnern zeigte sich der Trend nicht so ausgeprägt, allerdings war der Anteil von Verordnungen mit mehr als 3 Partnern am geringsten
- Bei einigen Wirkstoffen (z.B. Amlodipin, Alfacalcidol, Ranitidin, Irbesartan, Olanzapin) war der Anteil von NV-Kennzeichen bei Kassen mit nur einem Rabattpartner extrem hoch (9 bis 39%), bei Kassen mit mindestens zwei Rabattpartnern erheblich geringer
- Auch die Wirkstoff-bezogene Betrachtung zeigt, dass mehr als 3 Rabattpartner den NV-Anteil nicht zwingend senken

IGES Institut

Dr. Ariane Höer (ariane.hoer@iges.com)

Lukas Maag (lukas.mag@iges.com)

www.iges.com

[deutsche-apotheker-zeitung.de](https://www.deutsche-apotheker-zeitung.de)

BMG verteidigt Exklusivverträge und Rabattvertragssystem

Benjamin Rohrer

3-4 Minuten

Doch auch dies dürfte nicht der letzte Stand sein. Nach Informationen von DAZ.online stehen die Regierungsfaktionen und das BMG weiterhin in Kontakt diesbezüglich. Denn: Union und SPD hatten dem Ministerium sogenannte Prüfbitten an die Hand gegeben – ein Papier, in dem mehrere Neuregelungsvorschläge und -ideen enthalten sind. DAZ.online liegen die Kommentierungen des BMG zu diesen Vorschlägen vor. Und daraus geht hervor, dass das Ministerium zumindest derzeit eine verpflichtende Mehrfachvergabe ablehnt, diese „kann Lieferengpässe nicht verhindern“, heißt es dort.

Gegen die obligatorische Mehrfachvergabe sprechen aus Sicht des Ministeriums mehrere Punkte. Einerseits werden „pauschale, gesetzliche Vorgaben für Rabattverträge“ der Komplexität des Pharmamarktes nicht gerecht. Die vergaberechtlichen Instrumente zur Beschaffung von Arzneimitteln würden „unangemessen“ eingeschränkt. Und: Schon jetzt entscheide sich die Mehrzahl der Kassen für das Mehrpartnermodell. „Nach Pro Generika wurden 2018 bereits ca. 70 Prozent der Rabattverträge im Zwei- und Drei-Partnermodell vergeben“, heißt es weiter. Aus Sicht des BMG würde eine Streichung der Exklusivverträge auch „den

Wettbewerb schwächen, voraussichtlich zu höheren Preisen führen und damit das Einsparpotential der Rabattverträge grundsätzlich in Frage stellen“. Dass Mehrfachvergaben grundsätzlich Engpässe vermeiden, bezweifelt das Ministerium. Schließlich gebe es schon bei der Wirkstoffherstellung in China und Indien häufig Monopole. Schon dort könnten die Engpässe ausgelöst werden, heißt es. Mit dieser Positionierung stellt sich das BMG gegen Forderungen aus beiden Regierungsfractionen: Sowohl [die Union](#) als auch die [SPD im Bundestag](#) hatten die Streichung der Exklusivverträge in Positionspapieren gefordert.

Das BMG schlägt auch einen weiteren Vorschlag aus, den die Unionsfraction ins Spiel gebracht hatte. [Zur Erinnerung: In einem Positionspapier hatte die Union vorgeschlagen, dass Rabattverträge künftig nur noch kassenübergreifend und auf Landesebene ausgeschrieben werden sollen.](#) Die Union wollte damit gegen die Vielzahl der Verträge vorgehen und insbesondere die Arbeit der Apotheker erleichtern. Doch das BMG will hier keine größeren Änderungen am Rabattvertragssystem vornehmen. Es gebe mehrere Gründe, die gegen eine „Zentralisierung des Systems“ durch eine einheitliche Vergabe sprechen. Unter anderem würde der Wettbewerb zwischen den Kassen geschwächt. So könnten „Krankenkassen-Kartelle“ auf der einen und „Herstellermonopole“ auf der anderen Seite entstehen. Kleinere und mittelständische Unternehmer würden somit benachteiligt. Außerdem zeige das Beispiel der Versorgung mit parenteralen Zubereitungen aus Fertigarzneimitteln in der Onkologie, dass sich einheitliche Ausschreibungen nicht bewährt hätten, so das Ministerium.

Melanie Schröder · Jonas Lohmüller ·
Carsten Telschow · Katja Niepraschk-von Dollen ·
Anette Zawinell · Jana Bauckmann



Der GKV-Arzneimittelmarkt Bericht 2020

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Melanie Schröder, Jonas Lohmüller, Carsten Telschow,
Katja Niepraschk-von Dollen, Anette Zawinell, Jana Bauckmann

Wissenschaftliches Institut der AOK (WIdO)
im AOK-Bundesverband GbR
Rosenthaler Str. 31, 10178 Berlin

Geschäftsführender Vorstand:
Martin Litsch (Vorsitzender)
Jens Martin Hoyer (stellv. Vorsitzender)
<http://www.aok-bv.de/impressum/index.html>

Aufsichtsbehörde:
Senatsverwaltung für Gesundheit, Pflege
und Gleichstellung –SenGPG–
Oranienstraße 106, 10969 Berlin

Ansprechpartner im
Wissenschaftlichen Institut der AOK (WIdO):
Dr. Carsten Telschow, 030 34646-2111
Dr. Melanie Schröder, 030 34646-2152

Redaktionelle Bearbeitung: Melanie Hoberg, Susanne Sollmann
Satz: Anja Füssel, Melanie Hoberg
Grafik: KomPart
Titelfoto: KomPart



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E-Mail: wido@wido.bv.aok.de
Internet: <http://www.wido.de>

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Vorwort

Das Wissenschaftliche Institut der AOK (WiDO) berichtet seit 1985 jährlich über aktuelle Trends des Arzneimittelmarktes und der Arzneimittelversorgung der aktuell mehr als 70 Mio. GKV-Versicherten. Zwischenzeitlich konnte, basierend auf den jährlich mehr als 800 Mio. Arzneimittelverordnungsdaten sowie den im WiDO verwendeten Methoden und aufgebauten Klassifikationen, ein umfassendes Berichtswesen aufgebaut werden.

Die vorliegende differenzierte Beschreibung des GKV-Arzneimittelmarktes gibt einen umfangreichen Einblick in das Verordnungsgeschehen und beleuchtet die Hintergründe der aktuellen Marktentwicklungen. Neben dem Geschehen im Gesamtmarkt werden die zentralen Marktsegmente der Patentarzneimittel, Biologika und Biosimilars sowie der Orphan Drugs differenziert dargestellt. Auch die Liefersicherheit von Arzneimitteln, die Auswirkungen der Arzneimittelrabattverträge, die Zusammensetzung der Distributionskosten und die Marktdaten pharmazeutischer Hersteller werden behandelt.

Der Bericht wird ergänzt durch umfangreiches statistisches Material zum Arzneimittelmarkt 2019, das auf unserer Webseite zum kostenfreien Download angeboten wird. Dieses umfasst unter anderem detaillierte Ergebnisse der Komponentenzerlegung des Umsatzes, mit deren Hilfe die Bewegungen im Arzneimittelmarkt im Jahr 2019 analysiert werden können. Dazu kommen Übersichten über Arzneiverordnungen nach Facharztgruppen sowie nach Altersgruppen und Geschlecht der Versicherten, die einen differenzierten Einblick in das Verordnungsgeschehen des Jahres 2019 geben. Darüber hinaus werden die methodische Herangehensweise und die verschiedenen Klassifikationen erläutert.

Des Weiteren ermöglicht das WiDO mit dem PharMaAnalyst auf unserer Webseite flexible Analysen zu den verordnungs- und umsatzstärksten Arzneimitteln sowie Wirkstoffen und Wirkstoffgruppen der Jahre 2016 bis 2019. Mit der Bereitstellung dieser Verordnungsdaten aller GKV-Versicherten unterstützt das WiDO unter anderem auch die Herausgeber des Arzneiverordnungs-Reports. Aber auch verschiedene internationale Projekte wie beispielsweise die Antibiotikasurveillance des European Centre for Disease Prevention and Control (ECDC) und die Routineberichterstattung der OECD greifen auf diese Ergebnisse zurück. Auch bei der nationalen Dauerberichterstattung des Bundesgesundheitsministeriums oder des Statistischen Bundesamtes helfen diese Daten, den deutschen Arzneimittelmarkt transparent zu machen.

Danken möchten wir allen Kolleginnen und Kollegen im WIdO, die an der Publikation beteiligt waren und in beeindruckender Weise den Beleg erbracht haben, dass ein solches Projekt trotz der zahlreichen Pandemie-bedingten Herausforderungen von den heimischen Arbeitsplätzen aus durchgeführt werden kann. Neben dem Team der Autorinnen und Autoren, die in knapper Zeit die profunden Analysen erstellt und die Ergebnisse beschrieben haben, sind auch alle Kolleginnen und Kollegen des Forschungsbereichs Arzneimittel im WIdO mit Kenan Ajanovic, Sandra Blankenburg, Sandra Heric, Heike Hoffmeister, Mehmet Kaplankiran, Birol Knecht, Ursula Meis, Ralf Mühlhaus-Priesterjahn, Mandy Orlamünde, Sabine Roggan, Manuela Stallauke, Manuela Steden und Sylvia Steinhaus zu nennen. Der Dank geht ebenfalls an Henriette Weirauch für die Unterstützung bei der Visualisierung wie auch an Frau Sybilla Weidinger vom KomPart-Verlag, die die Grafiken erstellt hat. Bedanken möchten wir uns gleichermaßen bei Roman Asriel, Anja Füssel, Melanie Hoberg, Anja Michels und Susanne Sollmann in unserem Backoffice, ohne deren Unterstützung mit Lektorat und Satz diese Buchpublikation nicht möglich gewesen wäre.

Berlin, im Juli 2020
Geschäftsführung des WIdO

Zentrale Ergebnisse auf einen Blick

Mit einem Anstieg von 5,7 % auf nun 46,7 Mrd. € im **Gesamtmarkt** setzt sich der Trend zu höheren Umsätzen der Gesetzlichen Krankenversicherung (GKV) für Arzneimittel stärker fort als in den Vorjahren. Die Anzahl der Verordnungen ist dabei nur geringfügig angestiegen. Eine Verordnung hat im Jahr 2019 durchschnittlich 67,73 € an Bruttoumsatz gekostet, was einem Anstieg um 4,5 % gegenüber dem Vorjahr entspricht. Dabei ist der Umsatzanstieg nicht auf eine allgemeine Teuerung der Arzneimittel zurückzuführen (Preiseffekt: -0,8), sondern maßgeblich auf den **Struktureffekt** (5,8 %), der 2019 die Verschiebung der Verordnungen innerhalb einer Arzneimittelgruppe hin zu teureren Arzneimitteln beschreibt. Besonders ausgeprägt ist der Struktureffekt bei den Wirkstoffgruppen der Onkologika, der Immunsuppressiva und der Antithrombotischen Mittel. Aus einem Ranking der nettokostenstärksten Arzneimittel geht hervor, dass das Immuntherapeutikum Humira nach dem Patentauslauf 2018 seinen jahrelangen Spitzenplatz zugunsten von Eliquis, einem der direkten oralen Antikoagulantien (DOAK), eingebüßt hat.

Insbesondere die Preise der neuen, **patentgeschützten Arzneimittel** entwickeln dabei zunehmend eine eigene Dynamik. So kostet heute ein Arzneimittel, das in den letzten drei Jahren auf den Markt gekommen ist, mit durchschnittlich knapp 14.000 € rund dreimal so viel wie ein „normales“ Patentarzneimittel. Der Umsatzanteil noch unter Schutzrechten stehender Arzneimittel von 47 % am Gesamtmarkt blieb über die letzten Jahre annähernd konstant und steht 2019 einem Verordnungsanteil nach Tagesdosen von 7 % gegenüber. Im Jahr 2010 waren es noch 43%.

Diese Entwicklungen vollziehen sich trotz des **Arzneimittelmarktneuordnungsgesetzes (AMNOG)**. Nach diesem Gesetz soll seit 2011 eine Frühe Nutzenbewertung mit anschließenden Preisverhandlungen dafür sorgen, dass der Preis eines neuen Arzneimittels an seinem Zusatznutzen für Patientinnen und Patienten orientiert ist. Dadurch werden Einsparungen mit Erstattungsbeiträgen realisiert, die für 2019 auf 3,6 Mrd. € zu beziffern sind. Allerdings könnte unter anderem eine Rückwirkung des Erstattungsbeitrags zum Tag der Markteinführung weitere Einsparungen ermöglichen.

Der sogenannte **Bestandsmarkt** ist durch patentgeschützte Arzneimittel ohne Konkurrenz gekennzeichnet, die vor 2011 auf den Markt gekommen sind. Dieses Segment wird durch ein Preismoratorium geregelt, das die Preise der betroffenen Arzneimittel zum Stichtag 1. August 2009 „einfriert“. Seit 2018 können Hersteller ihre Preise nun um die allgemeine Teuerungsrate des Vorjahres anpassen und so Preiserhöhungen durchsetzen. Zusammengefasst hat der **Inflationsausgleich** 2019 zu Mehrkosten in Höhe von 181 Mio. € geführt. Das zeigt, dass das Preismoratorium eine wirksame Durchsetzung von Preiserhöhungen in diesem Bereich verhindert und als Kostendämpfungsinstrument unverzichtbar ist.

Mit Nettokosten von 13,5 Mrd. € stellen die **Biologika** ein weiteres gewichtiges und mit einer Steigerung von 10 % gegenüber dem Vorjahr auch weiterhin stark wachsendes Marktsegment dar. Als Biologika (Biologicals, Biopharmazeutika) werden Arzneimittel bezeichnet, deren Wirkstoffe aus einem lebenden Organismus und meist nur mithilfe gentechnologischer Methoden hergestellt werden.

Sobald diese Arzneimittel patentfrei werden und über die europäischen Regularien **Biosimilars** zugelassen sind, wird auch ein Preiswettbewerb für Biologika ermöglicht. Die Marktdurchdringung dieser Nachahmer entwickelt sich mit durchschnittlich 44 % zwar positiv, sie liegt aber immer noch weit von den Nachahmeranteilen des generikafähigen Marktes entfernt. Neben einer kleineren Zweitanbieteranzahl im Vergleich zum generikafähigen Markt (durchschnittlich drei gegenüber acht Zweitanbietern 2019) fallen auch die Preisabstände im biosimilarfähigen Markt geringer aus. Wäre im Jahr 2019 konsequent das günstigste Präparat des biosimilarfähigen Marktes verordnet worden, hätten bis zu 792 Mio. € für die GKV eingespart werden können. Eine verpflichtende Substitution in der Apotheke, die im Jahr 2022 in Kraft treten soll, bietet Potenzial für weitere Einsparungen. Durch diese Regelung kann der Wettbewerb über Rabattverträge der Kassen in Gang gesetzt werden. Insgesamt zeigt sich eine ausgeprägte Heterogenität der bisherigen Biosimilaranteile über die Wirkstoffe nicht nur auf Ebene der GKV, sondern auch in einer **regionalen Betrachtung** über die verschiedenen Kassenärztlichen Vereinigungen (KV): Hier stehen Biosimilaranteile von bis zu 32 % wie bei den KVen Westfalen-Lippe, Bremen oder Niedersachsen Anteilen von maximal 12 % in Sachsen-Anhalt, Baden-Württemberg, dem Saarland und Sachsen gegenüber, wobei allerdings die regionalen Rahmenvereinbarungen zu berücksichtigen sind.

Die **Orphan Drugs**, also Arzneimittel gegen seltene Erkrankungen, sind mit lediglich 0,05 % aller verordneten Tagesdosen (DDD) im Jahr 2019 für knapp 10 % der ausgegebenen Nettokosten verantwortlich, was einem Nettokostenanstieg zum Vorjahr von 18,9 % entspricht. Die Nettokosten je Tagesdosis in Höhe von 223,13 € unterscheiden sich folglich deutlich vom Gesamtmarkt mit 1,00 € oder vom Patentmarkt mit 7,36 €. Insgesamt fällt auf, dass Arzneimittel, die eine Orphan-Designation erhielten, einen immer größeren Anteil an den Markteinführungen neuer Wirkstoffe einnehmen. Dies ist angesichts der Fülle an seltenen, schweren Erkrankungen erfreulich. Mit Blick auf die zu beobachtenden Indikationserweiterungen mehrerer Arzneimittel mit Blockbusterstatus und der erzielten Fortschritte in den punktuell molekularen Behandlungsmöglichkeiten, speziell in der Krebstherapie, sind die Kriterien für die öffentliche Förderung bei Zulassung wie auch die Sonderstellung im Rahmen der Frühen Nutzenbewertung von Arzneimitteln gegen seltene Erkrankungen zu hinterfragen.

Ein zentrales kostensenkendes Mittel stellen **Arzneimittelrabattverträge** dar. Seit 2003 haben die Krankenkassen mit dem § 130a Abs. 8 SGB V die Möglichkeit, mit Herstellern individuelle Rabattverträge abzuschließen. Seit dem 1. April 2007 sind die Apotheken auch verpflichtet, die kassenspezifischen Rabattverträge bei der Produktauswahl vorrangig zu bedienen, sofern die verordnende Ärztin oder der verordnende Arzt eine Substitution nicht ausschließt. Im Jahr 2019 waren unter den insgesamt 2.472 ambulant verordneten Wirkstoffen und Wirkstoffkombinationen 659 bei mindestens einer Krankenkasse rabattiert, was zu Einsparungen von 4,96 Mrd. € geführt hat. Das entspricht rund 10,9 % der Arzneimittelausgaben. Dabei werden 45,5 % aller Rabattvertragswirkstoffe mit Exklusivverträgen von nur einem Hersteller bedient, während der Rest auf Verträge nach dem Mehrpartner-Modell und auf Open-House-Verträge entfällt. Es wurde gezeigt, dass Rabattverträge nicht nur eine ausgabensenkende Wirkung, sondern auch positive Effekte auf die Anbietervielfalt und eine stabilere Versorgung der Patientinnen und Patienten haben.

Im Jahr 2019 wurde das Thema Lieferschwierigkeiten, und in diesem Zusammenhang die **Sicherheit in der Arzneimittelversorgung**, unter anderem auch im Bereich der Rabattverträge, kontrovers diskutiert. Durch eine Vielzahl von Produktionsschritten in einer globalisierten Welt kann es durchaus zu Lieferengpässen kommen: Von den im September 2019 am Markt befindlichen und zu Lasten der GKV verordneten über 66.000 Arzneimitteln waren 461 Arzneimittel beim Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) als vorübergehend nicht verfügbar gelistet, was einer hohen Liefersicherheit von 99,3 % entspricht. Auch Analysen des Nichtverfügbarkeitskennzeichens aus den Apotheken zeigen, dass die Ausprägung von Lieferengpässen über den gesamten Markt in Deutschland relativ gering ist und man insgesamt von einer hohen Liefersicherheit sprechen kann. Für die Patientinnen und Patienten bedeuten Lieferengpässe in der Regel auch keinen Versorgungsengpass: Sofern es mehrere pharmazeutische Unternehmen gibt, die einen generischen Wirkstoff in Arzneimitteln mit gleicher Darreichungsform, Stärke und Packungsgröße anbieten, kann meist ein problemloser Wechsel von einem Produkt auf das andere stattfinden.

Insofern ist nicht nachvollziehbar, warum ein **Einfluss der Rabattverträge auf die Lieferfähigkeit** und die Versorgung angenommen wird: In der Regel wird die Versorgung im durch Rabattverträge gekennzeichneten Generikamarkt über eine Vielzahl an wirkstoffgleichen Alternativen gewährleistet. Zudem zeigt sich, dass 93 % der wenigen nicht verfügbaren Arzneimittel als krankenhausesrelevant gekennzeichnet waren, wobei der Arzneimittelbedarf im Krankenhaus gerade meist nicht durch Rabattverträge geregelt ist. Letztlich bieten Rabattverträge durch bessere Möglichkeiten zur Kalkulation der Absatzmengen, durch Vorgaben zur Gewährleistung eines ausreichenden Arzneimittelbestands bereits bei Vertragsstart und während der Vertragslaufzeit sowie durch Konditionalstrafen bei Nichtlieferfähigkeit eher eine Möglichkeit, Lieferengpässe zu reduzieren.

Ein Arzneimittel geht bis zur Patientin oder zum Patienten über mehrere **Distributionsstufen**, die den Preis eines Arzneimittels bestimmen. Ausgehend vom Herstellerabgabepreis ergeben Großhandelszuschlag, Apothekenzuschlag, Notdienstzuschlag und Umsatzsteuer den Brutto-Apothekenverkaufspreis. Gesetzlich festgelegte Apotheken- und Herstellerabschläge sowie **Zuzahlungen** der Versicherten reduzieren wiederum die Kosten für die GKV. So kostet ein Arzneimittel mit einem Herstellerabgabepreis von 100,00 € die GKV 118,71 €. Dabei ist der absolute Wert der Zuzahlungen zwar über die letzten Jahre gestiegen, der Eigenanteil der Versicherten am Gesamtumsatz ist mit 5,4 % allerdings geringer als noch vor zehn Jahren (7,5 %).

Schließlich bleibt der Arzneimittelmarkt einer der lukrativsten Märkte überhaupt: Mit einer durchschnittlichen **EBIT-Marge** der 21 umsatzstärksten international agierenden Unternehmen von 24,7 % sticht der Arzneimittelmarkt sogar die ökonomisch sehr erfolgreiche IT-Branche aus - ein wirtschaftlicher Erfolg, der nicht zuletzt von den Beitragszahlern in der GKV mitfinanziert wird.

1 Der Arzneimittelmarkt 2019

1.1 Die Ausgabensituation im GKV-Arzneimittelmarkt 2019

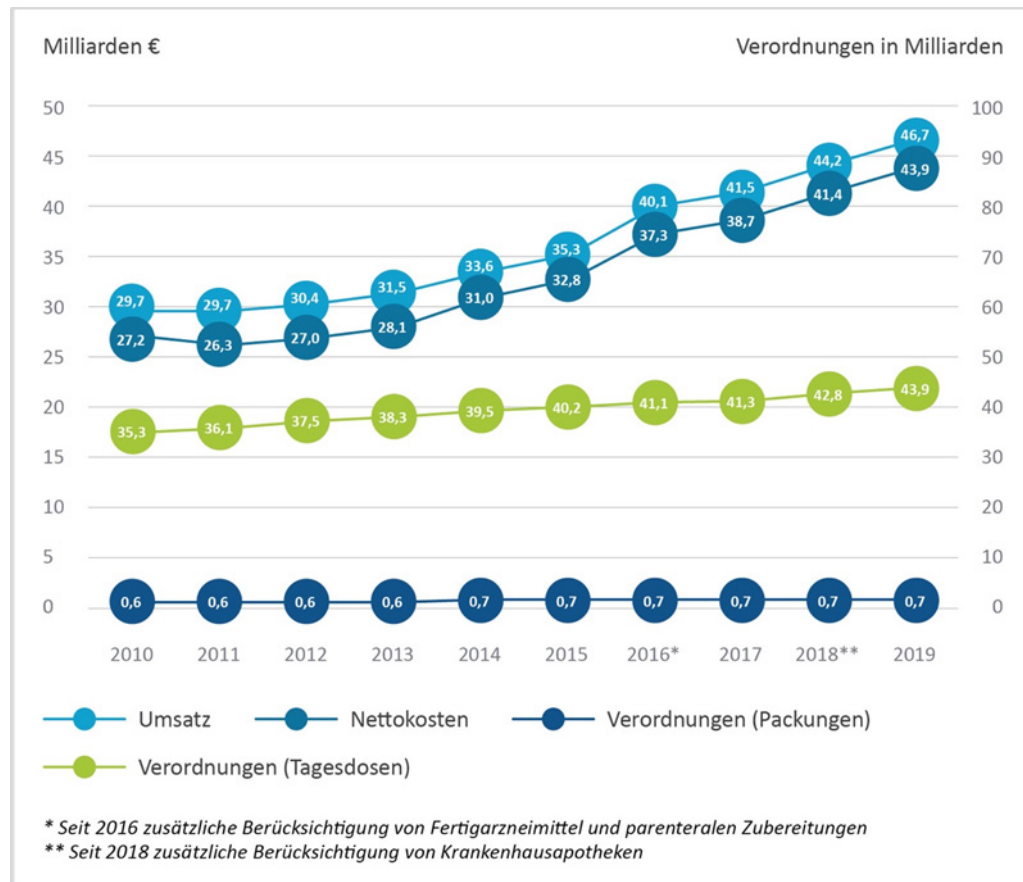
Im Jahr 2020 lagen die gesamten Ausgaben der GKV bei 249,3 Mrd. € und damit um 5,6 % über den Ausgaben des Vorjahres (KV 45). Zu den größten Ausgabenposten gehören Krankenhausbehandlungen mit einem Anteil von 30,6 %, gefolgt von den Arzneimitteln mit einem Anteil von 16,1 %. Insgesamt summieren sich die Ausgaben für alle im Rahmen der GKV verordneten Produkte aus Apotheken wie Arzneimittel und Impfstoffe auf 45,1 Mrd. € und sind gegenüber dem Vorjahr (+6,4 %) deutlicher angestiegen als im letzten Jahr (+3,7 %) (Bundesministerium für Gesundheit 2020a).

Ausgehend von diesen Ausgaben ermittelt der GKV-Arzneimittelindex den Bruttoumsatz und die Nettokosten des GKV-Arzneimittelmarktes¹. Der Bruttoumsatz ist im Jahr 2019 gegenüber dem Vorjahr insgesamt um 5,7 % (2.511 Mio. €) auf 46,7 Mrd. € angestiegen, was ein deutlich stärkeres Wachstum als in den Vorjahren darstellt (Abbildung 1-1). Dieser Anstieg kommt trotz einer nahezu konstanten Verordnungsmenge (690 Mio. gegenüber 683 Mio. Verordnungen im vorherigen Jahr) zum Tragen. Im folgenden Kapitel wird beschrieben, wie sich der Anstieg erklären lässt².

¹ Die Marktanalysen des GKV-Arzneimittelindex betrachten Bruttoumsätze bzw. Nettokosten. In diesen werden weder Ausgaben für Sprechstundenbedarf noch weitere Verordnungspositionen wie beispielsweise Verbandstoffe oder Teststreifen berücksichtigt. Zusätzlich sind darin die Zuzahlungen der Patientinnen/Patienten enthalten. Ausgehend von den Bruttoumsätzen werden für die Nettokosten die gesetzlichen Abschläge für Hersteller und Apotheken abgezogen. Die genaue Darstellung der berücksichtigten Ausgaben und der Berechnung des Umsatzes und der Nettokosten für Arzneimittel finden sich im ergänzenden elektronischen Anhang (WiDO 2020).

² Bei der Interpretation der Entwicklung ist zu berücksichtigen, dass sich die Datenbasis über die letzten Jahre weiterentwickelt hat: Seit 2016 umfasst der Datenkörper im GKV-Arzneimittelindex neben Fertigarzneimitteln auch parenterale Zubereitungen, Auseinzelnungen und Verblisterungen. Daten von Krankenhausapotheken im Rahmen der ambulanten Versorgung werden seit dem Datenjahr 2018 vollständig einbezogen (siehe auch WiDO 2020).

Abbildung 1-1: Umsatz, Nettokosten und Verordnungen des GKV-Arzneimittelmarktes seit 2010



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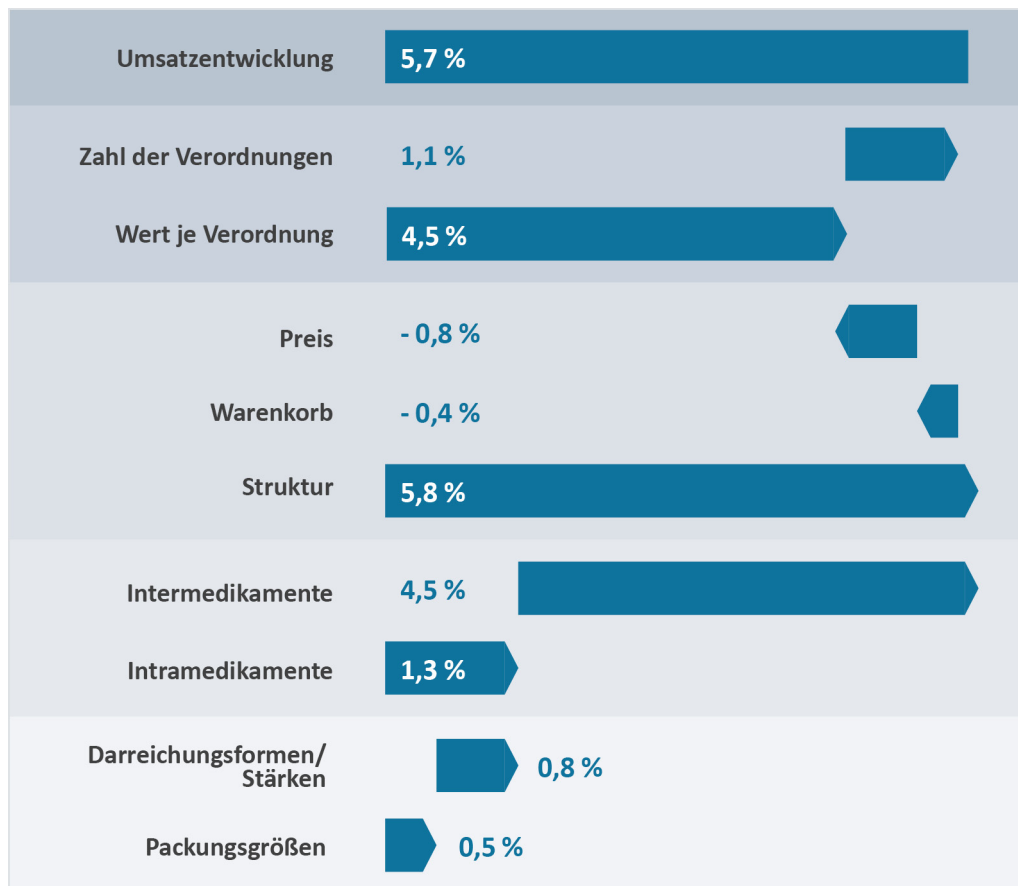
1.2 Wie erklärt sich der Umsatzanstieg im Jahr 2019?

Um die Ursachen des Umsatzanstiegs zu erklären, bietet sich das etablierte Konzept der Komponentenzerlegung³ der Umsatzentwicklung (Reichelt 1988) an, in dem die Effekte einzelner Einflussfaktoren (sog. Komponenten) offengelegt werden. Abbildung 1-2 zeigt den Einfluss der einzelnen Faktoren auf die Umsatzveränderung 2019 zu 2018.

Wie bereits zu Abbildung 1-1 beschrieben, zeigt sich auch in der Komponentenzerlegung, dass die Umsatzsteigerung um 5,7 % weniger durch den geringen Mengeneffekt (Anzahl der Verordnungen: +1,1 %) hervorgerufen wird, sondern vielmehr durch einen gestiegenen Wert je Verordnung. So hat eine Verordnung im Jahr 2019 durchschnittlich 67,73 € gekostet, während es im Vorjahr noch 64,78 € waren – das entspricht einem Anstieg um 4,5 %. Beruht der Umsatzanstieg also darauf, dass Arzneimittel einfach nur teurer geworden sind?

³ Eine detailliertere Beschreibung und Darstellung der Ergebnisse der Komponentenzerlegung der Umsatzentwicklung im Arzneimittelmarkt 2019 findet sich in WIdO (2020).

Abbildung 1-2: Komponentenerlegung der Umsatzentwicklung 2019 zu 2018



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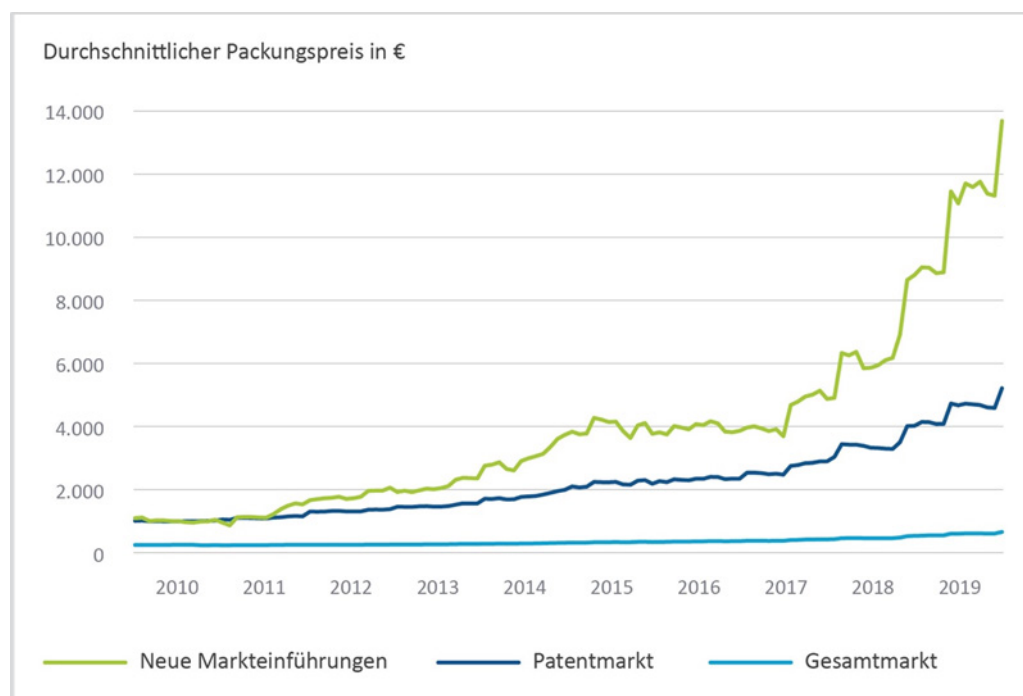
Um diese Frage zu beantworten, müssen mehrere Effekte gemeinsam betrachtet werden. Zunächst einmal ist der durchschnittliche Umsatz, der mit einer Packung erzielt wird, gestiegen („Wert je Verordnung“: +4,5 %). Demgegenüber steht ein geringer negativer Preiseffekt (-0,8 %), der den Effekt eines allgemeinen Preisrückgangs der Produkte beschreibt, die sowohl 2018 als auch 2019 im Handel waren. Ursächlich für diesen Rückgang können unter anderem gesetzliche Maßnahmen zur Preisregulierung sein: So stellt beispielsweise das Preismoratorium sicher, dass Hersteller die Preise lediglich im Rahmen eines Inflationsausgleichs erhöhen können, gleichzeitig sorgen Festbetragsanpassungen und die AMNOG-Erstattungsbeträge dafür, dass für viele Arzneimittel die Preise sogar abgesenkt wurden. Im Durchschnitt werden Arzneimittel, die auf den Markt sind, im Laufe der Zeit preisgünstiger.

Wie passt dies aber zu einem steigenden und umsatztreibenden Wert je Verordnung? Die Behandlung von Krankheiten mit Arzneimitteln wandelt sich ständig. Viele Erkrankungen werden heute mit anderen Arzneimitteln behandelt als noch vor wenigen Jahren. Das ist Ausdruck des Therapiefortschritts. In bestimmten Bereichen setzen sich einige Arzneimittel immer stärker im Markt durch. Sei es durch wissenschaftliche Erkenntnisse, durch Empfehlungen in ärztlichen Therapieleitlinien, durch Vorgaben der Selbstverwaltung im Gesundheitssystem oder des Gesetzgebers. Die durch diese Verschiebungen hervorgerufenen Umsatzeffekte werden über die Intermedikamentenkomponente abgebildet. Auch der Wechsel von einem günstigeren zu einem teureren Anbieter des gleichen Wirkstoffs zeigt sich in einer Änderung des Umsatzes. Verände-

rungen des Ordnungsverhaltens hin zu teureren Darreichungsformen oder Packungsgrößen bewirken als strukturelle Änderung ebenfalls eine Umsatzerhöhung (positive Intramedikamentenkomponente). Insgesamt betrachtet ergeben sich aus den aufgeführten strukturellen Änderungen – egal aus welcher Motivation – auch Umsatzänderungen.

Bei vielen Erkrankungen sind große Therapiefortschritte erkennbar – es gibt mittlerweile erheblich besser wirksame Mittel gegen Infektionskrankheiten wie Hepatitis-C, HIV, gegen Krebserkrankungen oder Autoimmunerkrankungen wie Rheumatoide Arthritis, chronisch entzündliche Darmerkrankungen oder Multiple Sklerose. Dennoch kommen immer wieder Zweifel auf, ob es tatsächlich der Innovationsgrad eines Arzneimittels ist oder eher das Ausnutzen der (scheinbar unbegrenzten) Zahlungsbereitschaft des Gesundheitssystems, die die Preissetzung der pharmazeutischen Unternehmen beeinflussen (Morgan et al. 2020). Dass sich die Preise für neue Arzneimittel (Arzneimittel, die in den letzten 36 Monaten den Markt betreten haben) seit Jahren von denen des Gesamt- und auch des gesamten Patentmarktes losgelöst haben, wird aus Abbildung 1-3 deutlich. So kostet heute ein Arzneimittel, das in den letzten drei Jahren auf den Markt gekommen ist, rund dreimal so viel wie der durchschnittliche Preis eines Patentarzneimittels. Noch vor wenigen Jahren war dieser Unterschied nicht so extrem ausgeprägt. Erst seit 2010 haben sich die Preise der neuen Arzneimittel zunehmend von denen im gesamten Patentmarkt entkoppelt.

Abbildung 1-3: Durchschnittliche Packungspreise in Segmenten des Arzneimittelmarktes seit 2010



Insgesamt hatte die strukturelle Veränderung im Therapie- und Verordnungsverhalten, also die Verschiebung der Verordnungen innerhalb einer Arzneimittelgruppe hin zu meist neueren und teureren Arzneimitteln, im Jahr 2019 den größten Einfluss auf die gesamte Umsatzentwicklung. Dadurch ist der Arzneimittelumsatz um 5,8 % angestiegen. Dies entspricht einem Euroäquivalent von 2,57 Mrd.

Besonders deutliche Struktureffekte zeigen sich erneut bei den Onkologika (Antineoplastische Mittel), den Immunsuppressiva und den Antithrombotischen Mitteln mit zum Teil deutlich zweistelligen Zuwachsraten. Durch die strukturelle Therapiever-schiebung allein in diesen drei Gebieten ist der Arzneimittelumsatz im Jahr 2019 um 1,52 Mrd. € angewachsen (Tabelle 1-1).

Tabelle 1-1: Struktureffekte auf den Bruttoumsatz in ausgewählten Wirkstoffgruppen des GKV-Arzneimittelmarktes 2019

Wirkstoffgruppe (ATC-Ebene)	Bruttoumsatz in Mio. €	Struktureffekt in %	Struktureffekt in €
Onkologika (L01)	6.822,4	16,1	957,7
Immunsuppressiva (L04)	7.182,9	5,5	366,8
Antithrombotische Mittel (B01)	2.753,1	7,7	195,1
Summe hier	16.758,4		1.519,6
Anteil hier an Gesamtmarkt	35,9 %		59,1 %
Gesamtmarkt	46.741,5	5,7	2.573,0

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Dabei haben auch einzelne Arzneimittel einen großen umsatzsteigernden Effekt. Tabelle 1-2 zeigt die größten Nettokostengewinner, also die Arzneimittel, die die stärksten Nettokostenzuwächse gegenüber dem Vorjahr verzeichnen. In Summe haben diese Kosten in Höhe von 2.543 Mio. € verursacht, was knapp ein Drittel des gesamten Nettokostenanstiegs darstellt.

Tabelle 1-2: Die fünf patentgeschützten Arzneimittel 2019 mit den höchsten Nettokostendifferenzen im Vergleich zu 2018

Präparat	Wirkstoff	Hauptindikationsgruppe	Nettokosten 2019 in Mio. €	Differenz Nettokosten zu 2018	DDD-Nettokosten
Keytruda	Pembrolizumab	Krebserkrankungen	593,6	287,3	280,53
Eliquis	Apixaban	Herz-Kreislauf-Erkrankungen	839,7	158,6	3,31
Imraldi	Adalimumab	Immuntherapie	120,0	109,1	38,26
Stelara	Ustekinumab	Immuntherapie	409,0	92,7	39,29
Revlimid	Lenalidomid	Krebserkrankungen	580,2	88,5	260,50
Summe hier			2.542,6	736,2	
Anteil hier an Gesamtmarkt			5,8 %	29,6 %	
Gesamtmarkt			43.859,4	2.486,5	1,00

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Die Warenkorbkomponente in Höhe von -0,4 % stellt lediglich einen Korrekturfaktor dar, der sich durch die außer Handel genommenen Präparate und Neueinführungen sowie saisonale Schwankungen im Warenkorb ergibt.

Wie verteilen sich die Arzneimittelausgaben der GKV auf die Hauptindikationsgruppen?

Tabelle 1-3 zeigt, wie sich ein Großteil der Nettokosten der GKV (rund 87 %) über die zehn nettokostenstärksten der insgesamt 18 Hauptindikationsgruppen⁴ verteilt. Demnach gibt die GKV am meisten, 18,7 % der Gesamtnettokosten für medikamentöse Krebstherapien aus, die wiederum lediglich 0,6 % des gesamten Verordnungsgeschehens (in DDD) darstellen. Ebenso verhält es sich mit Immuntherapeutika: Auch diese weisen mit 17,8 % einen hohen Nettokostenanteil auf, während ihr Verordnungsanteil mit 2,1 % vergleichsweise gering ist. Erst an dritter Stelle stehen Arzneimittel gegen Herz-Kreislauf-Erkrankungen – hinter denen sich klassische chronische Volkskrankheiten wie Bluthochdruck oder Koronare Herzerkrankung verbergen. Hier gibt die GKV rund sieben Mrd. € aus und deckt damit rund 50 % des gesamten Verordnungsgeschehens in Deutschland ab. So zeigt sich, dass jede zweite verordnete Tagesdosis auf ein Arzneimittel gegen Herz-Kreislauf-Erkrankungen entfällt.

⁴ Zur Definition und Zuordnung der Hauptindikationsgruppen vgl. WiDO (2020)

Tabelle 1-3: Nettokosten, verordnete Tagesdosen und DDD-Nettokosten der zehn umsatzstärksten Hauptindikationsgruppen im Jahr 2019 sowie deren Anteile am Gesamtmarkt

Rang	Hauptindikationsgruppe	Nettokosten in Mio. €	Anteil an Gesamt	DDD in Mio.	Anteil an Gesamt	DDD-Nettokosten in €
1	Krebserkrankung	8.206	18,7%	248	0,6 %	33,12
2	Immuntherapie	7.804	17,8%	924	2,1 %	8,45
3	Herz-Kreislauf-Erkrankungen	6.922	15,8%	21.847	49,7 %	0,32
4	Erkrankungen des Nervensystems	3.158	7,2 %	3.117	7,1 %	1,01
5	Infektionskrankheiten	2.673	6,1 %	386	0,9 %	6,92
6	Diabetes	2.605	5,9 %	2.336	5,3 %	1,12
7	Schmerzen und Entzündungen	2.338	5,3 %	1.779	4,1 %	1,31
8	Chronische Atemwegserkrankungen	2.103	4,8 %	1.387	3,2 %	1,52
9	Erkrankungen von Auge und Ohr	1.299	3,0 %	857	2,0 %	1,51
10	Magen-Darm-Erkrankungen	1.243	2,8 %	4.027	9,2 %	0,31
Summe und Anteil an Gesamt		38.351	87,4 %	36.909	84,0 %	1,04
Gesamtmarkt		43.859,4		43.932,0		1,00

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Für welche Arzneimittel wurde 2019 am meisten ausgegeben?

Die nettokostenstärksten Hauptindikationsgruppen zeigen sich auch exemplarisch in der Liste der einzelnen Arzneimittel, für die 2019 am meisten ausgegeben wurde (Tabelle 1-4). So entfallen, abgesehen von Lucentis, einem Mittel gegen die Augenerkrankung Makuladegeneration, alle Präparate der zehn nettokostenstärksten Arzneimittel auf Mittel gegen Krebserkrankungen, Immuntherapeutika oder Mittel gegen Herz-Kreislauf-Erkrankungen.

Zusammen ergeben die zehn Arzneimittel, die nur rund 1 % der Verordnungen nach Tagesdosen (DDD) ausmachen, einen Anteil von über 12 % der Nettokosten am gesamten Arzneimittelmarkt. Humira als jahrelang unangefochtener Anführer dieser Rangliste hat im Jahr 2019 nach Patentablauf gegen Ende des Vorjahres diese Vormachtstellung zugunsten der antithrombotisch wirkenden Mittel Eliquis und Xarelto eingebüßt. Somit stellt das Präparat Eliquis mit dem Wirkstoff Apixaban, eines der DOAK, mit Nettokosten von knapp 840 Mio. € das umsatzstärkste Arzneimittel in Deutschland im Jahr 2019 dar.

Tabelle 1-4: Nettokosten, verordnete Tagesdosen und DDD-Nettokosten der zehn nettokostenstärksten Arzneimittel im Jahr 2019 sowie deren Anwendungsgebiete und Anteile am Gesamtmarkt

Rang	Arznei- mittel	Hauptindikationsgruppe	Netto- kosten in Mio. €	Trend	DDD in Mio.	DDD-Net- tokosten in €
1	Eliquis	Herz-Kreislauf-Erkrankungen	839,7	↑	253,32	3,31
2	Xarelto	Herz-Kreislauf-Erkrankungen	761,2	●	231,71	3,28
3	Humira	Immuntherapie	696,6	↓	11,55	60,31
4	Keytruda	Krebserkrankungen	593,6	↑	2,12	280,53
5	Revlimid	Krebserkrankungen	580,2	↑	2,23	260,50
6	Opdivo	Krebserkrankungen	451,2	●	2,23	202,11
7	Avastin	Krebserkrankungen	442,1	↓	2,51	176,14
8	Stelara	Immuntherapie	409,0	↑	10,41	39,29
9	Lucentis	Erkrankungen von Auge und Ohr	383,7	↓	9,00	42,64
10	Zytiga	Krebserkrankungen	369,6	↑	2,93	126,27
Summe hier			5.526,9		528,0	
Anteil hier an Gesamt			12,6 %		1,2 %	
Gesamt			43.859,4		43.932,0	

Quelle: GKV-Arzneimittelindex

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Im Vergleich zu 2010 zeigt sich hier auch eine Dynamik: Hatten die zehn umsatzstärksten Arzneimittel im Jahr 2010 nur einen Kostenanteil von 10,9 % erreicht, stieg dieser Anteil auf 12,6 Prozent im Jahr 2019 an. Gleichzeitig ist der Anteil an allen verordneten Tagesdosen nur von 1,1 Prozent auf 1,2 Prozent gestiegen. Auch hier wird die Konzentration der Kosten auf wenige Arzneimittel deutlich.

1.3 Wie verteilen sich Umsätze und Verordnungen auf die Marktsegmente?

Der Arzneimittelmarkt kann nach zahlreichen Kriterien unterschieden werden. In Tabelle 1-5 wird er hinsichtlich der Kriterien Patentschutz, Biologika und Orphan Drugs differenziert. Es zeigt sich, dass der häufig diskutierte Patentmarkt sowohl umsatzmäßig als auch verordnungsseitig kleiner ist als der Markt der Arzneimittel, bei denen die Schutzfristen abgelaufen sind und somit Preiswettbewerb entstehen kann. Die Kosten je Tagesdosis (DDD-Nettokosten) der Patentarzneimittel sind jedoch mit 7,36 € im Durchschnitt zwölfmal so hoch wie die der Nicht-Patentarzneimittel. Der Markt für patengeschützte Arzneimittel wird aufgrund seiner hohen Kosten in Kapitel 2 näher beleuchtet. Der generikafähige Markt, mit 20,55 Mrd. € Nettokosten und 605,90 Mio. Verordnungen (38,88 Mrd. Tagesdosen) als größter Teil des Nicht-Patentmarktes ist sehr stark durch Rabattverträge zwischen Krankenkassen und pharmazeutischen Unternehmen gekennzeichnet. Diese waren in jüngerer Vergangenheit wieder Gegenstand gesellschaftlicher und politischer Diskussionen und werden in Kapitel 5 thematisiert.

Tabelle 1-5: Nettokosten und verordnete Tagesdosen sowie deren Anteile im GKV Arzneimittelmarkt 2019 nach Marktsegmenten

	Netto- kosten in Mrd. €	Verän- derung in %	DDD in Mrd.	Verän- derung in %	DDD- Netto- kosten in €	Netto- kosten an Gesamt	DDD an Gesamt
Gesamtmarkt	43,86	6,0	43,93	2,7	1,00		
Patentarzneimittel*	20,96	6,1	2,85	0,3	7,36	47,8 %	6,5 %
Nicht-Patentarznei- mittel*	22,87	5,6	41,07	2,9	0,56	52,2 %	93,5 %
Biologika	13,48	10,0	1,31	1,7	10,28	30,7 %	3,0 %
Nicht-Biologika	30,36	4,3	42,61	2,8	0,71	69,2 %	97,0 %
Orphan-Arzneimittel	4,43	18,9	0,02	12,3	187,76	10,1 %	0,1 %
Nicht-Orphan-Arznei- mittel	39,41	4,7	43,90	2,7	0,90	89,9 %	99,9 %

* Die Zuordnung erfolgt in monatlicher Abgrenzung: Laufen die Schutzfristen für einen Wirkstoff beispielsweise im Juli 2019 aus, so zählen die Arzneimittel bis Juli 2019 zum Patentmarkt und danach zum Zweitanbietermarkt

Quelle: GKV-Arzneimittelindex

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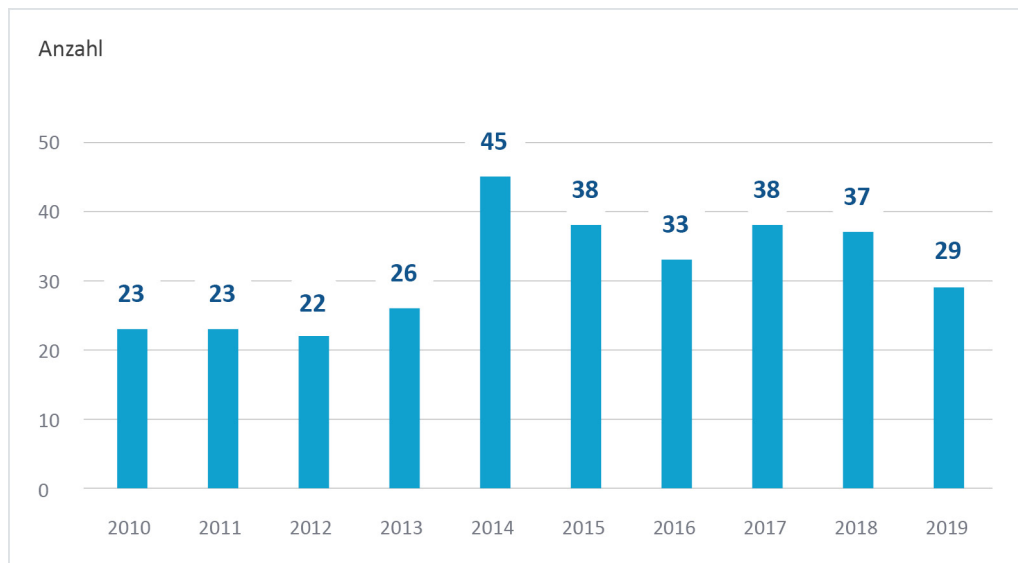
Bei Biologika, auf die 31 % der Umsätze des Gesamtmarktes entfallen, handelt es sich mit durchschnittlichen Tagesdosiskosten von 10,28 € insbesondere um vergleichsweise teure Arzneimittel, die gerade im Zusammenhang zu den viel diskutierten Nachahmerprodukten, den Biosimilars, in Kapitel 3 im Fokus stehen. Bei diesen Arzneimitteln zeigt sich der Trend hin zur zielgerichteten Therapie mit Angriff an definierte biologische Zielstrukturen im Körper - eine Strategie, die sich zunehmend auch bei verbreiteteren Erkrankungen durchsetzt (exemplarisch in einem Exkurs zu neuen Arzneimitteln des Jahres 2019 in Kapitel 1.4).

Ein weiteres Segment des Arzneimittelmarktes, das mit besonders hohen Tagesdosiskosten auffällt, sind die Arzneimittel bei seltenen Erkrankungen, die sogenannten Orphan-Arzneimittel. Dies wird auch daran deutlich, dass nur 0,045 % der verordneten Tagesdosen einen Nettokostenanteil von 10 % erreicht. Hier kostet eine Tagesdosis im Durchschnitt 187,76 €, mehr als das Zweihundertfache der Therapie mit Nicht-Orphan-Arzneimitteln. Zwar werden diese in der Regel jeweils nur für wenige Patientinnen und Patienten angewendet, aber es kommen immer mehr Orphan-Arzneimittel in den Markt (siehe Kapitel 4). Zusammengenommen haben sie inzwischen einen beträchtlichen Marktanteil erreicht.

1.4 Welche neuen Arzneimittel gibt es im Jahr 2019?

Im Jahr 2019 wurden in Deutschland 29 neue Wirkstoffe in den Markt eingeführt. Gegenüber den 37 Wirkstoffen im Vorjahr sind dies zwar weniger, die Anzahl entspricht aber in etwa dem Mittel der letzten Jahre (Abbildung 1-4). Auch einige Trends setzen sich im Jahr 2019 fort: Es gibt vermehrt zielgerichtete onkologische Arzneimittel (11) – hier hauptsächlich aus der Wirkstoffgruppe der Proteinkinase-Inhibitoren – sowie Arzneimittel zur Immuntherapie (5) und zur Behandlung von Erkrankungen des Blutsystems (4). Rund die Hälfte aller Neueinführungen sind Arzneimittel, die zur Behandlung seltener Erkrankungen zugelassen wurden (Orphan Drugs) (Tabelle 1-6).

Abbildung 1-4: Anzahl neuer Arzneimittel 2010 bis 2019



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Zudem erfolgt bei einem relevanten Teil der Arzneimittel (11) die Zulassung über andere Verfahren als dem Standard der zentralen EU-Zulassung, beispielsweise über Sonderwege wie einer bedingten Zulassung oder einem nationalen Inverkehrbringen im Rahmen des deutschen Arzneimittelgesetzes nach § 4b⁵. Hierbei sind auch Arzneimittel für neuartige Therapien (ATMP) zu nennen, von denen im Jahr 2019 bereits vier Wirkstoffe in den Markt kamen (Tabelle 1-6). Unter dem Begriff ATMP werden Gentherapeutika (Zynteglo, Luxturna), somatische Zelltherapeutika (Alofisel), biotechnologisch bearbeitete Gewebeprodukte (Obnitix) sowie Tumorimpfstoffe zusammengefasst. Insbesondere die beiden letztgenannten Arzneimittel aus mesenchymalen Stromazellen zeigen die unterschiedlichen Möglichkeiten des Marktzugangs solcher neuen Therapiekonzepte auf. Während das Arzneimittel Alofisel (indiziert zur Behandlung komplexer Analfisteln bei Erwachsenen mit Morbus Crohn) europäisch zugelassen wurde und mit transparenten Informationen über den Zulassungsprozess im European public assessment report (EPAR) dokumentiert ist, fehlen diese Informationen für das prinzipiell ähnliche Arzneimittel Obnitix (indiziert für Patientinnen und Patienten nach allogener Stammzelltransplantation mit steroidrefraktärer, akuter GvHD (graft-versus-host disease)-Reaktion), da dieses nur national über das Paul-Ehrlich-Institut (PEI) in den Verkehr gebracht wurde.

⁵ Eine Sondervorschrift für Arzneimittel für neuartige Therapien, zuständig ist in Deutschland das Paul-Ehrlich-Institut (PEI)

Tabelle 1-6: Neue Arzneimittel 2019

Wirkstoff	Handelsname	Hauptindikationsgruppe	Markt-einführung	Orphan-Arz-neimittel	ATMP	Standardzu-lassung EU	Höchster Preis (AVP) in € ^{##}
Doravirin	Pifeltro	Infektionskrankheiten	15.01.2019	nein		ja	2.042,96
Lamivudin, Tenofoviridisoproxil und Doravirin	Delstrigo						2.484,21
Brigatinib	Alunbrig	Krebserkrankungen	15.01.2019	nein		ja	7.333,08
Vonicog alfa	Veyvondi	Erkrankungen des Blutsystems	15.01.2019	nein*		ja	1.598,50 (AEP)
Damoctocog alfa pegol	Jivi	Erkrankungen des Blutsystems	01.01.2019	nein*		ja	4.470,00 (AEP)
Lanadelumab	Takhzyro	Erkrankungen des Blutsystems	01.02.2019	ja		nein	104.236,92
Apalutamid	Erleada	Krebserkrankungen	01.02.2019	nein		ja	4.143,81
Rucaparib	Rubraca	Krebserkrankungen	01.03.2019	nein*		nein	4.647,57
Galcanezumab	Emgality	Schmerzen und Entzündungen	01.04.2019	nein		ja	2.027,36
Voretigen Neparvovec	Luxturna	Erkrankungen von Auge und Ohr	15.04.2019	ja	ja	ja	345.000,00 (KEP)
Dacomitinib	Vizimpro	Krebserkrankungen	01.05.2019	nein		ja	4.819,17
Anthrax-Antigen	BioThrax	Infektionskrankheiten	01.05.2019	nein		Nein	1.148,86
Fremanezumab	Ajovy	Schmerzen und Entzündungen	15.05.2019	nein		ja	2.027,36
Lorlatinib	Lorviqua	Krebserkrankungen	01.06.2019	nein		nein	10.401,42
Risankizumab	Skyrizi	Immuntherapie	01.06.2019	nein		ja	6.153,55
Chlormethin	Ledaga	Krebserkrankungen	15.05.2019	ja		ja	2.951,81
Cemiplimab	Libtayo	Krebserkrankungen	01.08.2019	nein		nein	7.623,26
Ravulizumab	Ultomiris	Immuntherapie	01.08.2019	nein*		ja	5.694,92
Turoctocog alfa pegol	Esperoct	Erkrankungen des Blutsystems	01.08.2019	nein*		ja	3.600,00 (APU)
Pegvaliase	Palynziq	Stoffwechselerkrankungen	01.07.2019	ja		ja	4.960,12
Andexanet alfa	Ondexxya	Herz-Kreislauf-Erkrankungen	01.09.2019	nein		nein	12.800,00 (KEP)
Temocillin	Temopen	Infektionskrankheiten	01.10.2019	nein		nein	65,76 (KEP)
Volanesorsen	Waylivra	Herz-Kreislauf-Erkrankungen	15.08.2019	ja		nein	20.281,37
Ropeginterferon alfa-2b	Besremi	Immuntherapie	15.09.2019	nein*		ja	2.778,26
Humane allogene mesenchymale Stromazellen	Obnitix	Immuntherapie	15.09.2019	ja	ja	nein	46.341,59
Larotrectinib	Vitrakvi	Krebserkrankungen	15.10.2019	nein*		nein	6.623,56
Darvadstrocel	Alofisel	Immuntherapie	01.12.2019	ja	ja	ja	51.400,00 (APU)
Neratinib	Nerlynx	Krebserkrankungen	01.12.2019	nein		ja	6.462,07
Gilteritinib	Xospata	Krebserkrankungen	01.12.2019	ja		ja	22.732,77
Axicabtagen Ciloleucel	Yescarta	Krebserkrankungen	01.12.2019	ja	ja	nein	282.000,00 (KEP)

AVP: Apothekenverkaufspreis, APU: Abgabepreis des Herstellers; KEP: Krankenhauseinkaufspreis. Wenn kein AVP in die Preisverzeichnisse gemeldet wird, ist der jeweils nächste Preis in dieser Reihenfolge angegeben.

* Arzneimittel, deren Status als Orphan-Arzneimittel aufgehoben wurde

Eine weitere interessante Entwicklung vollzieht sich bei der Migräneprophylaxe: Nachdem bereits im Jahr 2018 der erste Antikörper (Erenumab, Aimovig) zur Migräneprophylaxe für Patientinnen und Patienten mit mindestens vier Migränetagen pro Monat in Deutschland eingeführt wurde, sind im vergangenen Jahr zwei weitere Antikörper (Galcanezumab, Emgality und Fremanezumab, Ajovy) mit gleichem Anwendungsgebiet hinzugekommen. Zur Prophylaxe der Migräne kamen bisher eine Reihe von Wirkstoffen mit hauptsächlich anderen Anwendungsgebieten mit zum Teil erheblichen Nebenwirkungen zum Einsatz. Diese drei neuen Antikörper haben mit der spezifischen Ausrichtung gegen körpereigene migräneauslösende Vorgänge ein neues Wirkprinzip und greifen so direkt in die Pathophysiologie der Migräne ein. Insgesamt wird geschätzt, dass es in Deutschland 1,4 bis zu 1,5 Mio. Patientinnen und Patienten gibt, für die eine Migräneprophylaxe therapeutisch sinnvoll ist.

Der Gemeinsame Bundesausschuss (G-BA) kommt in den Nutzenbewertungen aller drei neuen Antikörper zu dem Ergebnis, dass diese Mittel zur Prophylaxe bei Migränpatientinnen und -patienten einen beträchtlichen Zusatznutzen haben können (Gemeinsamer Bundesausschuss 2019a, Gemeinsamer Bundesausschuss 2019b). Allerdings gilt dies lediglich für erwachsene Patientinnen und Patienten, die auf keine der bisherigen unspezifischen Wirkstoffklassen ansprechen, diese nicht vertragen oder dafür nicht geeignet sind. In Deutschland wird die Anzahl der Betroffenen auf nur 14.000 bis 15.000 Patientinnen und Patienten geschätzt, also ca. 1,0 % aller Migränpatientinnen und -patienten. Dementsprechend konnte für 99,0 % der Patientinnen und Patienten ein Zusatznutzen nicht belegt werden.

Die Arzneimittelkommission der deutschen Ärzteschaft (AKdÄ) bewertet die prophylaktische Wirksamkeit der Migräne-Antikörper lediglich als moderat (AkdÄ 2020, Dicheva-Radev et al. 2020). Auch wenn es Hinweise auf vergleichsweise bessere Verträglichkeit gegenüber den herkömmlichen Migräneprophylaxemitteln gibt, empfiehlt die AKdÄ den Einsatz der drei Antikörper ebenfalls nur nach Versagen anderer Arzneimittel zur Migräneprophylaxe oder bei deren Unverträglichkeit. Nicht nur die deutlich höheren Jahrestherapiekosten von ca. 7.600 € bis zu 16.600 € je Patientin oder Patient gegenüber lediglich 43 € bis ca. 300 € für die bisher verfügbaren Medikamente mögen für diese Beurteilung ausschlaggebend sein. Gravierender ist, dass nach Einschätzung der AkdÄ mit den bisher erhobenen Daten die langfristige Sicherheit der Antikörper nicht ausreichend beurteilt werden kann und zudem mit den herkömmlichen Mitteln eine Verringerung der Migräneattacken durchaus erreicht werden konnte. Auch das Risiko für Patientinnen und Patienten mit kardiovaskulären Erkrankungen ist momentan nicht einschätzbar, da diese in den Zulassungsstudien ausgeschlossen wurden. Dies ist insofern problematisch, da das Risiko für kardiovaskuläre Ereignisse durch Migräne erhöht ist und das Risiko aufgrund des Wirkmechanismus zusätzlich erhöht zu sein scheint (AkdÄ 2020).

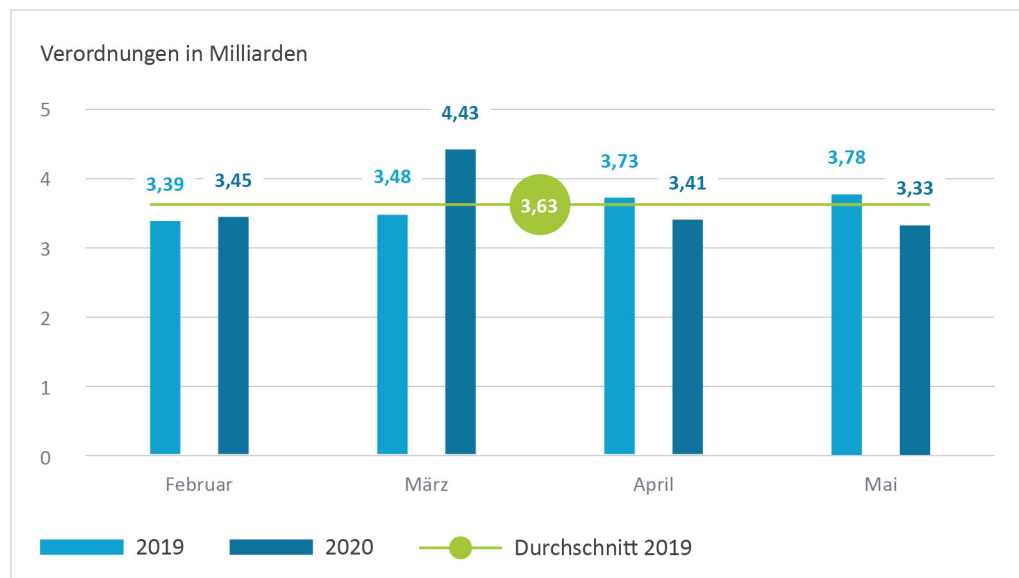
Im Jahr 2020 entfielen insgesamt 2,8 Mio. DDD auf diese neuen Antikörper zur Migräneprophylaxe, das entspricht Nettokosten von 54,0 Mio. € und bereits nach kurzer Marktpräsenz einer dauerhaften Prophylaxe für mindestens 7.000 Patientinnen und Patienten in der GKV.

1.5 Kurzer Ausblick auf den Arzneimittelmarkt 2020: Verordnungen in der Pandemie

Das Verordnungsgeschehen im Arzneimittelmarkt ist zu Beginn des Jahres 2020, insbesondere im Monat März, von einer im Vergleich zum Vorjahr deutlich höheren Verordnungsmenge geprägt. Es ist zu vermuten, dass sich dies durch das Anlegen von Vorräten erklären lässt, die als Reaktion auf die angekündigten Kontaktbeschränkungen infolge der Coronavirus-Pandemie getätigt wurden.

Wie in Abbildung 1-5 ersichtlich wird, fällt die Anzahl der verordneten Tagesdosen (DDD) mit 4,4 Mrd. im März 2020 sowohl gegenüber dem Vormonat 3,45 Mrd. als auch gegenüber dem Vorjahreswert (3,48 Mrd.) hoch aus. Im Schnitt sind 2019 etwa 3,63 Mrd. Tagesdosen verordnet worden, sodass der Monat März auch von einem mittelfristigen Trend abweicht. Im Folgemonat April 2020 kommt es dann zu einem vergleichsweise starken Absinken der verordneten Tagesdosen auf 3,41 Mrd., was im Vergleich zum Vorjahreswert (3,73 Mrd. DDD) einem prozentualen Rückgang von 8,6 % zum Vorjahresmonat entspricht. Im Mai sank der Verbrauch noch weiter auf 3,33 Mrd. DDD ab, was einem Rückgang um 11,9 % im Vergleich zum Mai 2019 entspricht.

Abbildung 1-5: Verordnungen in Tagesdosen für die Monate Februar bis Mai 2020 im Vergleich zum Vorjahr und zum monatlichen Durchschnitt 2019



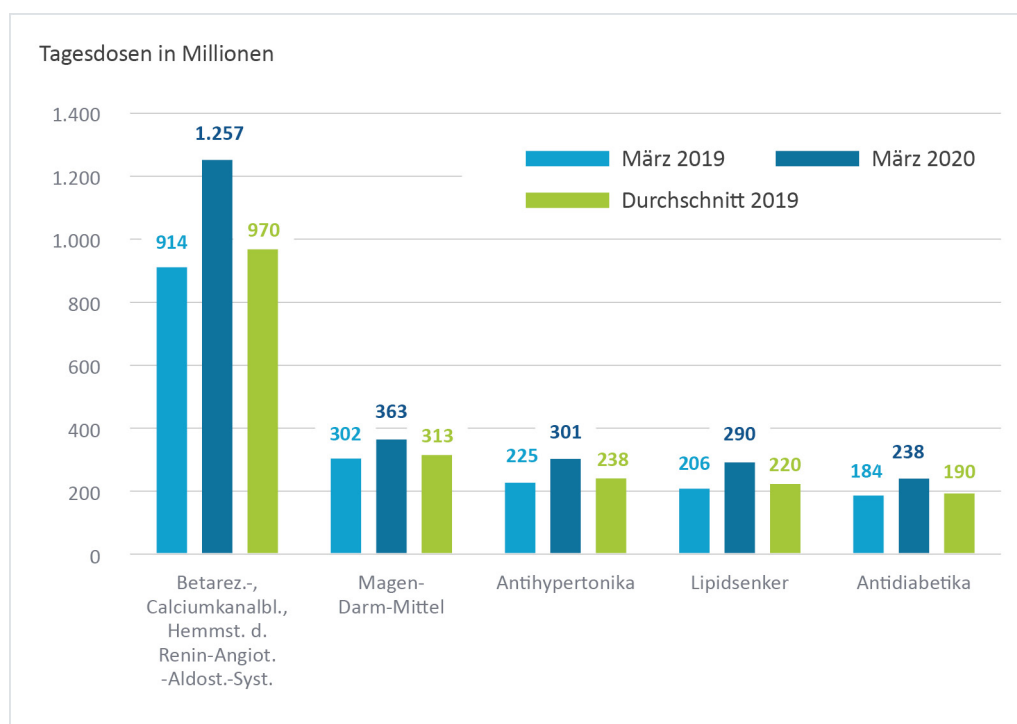
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Vergleichsweise geringer sind die Bewegungen bei der Anzahl der verordneten Packungen im gleichen Zeitraum: Diese steigen im März um lediglich 19 % (Tagesdosen 27 %). Dass die verordneten Packungen gegenüber den verordneten Tagesdosen weniger stark ansteigen, kann ein Hinweis darauf sein, dass vermehrt größere Packungen verordnet wurden, die bei der Behandlung von chronisch erkrankten Arzneimittelpatientinnen und -patienten eingesetzt werden.

Ähnlich wie bei den verordneten Tagesdosen verläuft die Entwicklung der Nettokosten. Im März sind diese im Vergleich zum Vorjahresmonat um 26,2 % von 2,86 Mrd. € auf 3,61 Mrd. € angestiegen, während sie im April von 2,99 Mrd. € im Jahr 2019 auf 2,87 Mrd. € im Jahr 2020 um 3,9 % gesunken sind, im Mai lag der Rückgang bei 6,8 %.

Betrachtet man die fünf verordnungsstärksten Indikationsgruppen für den Verordnungsmonat März 2020 im Vergleich zum Vorjahreswert, erkennt man bei faktisch allen diesen Gruppen einen deutlichen Anstieg der verordneten Tagesdosen im Vergleich zum Vorjahresmonat (Abbildung 1-6).

Abbildung 1-6: Verordnete Tagesdosen in den fünf verordnungsstärksten Indikationsgruppen im März 2020 im Vergleich zum Vorjahresmonat und monatlichen Durchschnitt 2019



Quelle: Wissenschaftliches Institut der AOK (WIdO), Datenstand 03.06.2020

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Zu den verordnungsstärksten Gruppen im März 2020 gehören Herz-Kreislauf-Mittel (Betarezeptoren-, Calciumkanalblocker und Hemmstoffe des Renin-Angiotensin-Aldosteron-Systems), Antihypertonika und Lipidsenker sowie Magen-Darm-Mittel und Antidiabetika. Angesichts der im Februar 2020 kurzfristig erwarteten Kontaktbeschränkungen ab März haben sich vermutlich vor allem chronisch erkrankte Patientinnen und Patienten insbesondere bei diesen verordnungsstarken Arzneimittelgruppen einen Vorrat angelegt, der sich im Verordnungsanstieg niederschlägt. Während bei den Antihypertonika ein Verordnungsanstieg von „nur“ 19,9 % zu verzeichnen ist, lassen sich in den anderen Gruppen Steigerungen von bis zu 37,5 % beobachten. So wurden bei den Betarezeptorenblockern, Calciumkanalblockern und Renin-Angiotensin-Aldosteron-Hemmstoffen im März 2020 knapp 1,3 Mrd. Tagesdosen verordnet, knapp 400 Mio. Tagesdosen mehr als im Vorjahresmonat (+37,6 %). Auch bei den Antidiabetika sind die Zuwächse mit +41 % deutlich sichtbar. Wie im Gesamtmarkt kann auch bei diesen Gruppen in den darauffolgenden Monaten April und Mai im Vergleich zum

Vorjahresmonat ein Rückgang der Verordnungen beobachtet werden: In den erwähnten fünf Gruppen liegt dieser Rückgang im April zwischen -2,1 % (Lipidsenker) und -10,8 % (Magen-Darm-Mittel).

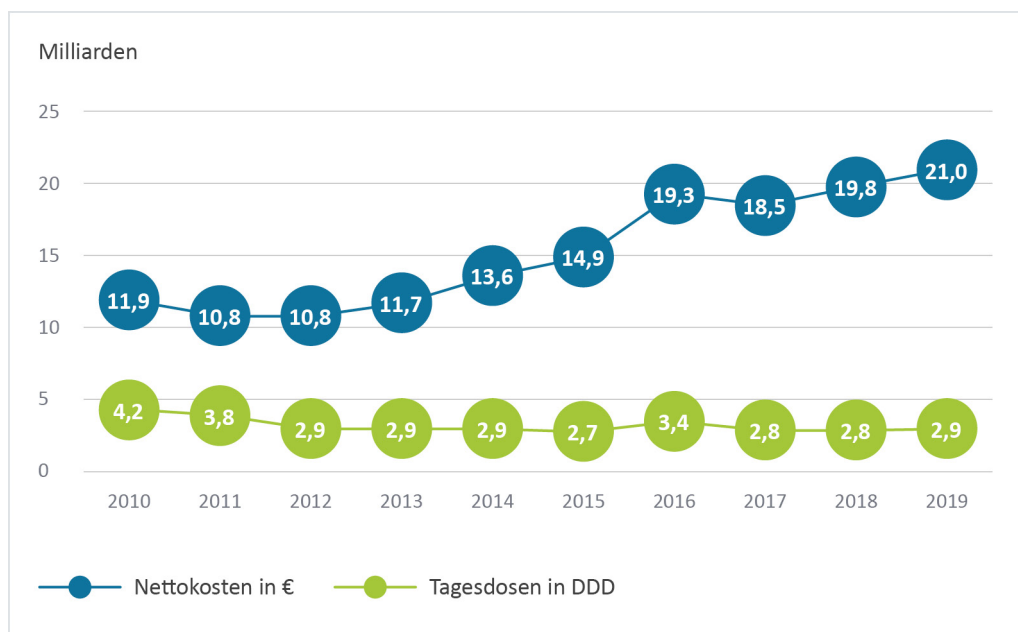
Insgesamt ist durch die sinkenden Verordnungszahlen im April und Mai zum jetzigen Zeitpunkt zu vermuten, dass sich das Anlegen von Vorräten auf den Monat März 2020 beschränkt hat und sich auch in den folgenden Monaten eine eher unterdurchschnittliche Verordnungsmenge zeigt, da zunächst die Vorräte der Großpackungen aufgebraucht werden. Die weitere Entwicklung, besonders in Verbindung mit ggf. weiteren einschränkenden Maßnahmen aufgrund der Pandemie, bleibt abzuwarten.

2 Der Markt der neuen und patentgeschützten Arzneimittel

2.1 Marktdynamik im Patentarzneimittelmarkt

Aus Wettbewerbssicht ist es entscheidend, ob für ein Arzneimittel bzw. seinen Wirkstoff noch Patente oder weitere Schutzfristen gültig sind. Ist ein Patent noch gültig, so ist der Markteintritt von Wettbewerbern mit dem gleichen Wirkstoff nicht möglich. Hersteller genießen in diesem Fall eine auf maximal 20 Jahre befristete Nutzungsexklusivität, welche durch ein „ergänzendes Schutzzertifikat“ sowie Unterlagenschutz um maximal fünf weitere Jahre verlängert werden kann. Vor dem Hintergrund eines Entwicklungszeitraums von etwa zehn Jahren zwischen Patentanmeldung und marktfähigem Produkt kann somit von einer durchschnittlich zehn- bis fünfzehnjährigen tatsächlichen Marktexklusivität ausgegangen werden (Schweitzer/Lu 2018).

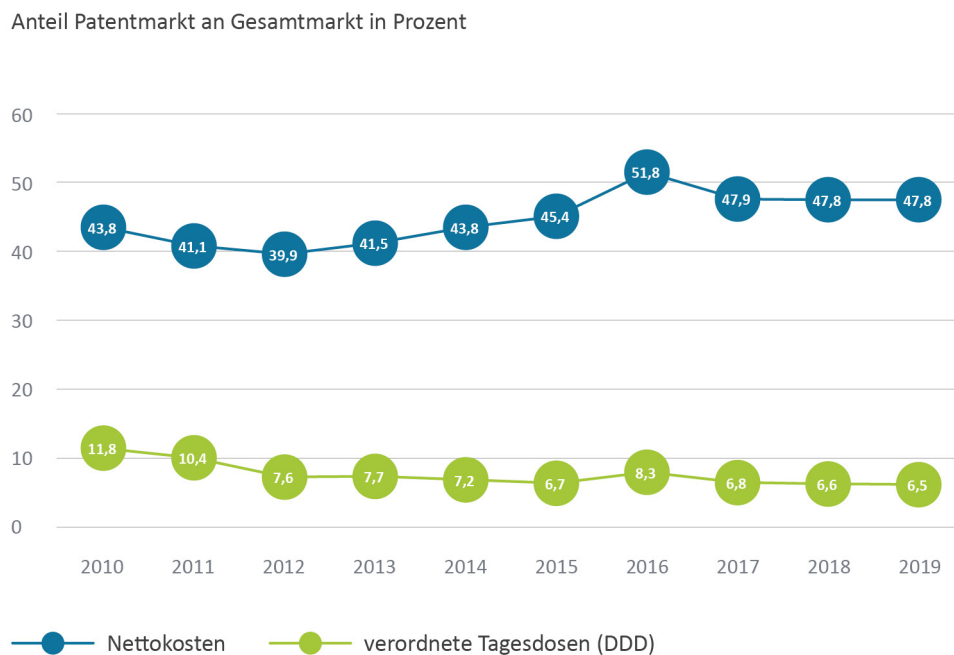
Abbildung 2-1: Verordnungen in Tagesdosen und Nettokosten im Patentmarkt seit 2010



Die Kosten für diesen Patentmarkt lagen 2019 bei 21,0 Mrd. € und haben sich gegenüber 2010 beinahe verdoppelt. Die Verordnungen entwickelten sich gegenläufig und sanken im gleichen Zeitraum (Abbildung 2-1). Folglich haben sich die durchschnittlichen DDD-Nettokosten 2019 gegenüber 2010 beinahe verdreifacht. Während die gesetzlichen Krankenkassen für eine Tagesdosis eines patentgeschützten Arzneimittels 2010 noch durchschnittlich 2,85 € ausgegeben haben, sind es im Jahr 2019 bereits 7,36 €. Zum Vergleich: Im Gesamtmarkt stiegen die DDD-Nettokosten im selben Zeitraum von 0,77 € auf 1,00 € (Abbildung 1-1). Dies zeigt, dass die Ausgaben und Preise im Patentmarkt deutlich stärker steigen als im restlichen Markt.

Auch in der Relation zum Gesamtmarkt nimmt der Patentmarkt eine gewichtige Rolle ein: Die Nettokosten für patentgeschützte Arzneimittel lagen 2019 bei 21,0 Mrd. €, was einem Anteil von 47,8 % am Gesamtmarkt entspricht. Dem steht ein Verordnungsanteil von lediglich 7 % gegenüber. Vor zehn Jahren lag der Nettokostenanteil des Patentmarktes bei vergleichbaren 43 % bei einem Verordnungsanteil von deutlich höheren 12 % (Abbildung 2-2).

Abbildung 2-2: Verordnungsanteil nach Tagesdosen und Nettokostenanteil des Patentmarktes seit 2010



Wie bereits in Kapitel 1 Abbildung 1-3 gezeigt, sind es nicht nur die Arzneimittel des Patentmarktes, die immer teurer werden, sondern insbesondere die neuen Arzneimittel, die innerhalb der letzten 36 Monate auf den Markt gekommen sind. Während die teuerste Packung aller neuen Markteinführungen im Zeitraum von 2009 bis 2011 knapp 58.000 € kostete (für das Arzneimittel Vpriv zur Behandlung der Enzymmangelkrankheit Morbus Gaucher Typ 1), war es im Zeitraum von 2018 bis 2020, das Arzneimittel Luxturna mit 345.000 €. Dieses wird zur Behandlung von Sehverlust aufgrund einer erblichen Netzhautveränderung eingesetzt. Der Preis der teuersten Packung im Markt hat sich damit innerhalb von zehn Jahren mehr als versechsfacht. Dabei scheinen die Grenzen nach oben offen zu sein: Zolgensma, das aktuell teuerste Arzneimittel der Welt ist seit Mai 2020 auch in Europa zugelassen und seit dem 1. Juli 2020 auch auf dem deutschen Markt mit einem Listenpreis von 1,945 Mio. € verfügbar (Deutsches Ärzteblatt 2020). Dieses Gentherapeutikum ist zugelassen für die Behandlung von Kindern mit Spinaler Muskelatrophie, einer genetisch bedingten Muskelerkrankung, die durch schwere Lähmungserscheinungen geprägt ist.

Die Entwicklung an der Preisspitze spiegelt sich in den durchschnittlichen Preisen aller neuen Markteinführungen wieder. Allein in den letzten zwei Jahren – im Zeitraum von Januar 2018 bis Dezember 2019 – ist mit Einführung mehrerer extrem teurer Präparate der durchschnittliche Packungspreis der Marktneueinführungen von 4.875 € auf 13.687 € angestiegen (Abbildung 1-3). Im gleichen Zeitraum sind die Durchschnittspreise im restlichen Patentmarkt von 2.197 € auf 2.417 € vergleichsweise moderat um 10 % ebenfalls gestiegen.

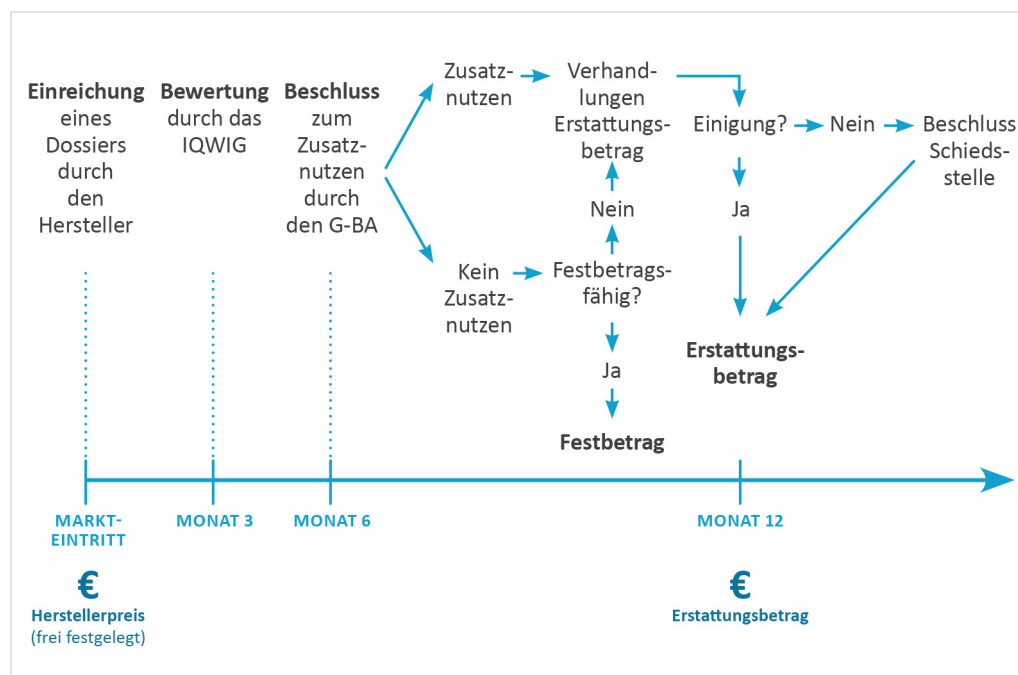
2.2 Frühe Nutzenbewertung und Preisentwicklung bei patentgeschützten Arzneimitteln seit 2011

Mit dem Ziel, steigende Ausgaben für Arzneimittel der gesetzlichen Krankenkassen zu reduzieren, ist am 1. Januar 2011 das AMNOG in Kraft getreten (Bundesministerium für Gesundheit 2016). Die damit eingeführte Frühe Nutzenbewertung (§ 35a SGB V) brachte eine ordnungspolitische Richtungsänderung: Erstmals fanden eine transparente und evidenzbasierte Einordnung patentgeschützter Arzneimittel mit neuen Wirkstoffen in ihren therapeutischen Kontext und eine nachgelagerte Erstattungspreisvereinbarung zwischen dem pharmazeutischen Unternehmen und dem GKV-Spitzenverband (GKV-SV) statt. Vor 2011 oblag die Preisgestaltung allein dem pharmazeutischen Unternehmen.

Der Preis eines neuen Arzneimittels wird durch diese Regelung an seinem Zusatznutzen für Patientinnen und Patienten gemessen, über den die Hersteller mit der Markteinführung einen Nachweis erbringen müssen. Dieser Nachweis kann unter anderem dadurch erfolgen, dass die Behandlung der indizierten Krankheit besser als zuvor erfolgt, der Heilungsprozess schneller verläuft, die Lebensqualität der Patientinnen und Patienten verbessert wird oder die Nebenwirkungen geringer sind als mit den bisherigen Therapieoptionen (Bundesministerium für Gesundheit 2016).

Der G-BA trifft auf Grundlage der wissenschaftlichen Bewertung der vorgelegten Nachweise die Entscheidung, ob ein Zusatznutzen vorliegt und welches Ausmaß dieser hat. Dieses Ergebnis ist die Grundlage für die darauffolgende Preisverhandlung zwischen dem GKV-SV und dem pharmazeutischen Unternehmen (Haas et al. 2019). Wenn kein Zusatznutzen festgestellt werden und das Arzneimittel keiner Festbetragsgruppe zugeordnet werden kann, wird die maximale Erstattungshöhe auf den Preis der vergleichbaren Therapien festgelegt. Wird hingegen einem neuen Arzneimittel ein Zusatznutzen attestiert, erfolgt die Preisverhandlung auf Grundlage der Nutzenbewertung unter Berücksichtigung des Wettbewerbs. Wenn in der Verhandlung keine Einigung erzielt wird, setzt eine Schiedskommission den Erstattungsbetrag fest, wobei dann auch das europäische Preisniveau einbezogen werden soll (GKV-Spitzenverband 2020). Der so ausgehandelte Erstattungsbetrag tritt ein Jahr nach Markteinführung in Kraft. Die ersten zwölf Monate müssen die gesetzlichen Krankenkassen den vom pharmazeutische Unternehmen festgelegten Preis vollständig erstatten (Abbildung 2-3).

Abbildung 2-3: Frühe Nutzenbewertung nach dem AMNOG



Quelle: eigene Darstellung in Anlehnung an SVR (2014)

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Mit dem Gesetz zur Stärkung der Arzneimittelversorgung in der GKV (AMVSG) wurden 2017 größere Justierungen am AMNOG vorgenommen. So wurden unter anderem mehrere Ausnahmetatbestände im Verfahren der Frühen Nutzenbewertung bzw. die nachfolgenden Preisverhandlungen für Kinderarzneimittel und Antibiotika geschaffen. Seitdem ist es auch möglich, bei der Vereinbarung von Erstattungsbeträgen bei nicht belegtem Zusatznutzen von der Vorgabe abzuweichen, dass der Erstattungsbetrag nicht zu höheren Jahrestherapiekosten führen darf als die wirtschaftlichste Vergleichstherapie. Dies wurde für begründete Einzelfälle – wenn es für die Patientin oder den Patienten eine wichtige Therapieoption bedeuten kann – vorgesehen (Bundesministerium für Gesundheit 2017). Seither wurden in über zwei Dritteln der Fälle höhere Preise für Arzneimittel ohne belegten Zusatznutzen vereinbart (Haas et al. 2019). Diese Ausnahme wurde somit in kurzer Zeit zur Regel.

Konnten die Ziele des AMNOG erreicht werden?

Mit dem AMNOG sollten zwei maßgebliche Ziele verfolgt werden: So ist es gelungen, Transparenz über den therapeutischen Stellenwert einer Arzneimittelinnovation herzustellen. Mit der abgeschlossenen Nutzenbewertung steht eine umfassende Bestandsaufnahme des aktuellen Informationsstandes für ein neues Arzneimittel zur Verfügung, die bei neuen Erkenntnissen – neue klinische Studien oder Auswertungen, Zulassungen für neue Anwendungsgebiete – regelhaft aktualisiert wird. So wurden bis Ende 2019 zu insgesamt 273 neuen Arzneimitteln Nutzenbewertungsverfahren durchgeführt. Darin zeigte sich für 172 Arzneimittel ein Zusatznutzen in wenigstens einer Teilpopulation, für 101 Arzneimittel konnte jedoch keinerlei zusätzlicher Nutzen im Vergleich mit den anderen verfügbaren Therapieoptionen gefunden werden. Diese Ergebnisse können somit einen Mehrwert für Patientinnen und Patienten und behandelnde Ärztinnen und Ärzte darstellen, um eine auf wissenschaftlicher Evidenz basierte Therapie durchführen zu können.

Zudem sollen die Ergebnisse der Frühen Nutzenbewertung demnächst niederschwellig und leicht erfassbar im Rahmen eines unabhängigen Informationssystems für Ärzte zur Verfügung gestellt werden (Bundesministerium für Gesundheit 2019). Allerdings lässt die geplante Ausgestaltung noch zu wünschen übrig. Da in der aktuell geplanten Form des Informationssystems zentrale Informationen fehlen, ist zu befürchten, dass Ärztinnen und Ärzte kaum in die Lage versetzt werden, einen tatsächlichen Überblick über den Stellenwert des betreffenden Arzneimittels im Therapiegebiet und die Einordnung der Kosten zu erhalten. Jedoch erscheint es allen Beteiligten klar, dass nur mit einer differenzierten Betrachtung der Ergebnisse zum Zusatznutzen ein Arzneimittel sinnvoll und wirtschaftlich einsetzbar ist (Litsch et al. 2019). Für die Ärztinnen und Ärzte wäre bei dem nunmehr beschrittenen Weg nicht erkennbar, für welche Patientengruppen das Arzneimittel überhaupt einen Zusatznutzen bietet. Zum anderen hat das AMNOG nicht nur ein Instrument zur evidenzbasierten Bewertung neuer Arzneimittel etabliert, sondern es wurde auch erstmals die Möglichkeit geschaffen, über die Preise dieser neuen Arzneimittel kollektiv zu verhandeln und so wirksam die Arzneimittelausgaben zu dämpfen. Doch konnte dieses Ziel des AMNOG auch erreicht werden?

Aus vergleichenden, länderübergreifenden Untersuchungen der Preisniveaus von Arzneimitteln (eine aktuelle Übersicht ist bei Schneider/Vogler 2019 zu finden) geht Deutschland regelmäßig als Hochpreisland für patentgeschützte Arzneimittel hervor (Vogler et al. 2014, Busse et al. 2016, Vogler et al. 2016, Busse et al. 2017). Dabei muss berücksichtigt werden, ob die ggf. virtuellen Listenpreise oder die faktischen verhandelten Preise im Preisvergleich genutzt werden. Eine Herausforderung in Deutschland besteht darin, dass pharmazeutischen Unternehmen mit ihren neuen Arzneimitteln direkten Zugang zum Markt haben. So gibt es in Deutschland auch trotz AMNOG keine sogenannte vierte Hürde, mit der nach der erfolgreichen europaweiten Zulassung zunächst die nationalen erstattungsrechtlichen Voraussetzungen festgelegt werden, bevor die neuen Arzneimittel den Patientinnen und Patienten verordnet werden können (Vogler 2018). Diese Freiheit wird von den Herstellern zur vergleichsweise frühzeitigen Markteinführung genutzt: In Deutschland sind neue Arzneimittel häufig früher im Markt als in anderen Ländern (Busse et al. 2015, Lackner et al. 2017).

Dazu kommt die Möglichkeit der freien Preisbildung, die zwar gegenüber der Zeit vor dem AMNOG mit zwölf Monaten kürzer ist, aber trotzdem innerhalb dieses Zeitraumes unbeschränkt gilt. Somit können pharmazeutische Unternehmen mögliche Abschläge, die durch die nachgelagerte Preisverhandlung entstehen, vorher einpreisen, um so den angestrebten Zielpreis als Verhandlungsergebnis zu erreichen. Schon ein nur geringer Zusatznutzen in einer kleinen Teilpopulation bedingt in der Regel einen Preisaufschlag gegenüber dem bisherigen Therapiestandard. Auswertungen des GKV-SV, der für die Krankenkassen zentral die Verhandlungen um die Erstattungsbeträge führt, zeigen, dass selbst für Arzneimittel ohne belegten Zusatznutzen bereits zu 70 % ein Aufschlag auf die Kosten des wirtschaftlichsten Therapiestandards möglich war (Haas et al. 2019). Dem intendierten Zweck des AMNOG, die Preise vorrangig am Nutzen zu orientieren, widerspricht diese Anpassung.

Folglich kann trotz AMNOG festgestellt werden, dass die gesetzlichen Rahmenbedingungen in Deutschland hohe Preise für Markteinführungen begünstigen. Eine Forderung, die insbesondere von Kostenträgerseite in den vergangenen Jahren immer wieder formuliert wurde, ist die rückwirkende Geltung des verhandelten Erstattungsbetrags ab dem ersten Tag (GKV-Spitzenverband 2016, Stoff-Ahnis 2020).

Führt das AMNOG zu Versorgungsproblemen?

Einerseits wird als wesentlicher Verdienst des AMNOG hervorgehoben, dass in einem geregelten Verfahren mit transparenter, auf Evidenz basierender Methodik der Stellenwert eines neuen Wirkstoffs in seinem therapeutischen Umfeld bewertet werden kann. Folglich wird schon zu einem frühen Zeitpunkt deutlich, welche Arzneimittel therapeutisch einen Nutzen haben und welche aus therapeutischer Sicht verzichtbar sein könnten. Andererseits wird argumentiert, dass das AMNOG zu Versorgungsdefiziten führe, da es Marktrückzüge der pharmazeutischen Unternehmen verstärke (Cassel/Ulrich 2019).

Seit 2011 wurden insgesamt 46 Arzneimittel nach oder während der Nutzenbewertung wieder vom Markt genommen. 16 davon sind dem Markt nur kurzzeitig aus verhandlungstaktischen Gründen entzogen worden und inzwischen nach erneuten Bewertungsverfahren mit meist besserer Evidenzgrundlage oder nach letztlich doch erfolgter Preiseinigung wieder im Markt. Die restlichen 30 nicht mehr im Markt befindlichen Arzneimittel bedeuten aber nicht ein Versagen des AMNOG, sondern sind vielmehr Ausdruck seines Funktionierens: Für die zurückgezogenen Arzneimittel konnte meist kein Zusatznutzen gezeigt werden und die Hersteller waren in der Folge nicht bereit, den dann zwingend niedrigeren Erstattungsbetrag auf dem Niveau der jeweiligen Vergleichstherapie zu akzeptieren. Das Ziel, die Spreu vom Weizen zu trennen, wurde erreicht. Von den Herstellern wurde in diesen Fällen die Marktrücknahme in Deutschland vermutlich in Kauf genommen, um zu verhindern, dass ein niedriger deutscher Preis als Referenzpreis in die Arzneimittelpreisbildung anderer Länder Eingang findet (AkdÄ 2013). Zehn der 30 Arzneimittel hatten zunächst einen Zusatznutzen, wurden im Laufe der Zeit aber wegen mangelnder Wirksamkeit oder zunehmender Produktkonkurrenz von den Herstellern weltweit vom Markt genommen, oder es wurden keine Gründe für die Marktrücknahme in Deutschland gegeben.

Mit den 31 endgültig zurückgezogenen Arzneimitteln wurden während ihrer Marktpräsenz Nettokosten von insgesamt 1,62 Mrd. € erzielt, für alle 15 inzwischen wieder in den Markt zurückgekehrten Arzneimittel entstanden vor dem Zeitpunkt ihres Rückzugs weitere Nettokosten in Höhe von knapp 800 Mio. €, zusammen also über 2,4 Mrd. €. Diese Kosten entstanden für Arzneimittel, für die meist mindestens gleichwertige und wirtschaftlichere Alternativen zur Verfügung stehen. Allein für die Antidiabetika Eucreas und Icandra mit der Wirkstoffkombination Vildagliptin/Metformin entstanden seit 2011 bis zu deren Marktrücknahmen 2015 wegen nicht belegten Zusatznutzens Nettokosten in Höhe von 296 Mio. €. Der über die Schiedsstelle festgelegte Erstattungsbetrag mit über 50 % Abschlag wurde in leicht modifizierter Form erst 2018 vom Hersteller akzeptiert. Die Produkte wurden wieder angeboten, auch wenn noch immer kein Zusatznutzen belegt ist.

Dieses Ergebnis unterstreicht auch generell die Problematik des schnellen, freien Marktzugangs im ersten Jahr ohne eine sogenannte vierte Hürde, wie sie in anderen Ländern üblich ist. Gerade bei versorgungsrelevanten Arzneimitteln kann es ein Vorteil sein, wenn bereits nach der Zulassung und vor Marktzugang eine Bewertung durchgeführt wird. Denn ein früher, unbeschränkter Marktzutritt birgt auch immer ein Sicherheitsrisiko für die Patientinnen und Patienten, da das Nebenwirkungsspektrum bei Markteintritt häufig noch nicht vollständig bekannt ist. Zudem könnte auf einen nachträglichen Marktrückzug des Produktes verzichtet werden, womit unnötige Belastungen der betroffenen Patienten vermieden würden.

Marktrückzüge gibt es auch nicht erst seit Einführung des AMNOG, denn sowohl aus wirtschaftlichen als auch therapeutischen Gründen sind Beispiele bekannt (Ujeyl/Schlegel 2015). Besonders bedenklich ist es, wenn Arzneimittel mit unsicheren Daten frühzeitig in den Markt kommen und sich im Zuge des breiten Einsatzes Sicherheitsbedenken herausstellen, die zu einer Rücknahme des Arzneimittels führen. Ein frühzeitiger Markteintritt mit geringer Datengrundlage birgt die große Gefahr, dass beispielsweise nicht vorhergesehene Nebenwirkungen zu Lasten der Patientinnen und Patienten auftreten, die durch klinische Studien bereits im Vorfeld hätten erkannt werden können. Eine weitere Gefahr ist, dass das Arzneimittel bei der Anwendung an größeren, nicht selektierten Patientengruppen keine Wirkung zeigt. Für das Antiepileptikum Trobalt ergab schon das AMNOG-Verfahren 2012 keinen Zusatznutzen. Der Hersteller hat das Mittel zunächst frühzeitig vom deutschen Markt genommen. Mitte 2017 erfolgte dann auch weltweit der Rückzug, da Trobalt offenbar sein therapeutisches Versprechen in der Praxis nicht ausreichend einlösen konnte (Tröbitscher 2017). Auch die aufgrund der Coronavirus-Pandemie geführten Debatten um eine frühzeitige Zulassung von hinsichtlich Wirksamkeit und Unbedenklichkeit nicht ausreichend geprüften Arzneimitteln gegen COVID-19 sind in diesem Kontext anzuführen (BfArM 2020, Der Arzneimittelbrief 2020, Müller 2020).

Wie erfolgreich sind die aktuellen Möglichkeiten zur Preisfindung im Rahmen des AMNOG?

Um die Frage zu beantworten, welche Einsparungen durch die Preisverhandlungen in den letzten Jahren erreicht wurden, können die Differenzen der Listenpreise bei Markteinführung und den sich nach den Verhandlungen auf Basis der Erstattungsbeiträge ergebenden Preisen gebildet und über die Zeit aufsummiert werden. Danach konnten im Jahr 2019 die Ausgaben um insgesamt 3,61 Mrd. € bei einem Bruttoumsatz von 12,68 Mrd. € verringert werden. Zu vermuten ist allerdings, dass pharmazeutische Hersteller mit hohen Preisen bei Markteintritt einstiegen, die dann bei der folgenden Preisverhandlung reduziert werden. So steigen trotz dieser Preisabschläge nach den Preisverhandlungen die Gesamtausgaben im Patentmarkt weiter an (siehe oben).

Die Ergebnisse der Nutzenbewertung und die Differenzen zwischen dem ursprünglichen Listenpreis der Hersteller (Preis des pharmazeutischen Unternehmers (PPU)) und dem aktuell verhandelten Erstattungspreis (APU) für die neuen Arzneimittel sind in Tabelle 2-1 gelistet. Auffällig ist auch in diesem Ausschnitt, dass eine Vielzahl von Präparaten als höchstes Ergebnis der Nutzenbewertung keinen bzw. keinen belegbaren Zusatznutzen attestiert bekommen. Auch wenn in der Vergangenheit gezeigt werden konnte, dass sich der mittlere Preisabstand zwischen Arzneimitteln mit Zusatznutzen von denen ohne Zusatznutzen signifikant unterscheidet (Schröder/Telschow 2017), so stellt Tabelle 2-1 exemplarisch dar, wie unterschiedlich diese Preisreduzierungen auch innerhalb einer Zusatznutzenkategorie ausfallen können.

Demnach erhalten Arzneimittel insgesamt einen Abschlag zwischen 5 % und 59 % während sich das Bild zwischen Arzneimitteln nach Zusatznutzen nicht stark unterscheidet. Arzneimittel mit Zusatznutzen sind durch einen Abschlag zwischen 5 % und 51 % gekennzeichnet, während der Abschlag für Arzneimittel, für die kein Zusatznutzen attestiert werden konnte, zwischen 7 % und 59 % liegt. Erklärend ist zu beachten, dass die Markteinführungspreise vom pharmazeutischen Hersteller frei gewählt werden und sich die Rationalität bei der Festlegung der Preishöhe zwischen den pharmazeutischen Herstellern oder den verschiedenen Produkten deutlich unterscheiden dürfte.

Tabelle 2-1: Ergebnisse der Nutzenbewertung und die Differenzen zwischen dem ursprünglichen Listenpreis der Hersteller (PPU) und dem aktuell verhandelten Erstattungspreis (APU) für die neuen Arzneimittel des Jahres 2018, für die bis Mai 2020 ein Erstattungsbetrag verhandelt wurde

Präparat	Wirkstoff	Hauptindikationsgruppe	Höchstes Nutzenbewertungsergebnis	ursprünglicher Hersteller-Listenpreis (PPU) der verordnungstärksten Packung in €	Niedrigster Herstellerabgabepreis (APU) der verordnungstärksten Packung in €	Abschlag in %	Verordnungen des Präparates 2019 in Tsd.
Trelegy Ellipta	Vilanterol, Umeclidinium-bromid und Fluticasonfuroat	chronische Atemwegserkrankungen	Zusatznutzen ist nicht belegt	200,70	162,43	19,1	95,0
Elebrato Ellipta	Vilanterol, Umeclidiniumbromid und Fluticasonfuroat	chronische Atemwegserkrankungen	Zusatznutzen ist nicht belegt	200,70	162,43	19,1	55,8
Biktarvy	Emtricitabin, Tenofoviralfenamid und Bictegravir	Infektionskrankheiten	Zusatznutzen ist nicht belegt	2.340,00	2.167,50	7,4	43,4
Aimovig	Erenumab	Schmerzen und Entzündungen	beträchtlicher Zusatznutzen	535,76	383,36	28,4	40,7
Imfinzi	Durvalumab	Krebserkrankungen	beträchtlicher Zusatznutzen	552,00	472,53	14,4	39,3
Steglujan	Sitagliptin und Ertugliflozin	Diabetes	Zusatznutzen ist nicht belegt	249,90	177,01	29,2	35,5
Ocrevus	Ocrelizumab	Immuntherapie	geringer Zusatznutzen	6.750,00	5.125,00	24,1	22,6
Fasenra	Benralizumab	chronische Atemwegserkrankungen	geringer Zusatznutzen	2.762,50	2.079,31	24,7	14,0
Reagila	Cariprazin	Erkrankungen des Nervensystems	geringer Zusatznutzen	529,94	259,27	51,1	13,8
Veltassa	Patiromercalcium	Sonstige	Zusatznutzen ist nicht belegt	300,00	183,28	38,9	9,3
Adynovi	Ruriococog alfa pegol	Erkrankungen des Blutsystems	Zusatznutzen ist nicht belegt	2.340,00	1.804,00	22,9	7,1
Hemlibra	Emicizumab	Erkrankungen des Blutsystems	nicht quantifizierbarer Zusatznutzen	4.917,17	3.879,83	21,1	5,8
Symkevi	Ivacaftor und Tezacaftor	chronische Atemwegserkrankungen	beträchtlicher Zusatznutzen	5.491,78	5.217,19	5,0	5,6
Juluca	Dolutegravir und Rilpivirin	Infektionskrankheiten	Zusatznutzen ist nicht belegt	2.715,75	2.025,00	25,4	5,2
Ravicti	Glycerolphénylbutyrat	Stoffwechselerkrankungen	nicht quantifizierbarer Zusatznutzen	325,00	208,00	36,0	5,2
Crysvita	Burosumab	Erkrankungen des Muskel- und Skelettsystems	nicht quantifizierbarer Zusatznutzen	10.163,00	7.650,00	24,7	4,6
Ilumetri	Tildrakizumab	Immuntherapie	Zusatznutzen ist nicht belegt	4.122,90	2.792,00	32,3	4,3

...

Fortsetzung Tabelle 2-2: Ergebnisse der Nutzenbewertung und die Differenzen zwischen dem ursprünglichen Listenpreis der Hersteller (PPU) und dem aktuell verhandelten Erstattungspreis (APU) für die neuen Arzneimittel des Jahres 2018, für die bis Mai 2020 ein Erstattungsbetrag verhandelt wurde

Präparat	Wirkstoff	Hauptindikationsgruppe	Höchstes Nutzenbewertungsergebnis	ursprünglicher Hersteller-Listenpreis (PPU) der verordnungstärksten Packung in €	niedrigster Herstellerabgabepreis (APU) der verordnungstärksten	Abschlag in %	Verordnungen des Präparates 2019 in Tsd.
Braftovi	Encorafenib	Krebserkrankungen	Zusatznutzen ist nicht belegt	1.604,67	1.405,99	12,4	4,3
Alkindi	Hydrocortison	Immuntherapie	Zusatznutzen ist nicht belegt	145,00	102,00	29,7	4,1
Verzenio	Abemaciclib	Krebserkrankungen	Zusatznutzen ist nicht belegt	2.674,00	1.961,54	26,6	4,0
Mektovi	Binimetinib	Krebserkrankungen	Zusatznutzen ist nicht belegt	3.056,51	1.250,31	59,1	2,8
Sialanar	Glycopyrroniumbromid	Magen-Darm-Erkrankungen	nicht quantifizierbarer Zusatznutzen	491,00	400,00	18,5	2,0
Prevymis	Letermovir	Infektionskrankheiten	nicht quantifizierbarer Zusatznutzen	4.650,24	4.105,25	11,7	1,9
Onpattro	Patisiran	Erkrankungen des Nervensystems	beträchtlicher Zusatznutzen	8.529,41	7.583,33	11,1	1,8
Odomzo	Sonidegib	Krebserkrankungen	Zusatznutzen ist nicht belegt	5.837,50	4.440,00	23,9	0,5
Lamzede	Velmanase alfa	Stoffwechselerkrankungen	nicht quantifizierbarer Zusatznutzen	15.500,00	8.800,00	43,2	0,5
Cablivi	Caplacizumab	Herz-Kreislauf-Erkrankungen	nicht quantifizierbarer Zusatznutzen	4.609,93	3.577,89	22,4	0,4
Myalepta	Metreleptin	Stoffwechselerkrankungen	nicht quantifizierbarer Zusatznutzen	67.500,00	55.781,25	17,4	0,2
Tegsedi	Inotersen	Erkrankungen des Nervensystems	nicht quantifizierbarer Zusatznutzen	44.951,93	21.584,00	52,0	0,2
Vyxeos	Cytarabin und Daunorubicin	Krebserkrankungen	beträchtlicher Zusatznutzen	6.300,00	5.150,00	18,3	0,1
Mepsevii	Vestronidase alfa	Stoffwechselerkrankungen	nicht quantifizierbarer Zusatznutzen	2.039,00	1.480,00	27,4	0,0
Zinplava	Bezlotoxumab	Infektionskrankheiten	geringer Zusatznutzen	2.950,00	2.360,21	20,0	0,0
Mylotarg	Gemtuzumab ozogamicin	Krebserkrankungen	nicht quantifizierbarer Zusatznutzen	10.530,00	6.750,00	35,9	0,0
Ozempic	Semaglutid	Diabetes	geringer Zusatznutzen	136,40	73,63	46,0	0,0

Stellt man die Umsätze der Arzneimittel, die in den Jahren 2011 bis 2019 einer Frühen Nutzenbewertung unterzogen wurden und für die bis Ende 2019 ein Erstattungsbetrag verhandelt wurde, den Umsätzen gegenüber, die sich ergeben hätten, wenn der verhandelte Erstattungsbetrag bereits bei Markteinführung gegolten hätte, zeigen sich die Mehrbelastungen der GKV durch die herstellerseitige freie Preisbildung im ersten Jahr. Addiert man diese Mehrkosten, die aufgrund der freien Preisbildung im ersten Jahr angefallen sind, so ergeben sich in Summe 1.227 Mio. €, die die GKV in den Jahren 2011 bis 2019 hätte einsparen können, wenn die vereinbarten Erstattungsbeträge bereits ab der Markteinführung gültig gewesen wären. Allein für das Jahr 2019 summieren sich diese Mehrkosten auf 46 Mio. €. Umsätze von Festbetrags-Arzneimitteln und von Arzneimitteln ohne Erstattungsbeträge (wegen Marktrückzügen, fehlendem Preiskennzeichen oder noch fehlender Preiseinigung) sind in dieser Berechnung nicht enthalten, da die Preisdifferenzen für diese nicht berechnet werden können.

Doch nicht nur zur Markteinführung werden Erstattungsbeträge verhandelt; diese schließen sich im Regelfall auch nach einer Neubewertung an, wenn beispielsweise ein neues Anwendungsgebiet zugelassen wird und damit größere Patientenpopulationen neu erschlossen werden oder wenn sich die Bewertung des Zusatznutzens ändert, beispielsweise bei Vorliegen neuer Studienergebnisse. Auch hier sollte es möglich sein, den verhandelten Erstattungsbetrag zwölf Monate rückwirkend gelten zu lassen: Denn die Patientinnen und Patienten im neuen Anwendungsgebiet können schon ab dem Zeitpunkt der Zulassungserweiterung mit dem Arzneimittel behandelt werden, der neu verhandelte Preis steht aber erst später fest (Litsch et al. 2019). Bezieht man diese – sowohl positiven als auch negativen – Preisänderungen nach Neubewertungen in die Berechnung mit ein, so addieren sich die Mehrkosten seit 2011 sogar auf 1,75 Mrd. € für zu hohe Preise aufgrund bislang nicht möglicher rückwirkender Geltung, davon allein 180 Mio. € für das Jahr 2019. Die Hersteller profitieren also weiterhin deutlich von der freien Preisbildung.

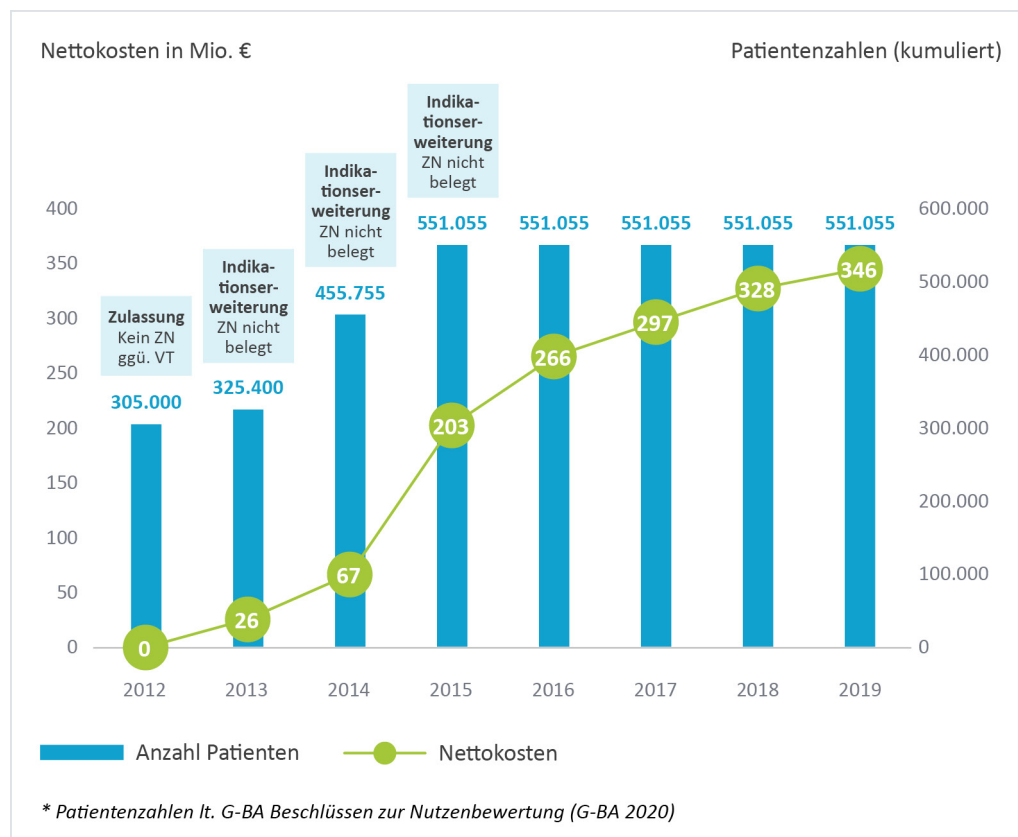
Wie passen die verhandelten Preise und Patientenzahlen bei Indikationserweiterungen zusammen?

Im Laufe des Produktlebens eines Arzneimittels kommt es in vielen Fällen zu einer Ausweitung der zugelassenen Anwendungsgebiete. Dabei stellt sich die Frage, ob Indikationserweiterungen, die auch mit einer größeren Anzahl an behandelbaren Patientinnen und Patienten einhergehen, in den nachfolgenden Preisverhandlungen angemessen Berücksichtigung finden. Exemplarisch wird hier der „Weg“ des Arzneimittels Eylea nachgezeichnet: Ende des Jahres 2012 wurde dieses Medikament zur Behandlung von Erwachsenen mit neovaskulärer altersbedingter Makuladegeneration ohne einen Beleg für einen Zusatznutzen gegenüber dem Wirkstoff Ranibizumab für eine Patientenpopulation von ca. 305.000 Patientinnen und Patienten zugelassen. In den folgenden drei Jahren erfolgten Zulassungserweiterungen auf insgesamt fünf Anwendungsgebiete¹. Ein Zusatznutzen konnte jedoch in keinem der Fälle belegt werden. In Summe hat sich bei Eylea die durch die Zulassung adressierte Patientenpopulation innerhalb von drei Jahren von ursprünglich 305.000 auf 550.000 nahezu verdoppelt. Der Erstattungsbetrag von Eylea ist allerdings, bezogen auf den ersten Erstattungsbetrag aus dem

¹ 2013: Behandlung von Erwachsenen mit einer Visusbeeinträchtigung aufgrund eines Makulaödems infolge eines Zentralvenenverschlusses; 2014: Behandlung einer Visusbeeinträchtigung aufgrund eines diabetischen Makulaödems bei Erwachsenen; 2015: Behandlung einer Visusbeeinträchtigung aufgrund eines Makulaödems infolge eines retinalen Venenastverschlusses und zur Behandlung von Visusbeeinträchtigung aufgrund einer myopen choroidalen Neovaskularisation

Jahr 2013, sogar um ca. 5 % angestiegen. Hier werden keine Kostenreduktionen erreicht, obwohl der Behandlungsumfang gemäß Patientenzahl eines der Kriterien für die Preisverhandlungen ist. Folglich stiegen auch die Nettokosten und sorgen dafür, dass dieses Arzneimittel 2019 mit über 345 Mio. € auf Rang 11 der nettokostenstärksten Arzneimittel der GKV rangiert (Abbildung 2-4). Zwar bietet das AMNOG für Arzneimittel, die ab 2011 in den Markt kamen, die Möglichkeit der erneuten Preisverhandlung bei neuen Anwendungsgebieten, die Preise (Erstattungsbeträge) werden aber nur selten trotz der Erweiterung der Patientenzahl reduziert. Auch wenn die Preisverhandlungen keinem festgelegten Algorithmus folgen, sollte anzunehmen sein, dass – gerade bei nicht belegtem Zusatznutzen – bei einer Erhöhung der behandelbaren Patientenzahl mit einer angemessenen Senkung des Erstattungsbetrags reagiert wird.

Abbildung 2-4: Nettokosten und Anzahl der von der Zulassung adressierten Patientinnen und Patienten nach Indikationserweiterungen für das Arzneimittel Eylea seit dessen Markteinführung 2012



Quelle: WIdO, Gemeinsamer Bundesausschuss (2020)

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Grundsätzlich sind Indikationserweiterungen positiv zu bewerten, da sie das Spektrum der verfügbaren Therapieoptionen erweitern. Wenn die Arzneimittel in den neuen Anwendungsgebieten jedoch keinen Zusatznutzen zu bestehenden Vergleichstherapien aufweisen, sollte sich dies im Preis niederschlagen. Beim Beispiel Eylea vergrößert sich die Patientenpopulation bei gleichem oder – wie hier – sogar steigendem Preis, ohne dass dies eine echte Verbesserung für die Versorgung darstellt.

Ist das AMNOG eine ausreichende Antwort auf den Trend zu immer teureren Patentarzneimitteln?

Der Arzneimittelmarkt befindet sich in stetem Wandel, die Entwicklung von Arzneimitteln wird durch eine Vielzahl von Faktoren beeinflusst. So sind unter anderem gesetzliche Rahmenvorgaben und Erstattungsbedingungen nicht zu unterschätzende Größen, die bei Herstellern die strategische Entscheidung zur Entwicklung eines Arzneimittels beeinflussen. Der medizinische Erkenntnisstand bietet heute deutlich mehr Möglichkeiten und Therapieansätze. Die Ursachen und die Entstehung von Krankheiten sind auch durch die Aufschlüsselung des menschlichen Genoms in vielen Gebieten heute besser erforscht als noch vor wenigen Jahren. So sind viele genetische und molekulare Strukturen im menschlichen Organismus, deren Veränderungen zu Erkrankungen führen, erst seit wenigen Jahren wissenschaftlich untersuchbar. Mit diesem Wissen können für eine zielgerichtete Behandlung andere Strategien verfolgt und neue Arzneimittel entwickelt werden.

Die damit ermöglichte differenzierte und zielgerichtete Behandlung bedingt aber auch, dass Arzneimittel bei Patientinnen und Patienten nur dann gut wirksam sind, wenn definierte biologische Prozesse die tatsächliche Ursache der Krankheit sind. Bei allen anderen sind diese Arzneimittel oft deutlich weniger effektiv, können durch Resistenzbildung umgangen werden oder sind einfach wirkungslos. Arzneimittel mit speziellen Wirkprinzipien, wie beispielsweise monoklonale Antikörper, sind in den vergangenen ca. 20 Jahren verstärkt entwickelt worden. Eine weitere Spezialisierung deutet sich mit den nun auf den Markt gekommenen Gentherapeutika wie Kymriah, Yescarta und Zolgensma an. Diese sind jeweils nur für sehr wenige Patientinnen und Patienten einsetzbar und dies zu bis vor kurzem noch unvorstellbar hohen Preisen.

Wenn jedoch mit diesen Arzneimitteln auch nur ein kleiner Teil einer Patientenpopulation sinnvoll behandelt werden kann, ist dies für die Industrie ein Argument zur Rechtfertigung hoher Preise, die sich nicht immer proportional zur Anzahl der behandelten Patientinnen und Patienten verhalten. Das zeigt das Beispiel Eylea zeigt (siehe oben). Doch was bedeutet diese Entwicklung für die damit verbundenen Gesamtkosten? Bei der Aufteilung einer Population in mehrere voneinander abgrenzbare Teilpopulationen entstehen fast zwangsläufig höhere Gesamtkosten, da sich diese aus der Multiplikation von Mengen und Preisen addiert über alle Teilpopulationen ergeben. Je mehr Teilpopulationen von einer zielgerichteten Behandlung profitieren können, umso höher ist die Wahrscheinlichkeit, dass die Gesamtkosten steigen. Diesen Aspekt nimmt das AMNOG bisher nicht in den Blick. Aktuell wird lediglich auf das Verhältnis zwischen Kosten und (Zusatz-)nutzen jedes einzelnen Arzneimittels gegenüber seiner Vergleichstherapie geachtet, aber nicht darauf, ob die aufgerufenen bzw. verhandelten Preise auch in der Gesamtheit angemessen sind und auf Dauer von der Solidargemeinschaft bezahlt werden sollten. Hierfür gibt es keinen Algorithmus. So wird es darauf ankommen, Nutzenbewertung und Preisfindung für diese und weitere Perspektiven zu öffnen, wenn der medizinische Fortschritt weiterhin finanzierbar sein und allen Patientinnen und Patienten mit Behandlungsbedarf uneingeschränkt zugutekommen soll.

2.3 Patentarzneimittel ohne Nutzenbewertung - der Bestandsmarkt

Nach wie vor ist der Patentmarkt auch durch den sogenannten Bestandsmarkt geprägt. Dieser umfasst aktuell oder ehemals patentgeschützte Arzneimittel ohne Zweitanbieter, die bereits vor Einführung des AMNOG im Jahr 2011 auf dem Markt waren. Aufgrund ihrer nach wie vor hohen Gesamt-Nettokosten besitzen diese Arzneimittel einen bedeutenden Stellenwert mit einem Marktanteil von ca. 43 % des Patentarzneimittelmarktes.

Eine im AMNOG ursprünglich verankerte Nutzenbewertung von versorgungsrelevanten Patentarzneimitteln des Bestandsmarktes wurde 2014 wieder aufgehoben (14. SGB-V-Änderungsgesetz). Zwar können seit 2017 mit dem AMVSG auch Bestandsmarkt-Arzneimittel ausnahmsweise für eine Nutzenbewertung herangezogen werden, doch nur, wenn für das Arzneimittel eine neue Zulassung mit neuem Unterlagenschutz erteilt wird. Da Arzneimittel mit bekannten Wirkstoffen unter den bestehenden EU-Regularien jedoch selbst bei sehr stark abweichenden Therapiegebieten gar keinen neuen Unterlagenschutz erhalten (GKV-Spitzenverband 2017), ist die Effektivität dieser Regelung zu hinterfragen. Erst im zweiten. Halbjahr 2019 wurde für den Wirkstoff Vigabatrin die erste Bestandsmarktbewertung für zwei neue Anwendungsgebiete begonnen, Anfang 2020 folgte für den Wirkstoff Ranibizumab ein weiterer Aufruf zur Nutzenbewertung.

Um die Preise und Kosten in diesem Bereich zu kontrollieren, wurde das Preismoratorium für die Arzneimittel des Bestandsmarktes, die nicht festbetrags geregelt sind, seit seiner Einführung 2009 bis heute aufrechterhalten und wird – nach wiederholter Evaluation – regelmäßig verlängert, aktuell gilt es bis Ende 2022. Liegen die Herstellerabgabepreise über den Preisen zum Stichtag 1.8.2009, so muss der Hersteller die Differenz zwischen Stichtagspreis und Herstellerabgabepreis in Form von Herstellerabschlägen abführen. Faktisch sind die Preise somit zum Stichtag eingefroren und können seit 2018 nur im Rahmen eines Inflationsausgleichs erhöht werden.

Im Laufe der vergangenen Jahre hat sich dieses eigentlich temporäre Instrument als unverzichtbar im Sinne der Ausgabendämpfung herausgestellt. Auch zukünftig wird das Preismoratorium für die Preis- bzw. Ausgabenregulierung insbesondere in den Marktsegmenten der generika- bzw. biosimilarfähigen Nicht-Festbetragsarzneimittel und der weiteren Altoriginale erforderlich sein, da diese zu großen Teilen weder im Wettbewerb stehen und bisher auch von keinen anderen Regulierungsinstrumenten erfasst werden.

Dass man bei Auslaufen des Moratoriums durchaus von Preisanstiegen ausgehen kann, zeigt die Ausnutzung des Inflationsausgleichs, den die Hersteller seit 2018 jährlich zum 1. Juli durch das AMVSG gewährt bekommen. In den ersten sechs Monaten des Jahres 2018 haben immer mehr Hersteller von der Möglichkeit Gebrauch gemacht, sodass am Ende des Jahres bereits für ein Viertel der Packungen eine Preisanpassung erkennbar war. Die Kosten auf Basis der Herstellerpreise erhöhten sich dadurch um ca. 55 Mio. €. Dieser Trend setzte sich mit der zweiten Runde zum 1. Juli 2019 noch deutlich stärker fort, sodass bis Ende des Jahres für 65 % der vom Preismoratorium betroffenen Arzneimittel die Preise erhöht wurden. Ausgabenseitig zeigt sich dies auch an einem Rückgang der Preismoratoriumsabschläge seit 2018, da die wegen früherer Preiserhöhungen zu zahlenden Abschläge nun abgeschmolzen werden. Zusammengefasst hat der Inflationsausgleich 2019 zu Mehreinnahmen der Hersteller in Höhe von 155 Mio. € auf Ebene der Herstellerabgabepreise geführt. Wegen der Zuschläge der Handelsstufen und der Mehrwertsteuer entspricht dies zusätzlichen Ausgaben für die GKV von 181 Mio. €.

Einige Hersteller haben erkannt, dass ältere Wirkstoffe auch für andere Indikationen eingesetzt werden können. Dies bedeutet zum einen geringere Aufwände für Forschung und Entwicklung und zum anderen keine gänzlich neue Zulassung mit entsprechendem umfassenden Studienprogramm. In Bezug auf das AMNOG besteht hier trotz erweiterter Regelung im AMVSG noch immer eine Regulierungslücke: Von der Nutzenbewertung und den nachfolgenden Preisverhandlungen scheinen die neuen Anwendungsgebiete alter Bestandsmarktwirkstoffe weitgehend nicht betroffen zu sein.

In der Wahl ihres Markteintrittspreises genießen die pharmazeutischen Unternehmen daher alle Freiheiten und wissen diese offenbar auch zu nutzen. So gab es in den vergangenen Jahren mehrere markante Beispiele, bei denen sich die Preise weder an den tatsächlichen Entwicklungs- oder Produktionskosten noch am damit verbundenen Nutzen für die Patientinnen und Patienten orientieren, sondern vielmehr am höchstmöglichen indikationsbezogenen Preisniveau (Schröder/Telschow 2017, Lohmüller et al. 2019) – natürlich aus ökonomischer Perspektive nachvollziehbar.

Altbekannte Wirkstoffe, deren kommerzieller Höhepunkt lange zurückzuliegen schien, werden dieser Strategie folgend vom Markt genommen und bald darauf als unverzichtbar und konkurrenzlos wieder mit neuem, deutlich höherem Preis eingeführt. Beispiele hierfür sind die Wirkstoffe Carmustin, Parathyroid oder Natrium-Pentosanpolysulfat (Schröder/Telschow 2017, Lohmüller et al. 2019). Zudem werden solche lang erforschten Wirkstoffe mit vergleichsweise geringen Aufwendungen für weitere Indikationen reaktiviert. Eine frühe Nutzenbewertung kann meist nicht durchgeführt werden, da diese nur für neue Präparate mit neuen Wirkstoffen anzuwenden ist. Doch selbst wenn die Präparate nach AMNOG bewertet würden, wäre eine Absenkung des Preises in einer Erstattungsbetragsverhandlung nach der Logik des AMNOG nur auf das Preisniveau der indikationsbezogenen Vergleichstherapie möglich. Sind die Preise des vergleichbaren Spektrums aber ebenfalls hoch oder gibt es gar keine adäquate Vergleichstherapie, so können nach heutigem Stand auch nicht die früheren Preise wirkstoffgleicher Präparate herangezogen werden. Die Entscheidung der Hersteller, die alten und meist sehr viel günstigeren, wirkstoffgleichen Präparate aus dem Handel zu nehmen, erscheint nachvollziehbar: Könnten diese doch unter Umständen Off-Label auch in den Indikationen der hochpreisigen „neuen“ Präparate eingesetzt werden.

3 Biologika und Biosimilars

Als Biologika (Biologicals, Biopharmazeutika) werden im engeren Sinne Arzneimittel bezeichnet, deren Wirkstoff aus einem lebenden Organismus hergestellt wird und deren Herstellung meist nur mithilfe gentechnologischer Methoden im großen Maßstab möglich ist. Sobald diese Arzneimittel patentfrei sind und über die europäischen Regularien Biosimilars zugelassen sind, wird ein Wettbewerb ermöglicht.

Bei einem Biosimilar handelt es sich gemäß der Europäischen Zulassungsbehörde um ein biotechnologisches Arzneimittel, „das einem anderen biologischen Arzneimittel, das bereits in der EU vermarktet wird, (dem sogenannten Referenzarzneimittel) sehr ähnlich ist“ (European Medicines Agency/Europäische Kommission 2019). Da es sich hierbei um Nachahmerprodukte handelt, können die Biosimilars in einer groben Annäherung aus Wettbewerbssicht auch als generische Biologika, also als Generika von bio- oder gentechnologisch hergestellten Arzneimitteln, betrachtet werden. Biosimilars sind seit 2006 in Europa verfügbar und haben in dieser Zeit als hinsichtlich Wirksamkeit und Sicherheit vergleichbare und meist preisgünstigere therapeutische Alternativen zunehmend an Bedeutung für die Arzneimitteltherapie gewonnen (Dicheva-Radev/Ludwig 2019). Zum biosimilarfähigen Marktsegment zählen die patentfreien Originalpräparate (Referenzarzneimittel) und die darauf beziehungsweise zugelassenen Biosimilars sowie weitere wirkstoffgleiche Erstanbieterpräparate. Als bioidentisch werden wirkstoffgleiche biotechnologisch hergestellte Arzneimittel aus demselben Herstellungsprozess bezeichnet. Diese sogenannten Bioidenticals können sowohl Originale als auch Biosimilars sein.

3.1 Übersicht über den Markt der Biologika und Biosimilars

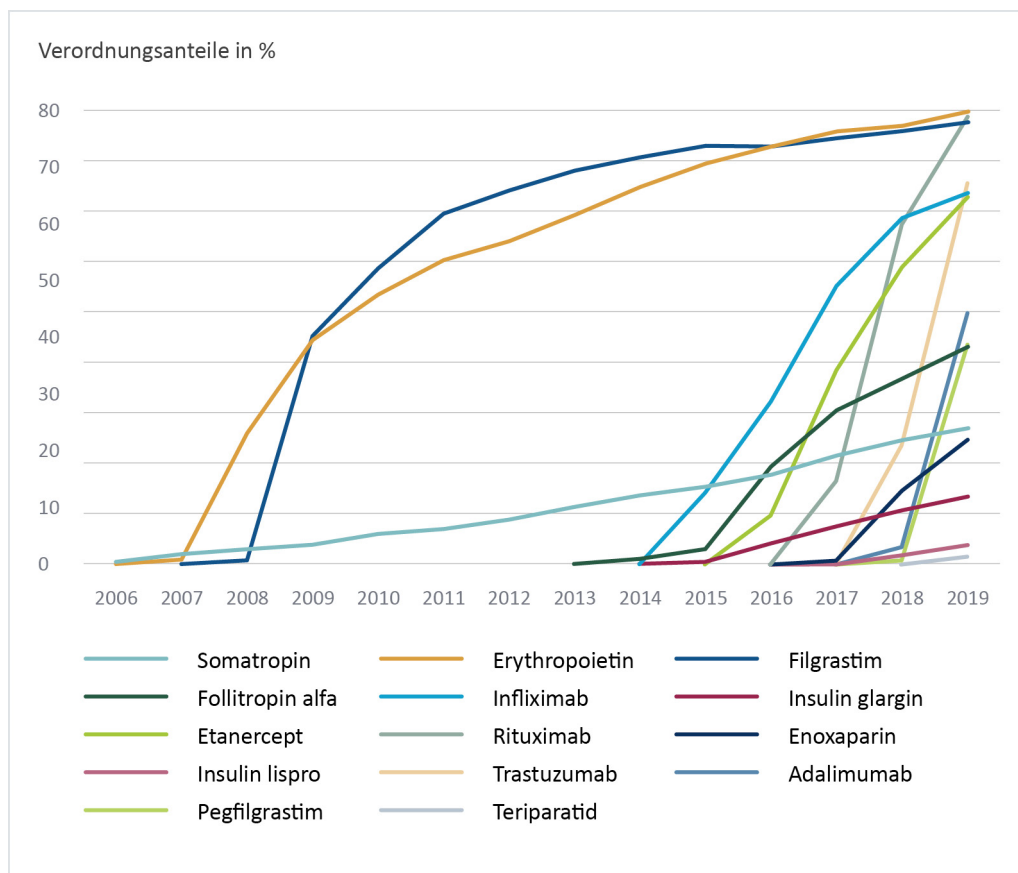
Die Nettokosten für den gesamten Biologikamarkt stiegen 2019 auf 13,5 Mrd. € an und machten somit fast ein Drittel des Gesamtmarktes für Arzneimittel aus (30,7 %). Die Dynamik dieses Marktsegments ist dabei ausgeprägter als im Gesamtmarkt: Während die gesamten Nettokosten 2019 im Vergleich zum Vorjahr um 6,0 % gestiegen sind, stiegen die Nettokosten für biologische Arzneimittel um 10,0 %. Die Verordnungen der Biologika wachsen zwar ebenfalls, allerdings stellen sie mit 1,31 Mrd. Tagesdosen gerade einmal 3,0 % des gesamten Arzneimittelmarktes.

Nachdem in den letzten Jahren die Schutzfristen einiger Blockbuster wie Humira mit dem Wirkstoff Adalimumab und Forsteo mit dem Wirkstoff Teriparatid abgelaufen sind und einige Nachahmer den Markt betreten haben, umfasst der biosimilarfähige Markt mit 4,04 Mrd. € nun rund 30 % der Nettokosten aller Biologika. Insgesamt handelte es sich innerhalb dieses biosimilarfähigen Marktes bei etwa jeder vierten Verordnung (nach Tagesdosen) um ein Nachahmerpräparat.

Wie entwickeln sich die Verordnungsanteile der Biosimilars?

Die Marktdurchdringung der Biosimilars hat sich für die einzelnen Wirkstoffe recht unterschiedlich entwickelt (Abbildung 3-1). Die – auch Jahre nach Zulassung – teilweise noch geringe Marktdurchdringung einiger Biosimilars steht einer sehr zügigen Marktdurchdringung anderer Biosimilars gegenüber. Insgesamt hat das Niveau der Nachahmeranteile in Höhe von 44 % das des generikafähigen Marktes bei weitem noch nicht erreicht (vgl. Kapitel 1).

Abbildung 3-1: Verordnungsanteile nach Tagesdosen der Biosimilars am biosimilarfähigen Markt 2006 bis 2019 je Wirkstoff, Legende sortiert nach Markteinführung



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So haben die Rituximab-Biosimilars im dritten Jahr nach ihrer Markteinführung einen Verordnungsanteil (in DDD) von 78,7 % erzielt, während der Verordnungsanteil der Biosimilars mit Somatropin auch nach vierzehn Jahren Marktverfügbarkeit immer noch deutlich unter 25 % liegt. Den niedrigsten Verordnungsanteil erzielten 2019 das Insulin lispro-Biosimilar (3,4 %) und die Teriparatid-Biosimilars (1,4 %), wobei letztere erst seit September 2019 auf dem Markt sind. Die Biosimilars zu Pegfilgrastim und Adalimumab, die erst Ende 2018 in den deutschen Markt eingeführt wurden, konnten 2019 bereits Verordnungsanteile von 38,6 % (Pegfilgrastim) respektive 44,1 % (Adalimumab) erzielen.

Der Anteil von Biosimilars variiert nicht nur auf Wirkstoffebene, sondern auch zwischen den verschiedenen Regionen in Deutschland. Betrachtet man die 17 KV, die mit Ausnahme von Nordrhein-Westfalen, das in die KV Nordrhein und die KV Westfalen-Lippe unterteilt ist, den Bundesländern entsprechen, lassen sich deutliche Unterschiede erkennen. Im Laufe der letzten zehn Jahre haben sich die verordnungsgewichteten, mittleren Anteilswerte der Biosimilars in DDD zwar in allen KVen erhöht, dies allerdings mit deutlich unterschiedlichen Anstiegen (Abbildung 3-2). Im Jahr 2010 lagen die Biosimilaranteile noch flächendeckend unter 5 %. Zu diesem Zeitpunkt waren nur für drei Wirkstoffe Biosimilars auf dem Markt: Somatropin (seit 2006), Erythropoietin (seit 2007) und Filgrastim (seit 2008). Seit 2013 werden jährlich weitere Wirkstoffe biosimilarfähig. Etwas zeitverzögert sind seitdem auch die Anteilswerte der Biosimilars in den KVen immer stärker angestiegen. Im Jahr 2019 befinden sich im oberen Viertel mit Anteilen von 22 % bis 32 % die KVen Westfalen-Lippe, Niedersachsen, Bremen, Hamburg und Schleswig-Holstein, während die KVen Saarland, Sachsen, Baden-Württemberg und Sachsen-Anhalt nur auf je 11 % bis 12 % Verordnungsanteile kommen und damit die Schlussgruppe bilden.

Abbildung 3-2: Prozentualer Verordnungsanteil nach Tagesdosen von Biosimilars an allen biosimilarfähigen Wirkstoffen je KV-Region seit dem Jahr 2010

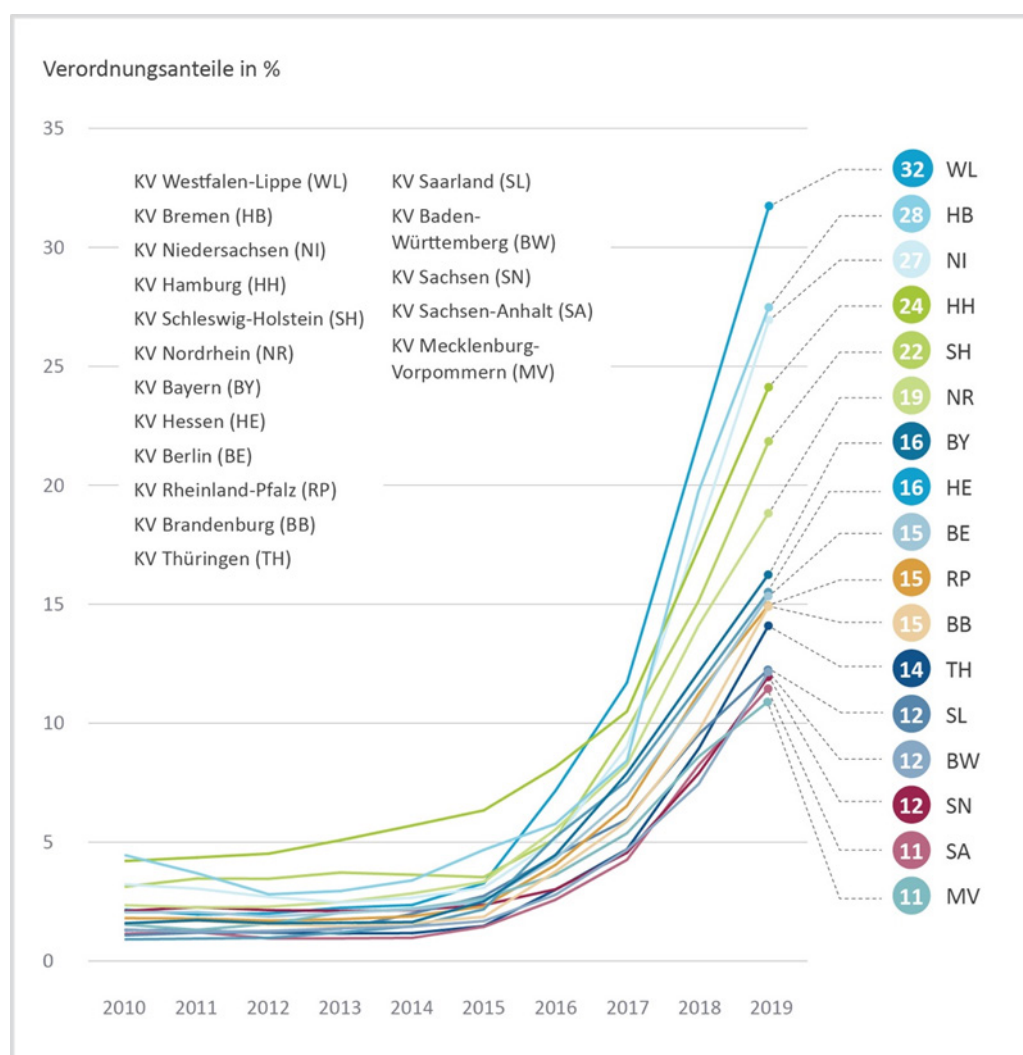


Abbildung 3-3 stellt diese Biosimilaranteile in DDD der Regionen für jeden biosimilar-fähigen Wirkstoff für das Jahr 2019 dar. Zur besseren Übersicht über die Rangfolge der KVen kennzeichnet eine farbliche Abstufung die Lage des regionalen Anteilswertes in der Verteilung (Quartilsbereiche) aller regionalen Anteilswerte je Wirkstoff. Das bedeutet, dass es für die einzelnen Wirkstoffe je ein Ranking der KVen gibt, anhand dessen die Erfüllungsquote jeder KV im Vergleich eingeordnet werden kann. Damit kann auch abgelesen werden, welche KVen besonders häufig überdurchschnittliche Biosimilarquoten aufweisen. So zeigt sich, dass sich die KVen Westfalen-Lippe und Niedersachsen bei fast allen Wirkstoffen immer unter den KVen mit den höchsten Biosimilarverordnungsanteilen (obere 50 % oder sogar 25 % der KVen) befinden. Die Bewertung der wirkstoffbezogenen Unterschiede bedarf jedoch einer differenzierten Einordnung unter Berücksichtigung der regionalen Vertragspolitik (siehe Abschnitt 3.2 „Gesetzliche Rahmenbedingungen“).

Die größte Spannweite zwischen den Biosimilaranteilen der KVen lässt sich beim Wirkstoff Follitropin alfa beobachten: Hier kann die KV Brandenburg mit knapp 94 % eine beinahe vollständige Abdeckung der Verordnungen durch Biosimilars vorweisen, während es in der KV Sachsen lediglich 23 % sind. Bei Teriparatid ist die Spannweite mit fünf Prozentpunkten am geringsten. Hier stehen die Biosimilars allerdings noch ganz am Anfang der möglichen Marktdurchdringung, da die ersten Biosimilars Movymia und Terrosa erst im September 2019 auf den Markt gekommen sind.

Die Insuline zeigen verordnungsgewichtet mit mittleren Anteilen von 11,5 % (Insulin glargin) und 2,5 % (Insulin lispro) eine insgesamt nur schwache Marktdurchdringung von Biosimilars auf. Deutlich über diesen Mittelwerten liegen die KVen Niedersachsen (19 % Insulin glargin, 11 % Insulin lispro) und Westfalen-Lippe (30 % Insulin glargin, 12 % Insulin lispro). Bei Insulin lispro liegen alle anderen KVen bei 3 % oder weniger. Beim Wirkstoff Erythropoietin bildet die KV Baden-Württemberg mit 40 % einen deutlichen Ausreißer zu den durchschnittlich 82 %. Der Wert verwundert weniger, wenn man einen Blick auf die Verordnungsmindestquoten für diesen Wirkstoff wirft (siehe Abschnitt 3.2 „Gesetzliche Rahmenbedingungen“): Für das Jahr 2019 lag die Vorgabe der KV Baden-Württemberg für die Verordnung von Erythropoietin-Biosimilars bei 23,0 % und damit deutlich unter denen der anderen KVen mit beinahe durchweg über 50 % (Rahmenvorgaben nach § 84 Abs. 6 SGB V für das Jahr 2019). Insgesamt befinden sich die KVen Westfalen-Lippe und Niedersachsen bei beinahe allen Wirkstoffen in den oberen 75 % der Anteilswerte. Das andere Ende der Verteilung bilden die KVen Saarland und Sachsen-Anhalt ab, hier ist das Gros der Anteilswerte den unteren 50 % zuzuordnen.

Abbildung 3-3: Verordnungsanteil nach Tagesdosen von Biosimilars im Jahr 2019, aufgeteilt nach Wirkstoff und den 17 Kassenärztlichen Vereinigungen (KV). Die Farben geben an, in welchem Quartil sich der Wert je Wirkstoff befindet.

	Erythropoietin	Filgrastim	Rituximab	Infliximab	Trastuzumab	Etanercept	Follitropin alfa	Adalimumab	Pegfilgrastim	Enoxaparin	Somatropin	Insulin glargin	Insulin lispro	Teriparatid	Ø (ungewichtet)	Ø (gewichtet)
Westfalen-Lippe	86	81	90	82	83	81	31	57	52	38	36	30	12	3	54,4	31,9
Niedersachsen	86	86	85	81	75	77	36	59	39	31	38	19	11	1	51,7	27,1
Bayern	89	80	85	64	77	72	69	43	49	19	21	7	1	1	48,3	16,3
Schleswig-Holstein	91	75	90	87	60	66	38	56	37	25	26	11	2	0	47,4	22,0
Bremen	91	99	66	70	63	62	29	48	53	52	43	12	0	0	49,2	27,6
Rheinland-Pfalz	86	82	72	62	68	66	42	46	41	21	27	10	1	1	44,7	15,0
Hamburg	93	84	70	68	55	70	25	44	44	20	32	13	2	1	44,5	24,3
Nordrhein	85	70	86	68	60	74	29	49	34	27	18	9	1	4	43,8	18,9
Sachsen	91	95	79	47	70	53	23	35	55	16	30	5	1	1	42,9	12,0
Baden-Württemberg	40	66	78	52	69	61	40	42	41	11	18	6	1	1	37,5	12,2
Brandenburg	80	92	64	50	59	47	94	38	25	17	3	14	3	0	41,9	15,0
Hessen	77	75	69	66	48	57	28	36	28	18	11	14	2	2	38,0	15,6
Berlin	80	59	70	38	55	47	42	29	28	19	24	12	1	1	36,2	15,4
Thüringen	87	86	67	58	54	47	37	34	34	24	21	9	1	1	40,0	14,2
Mecklenburg-Vorpommern	88	66	53	52	59	48	79	30	45	18	9	4	1	1	39,5	10,9
Saarland	77	79	75	59	45	55	27	36	8	16	11	7	1	5	35,8	12,2
Sachsen-Anhalt	66	78	71	49	50	55	50	33	26	14	15	9	1	0	37,1	11,5
Ø (ungewichtet)	82,0	79,6	74,7	62,0	61,7	61,1	42,2	42,1	37,7	22,6	22,6	11,3	2,5	1,4		
Ø (gewichtet)	81,0	77,8	79,1	71,2	63,6	60,4	41,9	45,5	38,6	24,2	18,5	13,5	4,3	1,8		

1. Quartil 2. Quartil 3. Quartil 4. Quartil

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Sind Biosimilars deutlich preisgünstiger als Original-Biologika?

Vergleicht man den Preisverfall der durchschnittlichen verordnungsungewichteten DDD-Kosten nach Patentablauf im biosimilarfähigen Markt mit der Entwicklung im generikafähigen Markt, zeigt sich, dass die mittleren Kosten chemischer Wirkstoffe deutlich stärker sinken als bei den Wirkstoffen mit Biosimilar-Wettbewerb (Schröder et al. 2019). Die unterschiedlichen Entwicklungen werden durch zwei Größen getrieben: Die relativ geringen Preisabstände zwischen Erst- und Zweitangebietern sowie die geringeren Verordnungsanteile der Biosimilars im biosimilarfähigen gegenüber dem generikafähigen Markt. So lag der Abstand der Nettokosten pro DDD eines Biosimilars im Vergleich zum Referenzprodukt im Jahr 2019 beim Wirkstoff Somatotropin bei bis zu 26,8 % zum Teil waren die Biosimilars sogar teurer als Originale bei Teriparatid hingegen nur bei 18,8 %.

Die vergleichsweise geringen Preisabstände der Biosimilars werden oft mit den hohen Anforderungen an die Entwicklung begründet. Unter anderem müssen für die Zulassung zusätzliche klinische Studien zur Vergleichbarkeit mit dem Referenzarzneimittel durchgeführt werden. Als Entwicklungskosten werden Größenordnungen von 60 bis 200 Mio. € genannt (Arbeitsgemeinschaft Pro Biosimilars 2015, Daubenfeld et al. 2016). Dies scheint zwar deutlich über denen für Generika zu liegen (ca. 5 Mio. €), allerdings auch erheblich niedriger als die ca. 0,9 bis 1,2 Mrd. €, die für die Entwicklung eines neuen Biologikums aufgewendet werden (Deutsche Apothekerzeitung 2008, Zylka-Menhorn/Korzilius 2014, Reinwald 2015, Verband forschender Arzneimittelhersteller 2015, Wouters et al. 2020). Vor dem Hintergrund der Entwicklungskosten, die bei einem Biosimilar bei etwa 12 % der Entwicklungskosten eines Originalprodukts liegen, bleibt bei Biosimilarpreisen von rund 87 % der DDD-Nettokosten der Originale noch Luft nach unten.

Es ist zu vermuten, dass die überschaubare Anbietervielfalt den Wettbewerb begrenzt: Im Jahr 2019 waren 24 Anbieter von 14 Biosimilars im deutschen Markt vertreten, wovon allerdings acht Originalanbieter mit ihren Zweitprodukten bzw. deren Tochterfirmen sind: Lilly, Medice, Sanofi-Aventis, Pfizer, Amgen, Biogen, MSD und Mundipharma. Mehr als zwei Drittel (69 %) der Gesamtnettokosten für Biosimilars im Jahr 2019 verteilen sich auf diese Originalanbieter. Durchschnittlich stehen für generikafähige Wirkstoffe knapp acht Zweitanbieter zur Verfügung, während es bei biosimilarfähigen Arzneimitteln im Schnitt nur drei Zweitanbieter sind. Dabei steigen die Preisabstände mit der Wettbewerbsintensität: Je mehr Zweitanbieter zu einem Wirkstoff im Markt sind, desto größer sind nicht nur die Verordnungsanteile der Biosimilars, sondern auch die Preisabstände zum Referenzprodukt (Schröder et al. 2019). Hier weist der noch begrenzte Markt der biosimilarfähigen Wirkstoffe keine Besonderheit auf.

Ausblick auf den biosimilarfähigen Markt

In den kommenden Jahren werden weitere Schutzfristen von noch patentgeschützten Biologika enden, was auch das Aufkommen neuer Biosimilars erwarten lässt. Gemäß dem Generics and Biosimilars Initiative Journal sollen in den kommenden fünf Jahren die Schutzfristen für 23 Wirkstoffe² in der Europäischen Union enden (GaBi Journal Editor 2019). Darunter befinden sich Wirkstoffe mit sehr hohen Nettokosten: Im Jahr 2019 kamen die Wirkstoffe Certolizumab pegol (168 Mio. €), Golimumab (210 Mio. €), Eculizumab (264 Mio. €), Pertuzumab (268 Mio. €), Ranibizumab (384 Mio. €), Ustekinumab (409 Mio. €) und Bevacizumab (442 Mio. €) zusammen auf Nettokosten von über 2 Mrd. €. Mit dem Patentablauf dieser Wirkstoffe sind entsprechend hohe Einsparungen durch günstigere Biosimilars möglich, sofern eine genügende Anzahl von biotechnologischen Arzneimittelherstellern diesen Markt erschließt.

² Brentuximab vedotin, Catumaxomab, Raxibacumab, Bevacizumab, Ofatumumab, Belimumab, Alemtuzumab, Certolizumab pegol, Ramucirumab, Obinutuzumab, Trastuzumab emtansin, Ranibizumab, Pertuzumab, Evolocumab, Golimumab, Eculizumab, Ustekinumab, Ipilimumab, Interferon beta-1b, Alglucosidase alfa, Belatacept, Liraglutid und Dulaglutid

3.2 Wie hoch ist die aktuelle Ersparnis im Biosimilar-markt und wie groß ist das weitere Potenzial?

Gesetzliche Rahmenbedingungen

Die gesetzlichen Rahmenbedingungen bieten aktuell drei Vorgaben, um mit Biosimilars zu sparen: Verordnungsquoten, Festbeträge und Rabattverträge.

Für die **Verordnungsquoten** vereinbaren die Kassenärztliche Bundesvereinigung (KBV) und der GKV-SV gemäß § 84 Abs. 6 SGB V jährlich die Rahmenvorgaben des Ausgabenvolumens für die insgesamt von den Vertragsärztinnen und -ärzten veranlassten Leistungen. Daraus ergeben sich unter anderem Zielvorgaben, wieviel mindestens (Verordnungsmindestquote) oder höchstens (Verordnungshöchstquote) von einer bestimmten Arzneimittelgruppe verordnet werden soll. Beispielsweise vereinbarte die KV Saarland für das Jahr 2020, dass mindestens 33,3 % der Verordnungen des Wirkstoffes Trastuzumab durch Biosimilars erfolgen soll, die KV Westfalen-Lippe vereinbarte für selbigen eine Verordnungsmindestquote von 85,8 % (GKV-Spitzenverband/Kassenärztliche Vereinigung 2019). Die Spanne zwischen den Verordnungsmindestquoten der 17 KVen ist entsprechend groß. Wenn eine Ärztin oder ein Arzt die vereinbarte Quote nicht einhält, droht in letzter Konsequenz eine Wirtschaftlichkeitsprüfung mit der Möglichkeit eines Entzugs der Zulassung. Trotzdem birgt dieses Instrument noch ein beachtliches Potenzial. So beziffert Insight Health in einem Gutachten für die Arbeitsgemeinschaft Pro Biosimilars für das Jahr 2019 eine bereits realisierte Einsparung von 343 Mio. € und in einem zusätzlichen Einspar-Szenario (Übertrag der höchsten arzneimittelbezogenen Verordnungsquote einer KV auf alle KVen) ein Potenzial in Höhe von 328 Mio. € (Pieloth/Sahin 2020).

Zudem können Arzneimittel, die bestimmte Merkmale teilen, einer **Festbetragsgruppe** zugeordnet werden, mit der eine Erstattungshöchstgrenze einhergeht. Nach den Regelungen des § 35 SGB V bestimmt der G-BA, für welche Gruppen von Arzneimitteln Festbeträge festgesetzt werden können. Im Einzelnen handelt es sich dabei um Arzneimittel mit entweder demselben Wirkstoff, pharmakologisch-therapeutisch vergleichbaren (insbesondere chemisch verwandten) Wirkstoffen oder therapeutisch vergleichbarer Wirkung (insbesondere Arzneimittelkombinationen). Festbeträge stellen damit eine indirekte Form der Preissteuerung dar, da sie nicht direkt in die Preisfestsetzung eingreifen, sondern Erstattungshöchstgrenzen setzen. Im Bereich der Biosimilars wird dieses Instrument noch zurückhaltend genutzt. So gibt es aktuell bei fünf der 14 biosimilarfähigen Wirkstoffe eine Festbetragsgruppe (Enoxaparin, Erythropoietin, Etanercept, Filgrastim und Infliximab, Stand 28.02.2020).

Seit 2003 haben Krankenkassen außerdem mit dem § 130a Abs. 8 SGB V die Möglichkeit, mit einem Hersteller kassenspezifische **Rabattverträge** abzuschließen. Seit dem 1. April 2007 sind die Apotheken verpflichtet, die kassenspezifischen Generika-Rabattverträge bei der Produktauswahl vorrangig zu bedienen, sofern die Ärztin oder der Arzt die Substitution nicht ausgeschlossen hat. Für Hersteller kann ein Rabattvertrag besonders dann attraktiv sein, wenn mit dem Vertrag eine gewisse Absatzsicherheit garantiert wird. Hier fehlt aber für Biologika – im Gegensatz zum Generikamarkt – ein entscheidender Mechanismus, nämlich die verpflichtende Substitution in der Apotheke. Schließt ein Hersteller einen Rabattvertrag für ein biosimilarfähiges Arzneimittel mit einer Krankenkasse ab, muss die Apotheke dieses nicht vorrangig abgeben, es sei denn es handelt sich um ein Bioidentical (siehe oben). Hierzu werden in Anlage 1 zum Rahmenvertrag nach § 129 Abs. 2 SGB V derzeit (Stand 1. April 2020) 21 bioidentische

Arzneimittel als austauschbar für sechs der 14 biosimilarfähigen Wirkstoffe gelistet. Zwar gibt es aktuell für alle biosimilarfähigen Wirkstoffe auch Rabattverträge der Krankenkassen, diese umfassen allerdings meist auch alle Anbieter. Eine Ausschreibung mit exklusiven Zuschlägen, wie bei den Generika seit vielen Jahren erfolgreich praktiziert, ist nicht effektiv, da in der Regel kein Austausch in der Apotheke erfolgt. Den Anbietern kann somit derzeit kein Anspruch auf Exklusivvermarktung für die Versicherten der ausschreibenden Krankenkasse zugesagt werden, was die Rabatthöhe weitestgehend auf das Preisniveau der jeweils günstigsten Anbieter beschränken dürfte.

Mit dem **Gesetz für mehr Sicherheit in der Arzneimittelversorgung** (GSAV), das am 16.08.2019 in Kraft getreten ist, wurde die verpflichtende Substitution nach § 129 Abs. 1 auch für im wesentlichen wirkstoffgleiche Biologika – unabhängig vom Herstellungsprozess – zwar beschlossen, allerdings tritt dieser Teil des Gesetzes erst mit einer Verzögerung von drei Jahren im Jahr 2022 in Kraft. Und auch dann müssen nur die Biosimilars in der Apotheke substituiert werden, für die der GB-A nach Evaluierung der Studienlage in der Arzneimittel-Richtlinie entsprechende Hinweise vorsieht.

Auf der Grundlage der aktuellen Möglichkeiten, liegt es also vor allem in der Hand der verordnenden Ärztinnen und Ärzte, durch den Einsatz von Biosimilars Einsparungen zu ermöglichen.

Wieviel konnte insgesamt im Jahr 2019 mit dem Einsatz preisgünstiger Biosimilars gespart werden und welches Einsparpotential blieb ungenutzt?

Durch die Abgabe der jeweils günstigeren Wettbewerbspräparate – in der Regel sind dies die Biosimilars anstelle eines Originals – konnten im vergangenen Jahr 459 Mio. € gespart werden. Wäre allerdings systematisch das – unter den gegebenen Marktbedingungen und Preisangaben – jeweils günstigste Produkt verordnet worden, wären im Jahr 2019 insgesamt zusätzliche Einsparungen in Höhe von 791,6 Mio. € möglich gewesen³. Da die selektiv verhandelten Rabatte für die im Biosimilarbereich nahezu flächendeckend abgeschlossenen Rabattverträge nicht bekannt sind, kann jedoch vermutet werden, dass ein großer Teil dieses Einsparpotenzials bereits über diese nachträglich gewährten Rabatte adressiert werden konnte (siehe unten).

Etwa ein Fünftel des gesamten möglichen Einsparpotenzials liegt beim Wirkstoff Adalimumab, was hohen Nettokosten in Verbindung mit einem relativ großen Preisabstand geschuldet ist: Wäre man bei den Verordnungen vollständig auf die günstigeren Anbieter umgestiegen, wären 289,1 Mio. € an Einsparungen für diesen Wirkstoff möglich gewesen, was über ein Drittel des gesamten Einsparpotenzials ausmacht. Obwohl die Marktdurchdringung der Biosimilars bei Adalimumab mit 45,5 % vergleichsweise hoch ist, gibt es nach wie vor einen Preisunterschied von etwa 37,0 % der DDD-Nettokosten zwischen dem Original Humira und den im Jahr 2019 auf dem Markt befindlichen fünf Biosimilars. Dank der wachsenden Marktdurchdringung der Biosimilars konnten 2019 durch die tatsächlich erfolgte Abgabe eines günstigeren Biosimilars 205,2 Mio. € bei Adalimumab eingespart werden. An zweiter Stelle der Wirkstoffe mit dem höchsten Einsparpotenzial folgt Infliximab. Hier blieben knapp 103,6 Mio. € an Einsparungen ungenutzt. Verhältnismäßig wenig (14,0 Mio. €) konnte realisiert werden und dies, ob-

³ Anders als in der Einsparpotenziallogik von Bauer et al. (2020), die auf Listenpreisen basiert, wurden und werden in dieser Berechnung stets die abgerechneten Preise verwendet, sodass die Hilfstaxenabschläge für individuelle Zubereitungen Berücksichtigung finden. Mit der Berechnung über die Nettokosten sind weiterhin die gesetzlichen Abschläge einbezogen.

wohl es für Infliximab sowohl einen Festbetrag als auch zwei bioidentische Arzneimittel gibt. Großes Einsparpotenzial existiert auch noch für Wirkstoffe, bei denen Biosimilars schon seit über zehn Jahren verfügbar sind: So kamen die ersten Biosimilars zum Wirkstoff Erythropoietin 2007 auf den Markt. Trotz des mittlerweile hohen Verordnungsanteils von Biosimilars bei Erythropoietin (vgl. Abbildung 3-1) und trotz eines Festbetrags, der die Preise der Erst- und Zweitanbieterpräparate auf ein vergleichbares Niveau senkt, wären hier noch immer Einsparungen in Höhe von 19,8 Mio. € möglich, wenn stets das günstigste vergleichbare Produkt verordnet worden wäre. Damit blieb in Summe im Jahr 2019 ein Einsparpotenzial von fast 800 Mio. € im biosimilarfähigen Markt ungenutzt. Inwieweit dieses Potenzial über den Weg der Rabattverträge gehoben werden konnte, muss an dieser Stelle aufgrund der nicht öffentlich bekannten Vertragskonditionen allerdings unbeantwortet bleiben.

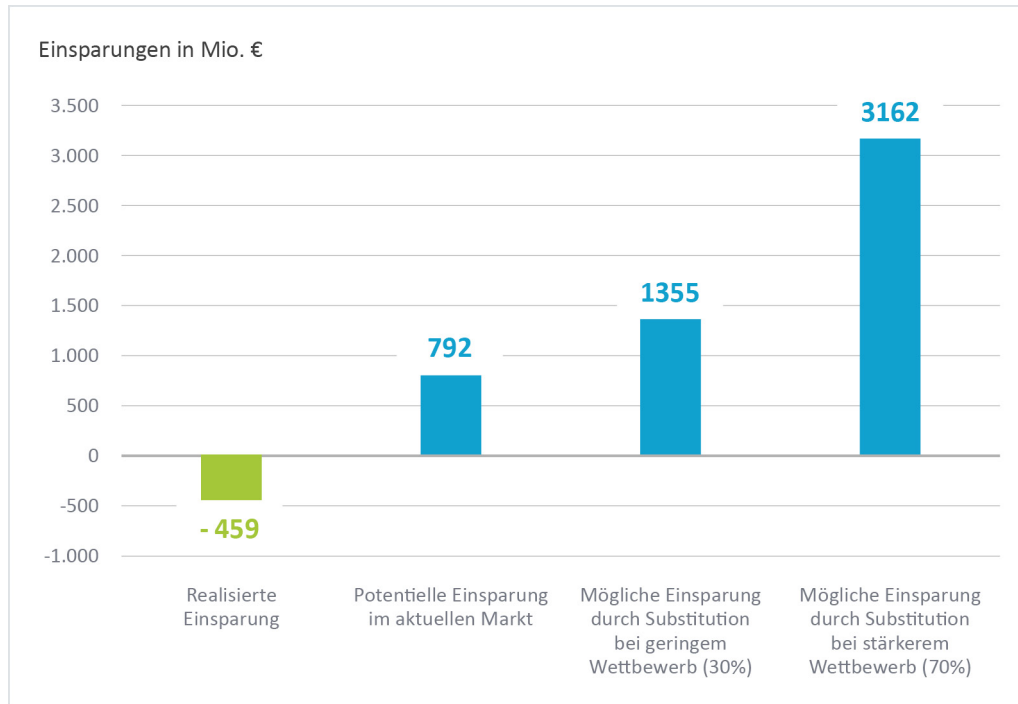
Die jetzigen Bedingungen zeigen, dass im Markt der biosimilarfähigen Arzneimittel große Summen eingespart werden könnten, die aktuell jedoch nicht annähernd ausgeschöpft werden: Fast zwei Drittel des Gesamtvolumens bleibt derzeit – ohne Berücksichtigung von Selektivrabatten – ungenutzt. Unter den Bedingungen des GSAV kann ab 2022 dieses Potenzial deutlich stärker gehoben werden, sofern der G-BA entsprechende Hinweise für alle biosimilarfähigen Wirkstoffe beschließt und die verordnenden Ärztinnen und Ärzte mit der Möglichkeit, den Austausch in der Apotheke zu unterbinden, verantwortungsvoll umgehen.

Sind damit bereits alle Einsparmöglichkeiten beschrieben?

Das berechnete Einsparpotenzial basiert auf dem Status quo, also einem Markt, der aktuell durch geringe Preisabstände und sehr heterogene Verordnungsanteile der Nachahmerprodukte charakterisiert ist. Wirft man hier einen Blick ins Ausland, eröffnen sich weitere Potenziale für Annahmen, wie sich Preise oder Verordnungen entwickeln könnten: In einigen europäischen Ländern ist für Biosimilars ein sogenannter „biosimilar price link“ vorgesehen, also ein definierter Preisabstand, den das Biosimilar zum Referenzprodukt haben muss. In Litauen und Frankreich liegt dieser bei bis zu 30 % (Vogler/Schneider 2017). Auch im deutschen Markt sind Beispiele vertreten, die sogar einen größeren Preisabstand zeigen: Beim Wirkstoff Adalimumab waren es im Jahr 2019 bereits bis zu 37 % Preisabstand der durchschnittlichen DDD-Nettokosten.

Dabei ist auffallend, dass die Preisabstände umso größer sind, je mehr Biosimilaranbieter um Marktanteile bei einem Wirkstoff konkurrieren. Simuliert man das Einsparpotenzial für alle biosimilarfähigen Wirkstoffe mit einem durchschnittlichen Preisabstand von 30 % der DDD-Kosten zum Original-Biologikum vor dessen Patentablauf bei alleiniger Verordnung von Biosimilars, lassen sich 2019 mögliche Einsparungen in Höhe von 1.355 Mio. € berechnen (siehe Abbildung 3-3). Auch wenn ein Preisverfall um 70 % für den deutschen Markt bisher nur bei Generika beobachtet werden konnte, zeigen auch einzelne Beispiele aus dem europäischen Ausland, dass größere Nachlässe als 30 % bei Biosimilars möglich sind: In Norwegen und dem Vereinigten Königreich konnten Rabatte von 70 % und darüber hinaus vereinbart werden (Generics and Biosimilar Initiative (GaBi) 2015, Vogler/Schneider 2017, Ärzte Zeitung online 2018, Vogler et al. 2019). Die Simulation von Nachlässen in dieser Größenordnung für den gesamten biosimilarfähigen Markt ergibt ein Einsparpotenzial für das Jahr 2019 von 3,16 Mrd. € (Abbildung 3-3). So wird deutlich, dass im Korridor zwischen beiden Szenarien – mit 30 % Preisabschlag bei einem schwachen Wettbewerb oder 70 % Preisabschlag bei einem starken Wettbewerb – weitere erhebliche Einsparungen im Milliardenbereich möglich sind.

Abbildung 3-4: Im Jahr 2019 realisierte Einsparungen durch den Einsatz von Biosimilars und Modelle zu Einsparpotentialen



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Bei der Interpretation der Einsparpotentiale ist zu berücksichtigen, dass über Rabattverträge vermutlich ein gewisser Teil der potentiellen Einsparungen bereits heute gehoben wird. So kann vermutet werden, dass sich dadurch das (auch nach Patentablauf stabile und meist deutlich höhere) Preisniveau der Originalprodukte dem der günstigeren Biosimilars über nachträglich gewährte Rabatte annähert. Für einen Teil des Biosimilarmarktes (sieben Wirkstoffe) wagen Bauer et al. (2020) erstmals eine Abschätzung der Einsparungen durch das existierende Rabattgeschehen. Auf Basis von „Marktkennntnissen der Autoren [...] ergänzt durch Ergebnisse eigens durchgeführter Experteninterviews“ nehmen sie die Existenz von Open-House-Verträgen in verschiedenen Formen (Preissicherungsrabatt, Grundrabatte, Mischformen) an und simulieren Einsparungen, die in den jeweiligen Szenarien zwischen 200 und 275 Mio. € liegen.

Wenngleich dies eine auf Annahmen beruhende erste Abschätzung des existierenden Rabattgeschehens darstellt, bleibt doch der Befund, dass erst durch die verstärkte Nutzung von Exklusivverträgen der Preiswettbewerb in Gang gesetzt werden kann, sodass das Preisniveau der Biosimilars weiter sinkt. Vor dem Hintergrund der Entwicklungskosten, die bei einem Biosimilar bei etwa 12 % der Entwicklungskosten eines Originalprodukts liegen (siehe Abschnitt 3.1), existiert bei der Preisgestaltung für die Hersteller offenbar weiterhin Luft nach unten.

Wie kann der Markt der Biosimilars nachhaltig gestaltet werden?

Es sollte beachtet werden, dass ein rigoroses Einspardiktat in dem vergleichsweise jungen Markt der Biosimilars die Gefahr birgt, dass Anbieter eher ferngehalten werden. Folglich wird es nur über das behutsame Austarieren von Einsparzielen und wettbewerbsfördernden Elementen gelingen, dauerhaft und langfristig zu angemessenen Kosten zu kommen (Reilly/Schneider 2020). Dieser Effekt wird sich nur einstellen, wenn sich der Wettbewerb mit der zunehmenden Anbietervielfalt verstärkt. Doch wie kann es dazu kommen? Rabattverträge mit exklusiven Zuschlägen können helfen, die Anbietervielfalt zu befördern, weil auch kleinere Anbieter dadurch eine höhere Absatzsicherheit erhalten. Das ist wegen der höheren Entwicklungskosten der Biosimilars im Vergleich zu den Generika umso wichtiger. Der Biosimilarmarkt ist derzeit durch wenige große Anbieter geprägt (siehe oben). Es ist anzunehmen, dass durch diese etablierte Anbieterstruktur gerade ausländische Anbieter dem zweifelsohne attraktiven deutschen Markt fernbleiben, da kaum Chancen auf relevante Marktanteile für hierzulande noch unbekannte Anbieter bestehen. Umso mehr, da aus Untersuchungen bekannt ist, dass die Wahrscheinlichkeit, ein Nachahmerpräparat auf den Markt zu bringen, geringer ist, wenn finanzielle Verflechtungen zwischen Herstellern von Original- und Nachahmerprodukten bestehen (Newham et al. 2018). Das GSAV kann eine wettbewerbliche Entwicklung auch im biosimilarfähigen Markt befördern, wenn die Krankenkassen die damit gegebene Möglichkeit für exklusive Ausschreibungen aufgreifen. Damit kann sich über die Rabattgewährung ein stärkerer Preiswettbewerb entfalten.

Die automatische Substitution wird aber auch ab 2022 nur unter bestimmten Bedingungen erfolgen können. So wurde mit dem GSAV dem G-BA die Aufgabe übertragen, Wirkstoffe dahingehend zu überprüfen, ob sie verpflichtend ausgetauscht werden können. Nur wenn es gelingt, diese Austauschlisten für möglichst viele Wirkstoffe zu erstellen und marktwirksam umzusetzen, wird eine umfängliche Wirkstoffsubstitution hin zu günstigen Produkten gefördert und kann Einsparmöglichkeiten bieten. Zudem helfen qualitätsgesicherte Studien zur Sicherheit der Austauschbarkeit sowohl den Ärztinnen und Ärzten als auch den Patientinnen und Patienten, unberechtigte Vorbehalte zu verringern und damit eine breitere Akzeptanz zu schaffen.

Was bedeutet ein Biosimilaraustausch für Patientinnen und Patienten und Ärztinnen und Ärzte?

Switching-Studien haben für eine Vielzahl an biologischen Wirkstoffen gezeigt, dass der Wechsel von einem zum anderen Präparat für die Patientinnen und Patienten unbedenklich ist (AkdÄ 2017). Dabei macht es auch keinen Unterschied, ob von einem Original zu einem Biosimilar oder in die andere Richtung umgestellt wird. Wichtig und sinnvoll ist die Begleitung der Therapie durch die Ärztin oder den Arzt, was bei den bislang von Biologika adressierten Krankheitsbildern ohnehin gegeben sein dürfte. Letztlich bleibt die Verordnung eines bestimmten Arzneimittels durch die Aut-idem-Regelung nach wie vor in der Hand der behandelnden Ärztin oder des behandelnden Arztes. Daher ist auch die Akzeptanz und Bereitschaft von Ärztinnen und Ärzten ein wichtiger Faktor im Verordnungsgeschehen von Biosimilars. Nach wie vor gibt es Vorbehalte, auch dann, wenn der Wechsel von einem Referenzprodukt zu einem Biosimilar nach Studienlage als unbedenklich gilt. Dennoch besteht bereits ein großes Einsparpotenzial, selbst wenn nur in den Fällen ein preisgünstigeres Biosimilar abgegeben würde, bei denen mit einem biosimilarfähigen Wirkstoff im Rahmen einer Ersteinstellung behandelt wird. Eine Analyse des Wissenschaftlichen Instituts der AOK (WiDO) konnte zeigen, dass im Jahr 2018 knapp 55 % der AOK-versicherten Patientinnen und Patienten, die mit einem biosimilarfähigen Wirkstoff behandelt wurden, eine Ersteinstellung erhielten (WiDO 2019b). Für mehr als die Hälfte der Fälle einer kostengünstigeren Biosimilar-Therapie wäre demnach kein Switch nötig gewesen.

4 Arzneimittel zur Behandlung von seltenen Erkrankungen

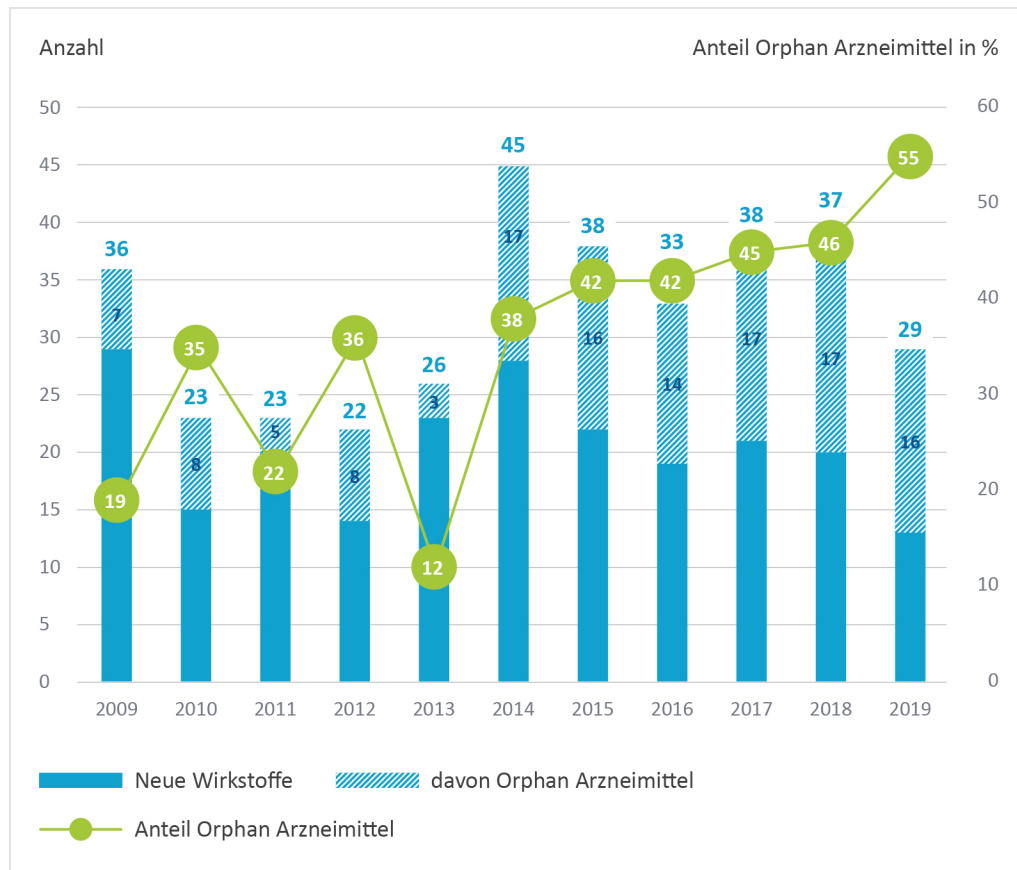
4.1 Marktdynamik bei Orphan Drugs

Arzneimittel gegen seltene Erkrankungen, sogenannte Orphan Drugs, erfahren immer wieder Aufmerksamkeit, da ihre Relevanz in der Arzneimittellandschaft seit einigen Jahren zunimmt und die „Mondpreis“-Diskussionen der vergangenen Jahre besonders diese Arzneimittel betrifft.

Aufgrund der geringen Anzahl an Patientinnen und Patienten und der damit einhergehenden geringeren Umsatzerwartung wurde die Entwicklung von Arzneimitteln gegen seltene Erkrankungen lange Zeit vernachlässigt. Um die Attraktivität der Entwicklung dieser Medikamente zu erhöhen und Forschung in diesem Gebiet zu fördern, wurden 2001 auch in der EU Anreizstrukturen geschaffen. So erhalten pharmazeutische Unternehmen, die bei der europäischen Zulassungsbehörde EMA für ihr Arzneimittel eine Orphan-Designation erfolgreich beantragt haben, finanzielle Anreize im Rahmen der Zulassung: Neben kostenfreier wissenschaftlicher Beratung, der Reduktion der Gebühren vor Marktzulassung um 50 % bzw. 100 % für kleinere Unternehmen, erhalten die Hersteller auch über den Patentschutz hinaus eine Marktexklusivität für zehn bzw. zusätzliche zwei Jahre bei pädiatrischen Indikationen. Einzelne europäische Länder gewähren Steuervergünstigungen (Frankreich, Niederlande und Großbritannien) und Forschungsförderungen (Deutschland, Frankreich, Niederlande) für Unternehmen oder bieten weitere regulatorische Erleichterungen wie reduzierte Anforderungen an die Nutzenbewertung zur Markteinführung in Deutschland (Roll et al. 2011).

Dass diese Regelungen Früchte tragen, wird sowohl auf europäischer Ebene als auch in der deutschen Arzneimittellandschaft deutlich. So steigt nicht nur die Anzahl der zugelassenen Orphan Drugs in Europa immer stärker an (European Medicines Agency 2018), auch in Deutschland wächst die Anzahl an verfügbaren Orphan Drugs seit Jahren stark, sodass 2019 bereits jeder zweite neue Wirkstoff im deutschen Markt bei Zulassung ein Arzneimittel gegen seltene Leiden ist (Abbildung 4-1). Davon entfallen die meisten Wirkstoffe auf onkologische Indikationen. Dass die Entwicklung von Orphan-Arzneimitteln zur punktuell molekularen Behandlung onkologischer Erkrankungen eher im Mittelpunkt des Forschungsinteresses der pharmazeutischen Unternehmen steht und nicht die Entwicklung von Arzneimitteln gegen seltene genetisch bedingte Erkrankungen, für die es häufig keine Therapieoptionen gibt, wird dabei kritisch betrachtet (Ludwig 2019).

Abbildung 4-1: Markteinführungen neuer Wirkstoffe und darunter Arzneimittel, die bei Zulassung eine Orphan-Designation besaßen

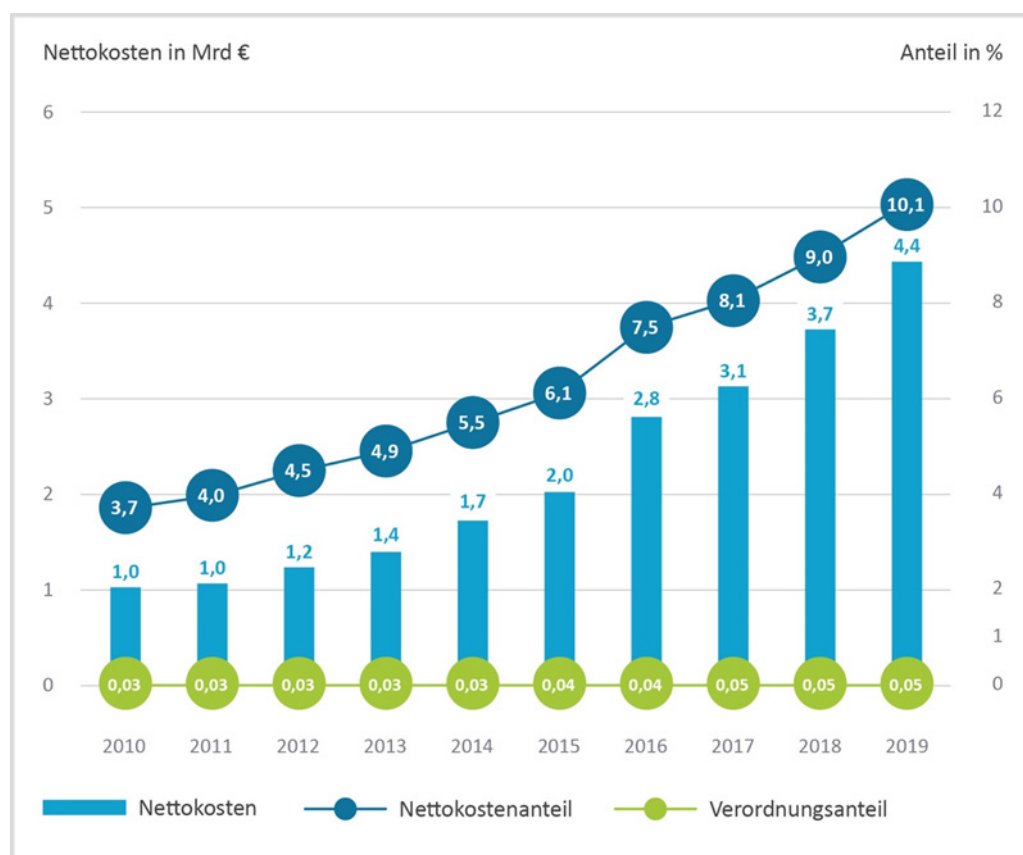


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Infolgedessen nehmen auch die Nettokosten und allerdings in deutlich geringerem Maße die Verordnungen der Arzneimittel zu, die jemals als Orphan Drug zugelassen wurden. Während Orphan-Arzneimittel 2010 noch Nettokosten in Höhe von 1 Mrd. € verursachten, was weniger als 5 % der Nettokosten des gesamten GKV-Marktes entsprach, haben sich diese Kosten in zehn Jahren vervierfacht und erreichen mit über 4,4 Mrd. € 2019 einen Nettokostenanteil von 10 % (Abbildung 4-2). Allein der Vergleich von 2019 zu 2018 zeigt: Mit einem Nettokostenwachstum in Höhe von 18,9 % ist die Nettokostenentwicklung in diesem Marktsegment deutlich dynamischer als im Restmarkt. Bis 2024 wird für den weltweiten Markt der Anteil der Orphan Drugs an den Gesamtausgaben auf 18 % prognostiziert (EvaluatePharma 2020). Für rund 40 % der Arzneimittel gegen seltene Erkrankungen, die sich in der Entwicklungspipeline befinden, wird 2024 der Status eines Blockbusters, also eines Arzneimittels, das jährlich mehr als 1 Mrd. \$ Umsatz erzielt, erwartet (EvaluatePharma 2018).

Dabei scheint gerade der deutsche Markt attraktiv für Hersteller von Arzneimitteln gegen seltene Erkrankungen zu sein: Im Vergleich zu 21 anderen europäischen Ländern ist in Deutschland nicht nur die höchste Anzahl von Präparaten dauerhaft verfügbar, diese Produkte treten auch am schnellsten in den Markt ein und die Orphan-Umsätze je Einwohner sind ebenfalls in Deutschland am höchsten. Deutschland stellt das einzige Land in dieser Gruppe dar, in dem eine volle Erstattung durch die Kostenträger erfolgt. In anderen Ländern gelten teilweise Einschränkungen der Verfügbarkeit oder hinsichtlich der Erstattung, beispielsweise erst bei nachgewiesenem therapeutischem Vorteil des betreffenden Arzneimittels (Gammie et al. 2015, Detiček et al. 2018).

Abbildung 4-2: Nettokosten sowie Nettokosten- und Verordnungsanteile der Orphan Drugs



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Warum gibt es immer mehr Arzneimittel gegen seltene Erkrankungen?

Als selten gilt eine Krankheit innerhalb der Europäischen Union, wenn sie nicht mehr als fünf je 10.000 Personen betrifft. Die Zahl der Erkrankten ist somit je Einzelkrankheit erst einmal gering. Durch Fortschritte in der Grundlagenforschung und zunehmende Möglichkeiten in der Gentechnologie wächst die Zahl der diagnostizierbaren seltenen Erkrankungen stetig (van Egmond-Fröhlich/Schmitt 2018). Mittlerweile sind bei steigender Tendenz rund 8.000 seltene Erkrankungen bekannt. Jährlich kommen ca. 100 bis 250 neue seltene Erkrankungen dazu (Boycott et al. 2017). Insgesamt sind in der EU rund 8 % aller Bürgerinnen und Bürger von mindestens einer dieser seltenen Erkrankungen betroffen (Richter et al. 2015 nach Falkenstein/Stark 2018).

Auch wenn die vermehrte Entwicklung von Orphan Drugs als Erfolg der finanziellen Anreize gewertet werden kann, wird diese Entwicklung nicht unkritisch betrachtet. Es wird argumentiert, dass vermehrt Arzneimittel gegen Leiden auf den Markt gebracht werden, die nicht per se als selten einzustufen sind. Hersteller würden die Anwendungsgebiete so zurechtschneiden, dass kleinere Indikationen entstehen, die dann die Kriterien der Orphan-Designation erfüllen (Simoens 2011). Aufgrund der Unterteilung einer Erkrankung nach speziellen Merkmalen (z. B. Biomarker) würden per se nicht seltene Erkrankungen zu seltenen Erkrankungen gemacht (Kesselheim et al. 2017). Dies wird anhand der nettokostenstärksten Orphan-Arzneimittel des Jahres 2019 (Tabelle 4-1) deutlich. Bei beinahe jedem dritten Arzneimittel handelt es sich um eines, dass aufgrund einer (meist anhand von Biomarkern vorgenommenen) Unterteilung oder Stratifizierung der Patientengruppe der Präzisionsmedizin¹ zuzuschreiben ist.

¹ Die auch als individualisierte oder personalisierte Medizin bezeichneten Therapiekonzepte nehmen die individuellen genetischen Charakteristika sowie bestimmte Stoffwechselvorgänge in den Fokus, durch die beispielsweise die Entstehung onkologischer Erkrankungen begünstigt wird (Leiner 2015).

Tabelle 4-1: Die 20 nettokostenstärksten Arzneimittel 2019, die einen Orphan-Drug-Status haben oder hatten

Rang	Präparat	Hauptindikationsgruppe	Markteintritt	Nettokosten in Mio. €	DDD in Mio.	DDD-Nettokosten	Personalisierte Medizin (vfa, 2020)
1	Revlimid	Immuntherapie	2007	580,3	2,2	260,50	nein
2	Imbruvica	Krebserkrankungen	2014	306,3	1,2	248,76	nein
3	Soliris	Immuntherapie	2007	263,6	0,2	1.149,30	nein
4	Darzalex	Krebserkrankungen	2016	246,9	1,4	181,20	nein
5	Jakavi	Krebserkrankungen	2012	237,7	1,6	150,38	nein
6	Myozyme	Stoffwechselerkrankungen	2006	111,1	0,1	1.286,90	nein
7	Replagal	Stoffwechselerkrankungen	2001	109,0	0,2	678,56	nein
8	Tasigna	Krebserkrankungen	2008	108,3	0,8	129,79	ja
9	Kalydeco	Chronische Atemwegserkrankungen	2012	93,4	0,1	721,69	ja
10	Ilaris	Immuntherapie	2009	86,0	0,4	233,05	nein
11	Glivec	Krebserkrankungen	2001	80,5	0,7	122,95	ja
12	Lynparza	Krebserkrankungen	2015	80,3	0,4	226,75	ja
13	Vidaza	Krebserkrankungen	2009	76,9	0,4	174,97	nein
14	Revolade	Erkrankungen des Blutsystems	2010	76,6	0,9	89,41	nein
15	Sprycel	Krebserkrankungen	2006	72,2	0,4	198,92	ja
16	Exjade	Sonstige	2006	63,1	0,7	96,05	nein
17	Sutent	Krebserkrankungen	2006	62,1	0,4	159,06	nein
18	Ofev	Krebserkrankungen	2015	61,5	0,6	104,85	nein
19	Strensiq	Stoffwechselerkrankungen	2015	58,7	0,0	1.344,37	nein
20	Orkambi	Chronische Atemwegserkrankungen	2015	58,4	0,1	420,80	ja
Summe				2.832,8	12,7	223,13	
Anteil Top 20 an Gesamtmarkt in %				6,5	0,03		
Gesamtmarkt				43.859,4	43.932,0	1,00	

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Da gerade die Onkologie ein attraktives Feld ist, um neue seltene Erkrankungen zu definieren (Loughnot 2005 nach Simoens 2011), wundert es nicht, dass onkologische Arzneimittel in Tabelle 4-1 mit zehn Präparaten die häufigste Hauptindikationsgruppe darstellen. Tatsächlich entfallen rund 42 % der Nettokosten der Orphan-Arzneimittel in Deutschland auf Krebserkrankungen. Die jährliche Anzahl an Krebsneuerkrankungen in Deutschland liegt bei 492.000 (Robert Koch-Institut 2019). Lediglich bei drei Präparaten in den Top 20 und bei rund 13 % Nettokosten aller Orphan-Arzneimittel handelt es sich um Arzneimittel zur Enzyersatztherapie, die bei der Therapie einer typischen schweren chronischen seltenen Erkrankung wie Morbus Pompe zur Anwendung kommen.

Angesichts dieser starken Präsenz von Onkologika stellt sich die Frage, ob mit den vor 20 Jahren für Orphan Drugs geschaffenen Anreizstrukturen tatsächlich noch die Arzneimittel gefördert werden, für die sie einmal entwickelt wurden. Hier wird vor allen Dingen das Prävalenzkriterium hinterfragt, da dies Fehlanreize bietet (Greiner 2012, Danzon 2018). So kommen Arzneimittel, die der Präzisionsmedizin zugeordnet werden und deswegen auch naturgemäß eine kleine Anzahl an Patientinnen und Patienten betreffen, in den Genuss einer Förderung, die für sie nicht intendiert war. Das Anreizinstrumentarium für Orphan Drugs zielt auf die Förderung der Entwicklung von Arzneimitteln gegen „echte“ seltene Erkrankungen ab und war nicht als Begleitinstrument der Präzisionsmedizin gedacht, die sich vermutlich auch unabhängig von den Anreizstrukturen für Orphan Drugs in dieser Form und in diesem Ausmaß entwickelt hätte. Vor dem Hintergrund knapper Ressourcen ist ein solcher Mitnahmeeffekt aus ökonomischer Perspektive kritisch zu bewerten.

Als Lösung wird zum einen gefordert, die Entwicklungen in der Medizin, beispielsweise in der Präzisionsmedizin, bei der Erteilung des Orphan Status zu berücksichtigen und die Anforderungen für die Erteilung des Orphan Status grundsätzlich zu überdenken (Ludwig/Schwabe 2019). Zum anderen sind Rückzahlungen der initialen finanziellen Förderungen denkbar, sobald die Umsätze eine definierte Schwelle überschreiten (Ludwig/Schwabe 2019).

Neben der in Frage zu stellenden Prävalenzgrenze lässt sich auch die in Europa geltende zehn- bis zwölfjährige Marktexklusivität hinterfragen. Gemäß dieser Marktexklusivität können andere Hersteller auch keine ähnlichen Arzneimittel in der gleichen Indikation auf den Markt bringen (Sydow/Throm 2019), was einen weitreichenderen Schutz als durch das Patentrecht darstellt. In den USA ist diese Marktexklusivität mit sieben Jahren deutlich kürzer, in Australien und Kanada gibt es Vergleichbares gar nicht (Roll et al. 2011). Dabei wurde 2018 die Definition der Ähnlichkeit zwar strenger gefasst, die Marktexklusivität an sich jedoch nicht begrenzt (Ludwig/Schwabe 2019). Eine Absenkung der Marktexklusivität würde die Preissetzungsmacht des Herstellers eindämmen und könnte folglich zu geringeren Preisen führen.

Ist ein Markt für seltene Krankheiten attraktiv für Nachahmer?

Einerseits kann aufgrund der geringen Patientenzahl bei seltenen Erkrankungen kaum davon ausgegangen werden, dass es einen Generikamarkt nach Ablauf des Patentschutzes bei Orphan-Arzneimitteln gibt. Andererseits wird argumentiert, dass bei Ablauf des Patentschutzes auch bei Orphan-Arzneimitteln die gleiche Marktdynamik greift wie bei anderen Arzneimitteln (Sydow und Throm, 2019). Wie sieht der generikafähige Markt bei Orphan-Arzneimitteln aus?

Von den 156 Arzneimitteln, die bei Zulassung eine Designation als Orphan Drug besaßen und 2019 am deutschen Markt verfügbar waren, waren für neun Arzneimittel tatsächlich Nachahmer im Markt. Für mindestens sechs weitere Arzneimittel kann angenommen werden, dass Schutzfristen abgelaufen sind, da diese bereits seit mehr als 15 Jahren angeboten werden. Für diese sechs haben bisher (noch) keine Nachahmer den Markt betreten. Tabelle 4-2 zeigt die neun Wirkstoffe mit Wettbewerb, ihre Nettokosten im Jahr 2019, die Zweitanbieterquote (nach Tagesdosen) sowie die Nettokostendifferenz der Generika gegenüber den Altoriginalen als Quotient. So wird deutlich, dass es einen relevanten Nachahmermarkt zu geben scheint, dies aber vor allen Dingen in den nettokostenstarken Märkten der onkologischen Präparate (die alle keine Orphan-Designation mehr besitzen): Hier gibt es oft große Zweitanbieteranteile und spürbare Preisabschläge gegenüber dem jeweiligen Altoriginal. Die kleineren Märkte der Arzneimittel gegen eher „klassische“ seltene Erkrankungen (Carglumsäure, Miglustad) weisen dabei wenige Anbieter, geringe Zweitanbieteranteile und auch geringe Preisabschläge auf.

Tabelle 4-2: Orphan-Arzneimittel mit Wettbewerb, ihre Nettokosten im Jahr 2019, die Zweitanbieterquote (nach Tagesdosen) sowie mittlere DDD-Nettokostendifferenz der Generika gegenüber den Altoriginalen

Wirkstoff	Hauptindikationsgruppe	Nettokosten in Mio. €	Zweitanbieteranteil (DDD)	Abstand der DDD-Nettokosten
Imatinib	Krebserkrankungen	113,5	64 %	0,23
Dasatinib	Krebserkrankungen	90,3	22 %	0,87
Bosentan	Herz-Kreislauf-Erkrankungen	40,5	74 %	0,52
Sildenafil	Herz-Kreislauf-Erkrankungen	38,7	79 %	0,85
Everolimus	Krebserkrankungen	26,4	50 %	0,42
Miglustad	Stoffwechselkrankheiten	15	17 %	0,89
Anagrelid	Krebserkrankungen	14,2	61 %	0,55
Iloprost	Herz-Kreislauf-Erkrankungen	6,6	12 %	1,35
Carglumsäure	Stoffwechselkrankheiten	1,5	0 %	0,94

Auf der einen Seite deutet sich also an, dass der Markt der klassischen Orphan-Arzneimittel nicht attraktiv für Nachahmer zu sein scheint. Dies ist aber bei Arzneimitteln gegen seltene Erkrankungen auch kaum anders zu erwarten, da der Patientenkreis eng begrenzt ist. Auf der anderen Seite gibt es Märkte für Orphan-Arzneimittel, die Nachahmern Raum zu bieten scheinen. Hier sind die Zulassungen in der Regel um weitere Indikationen erweitert worden, sodass die Gesamtpatientenzahl über der Grenze von fünf von 10.000 liegt. Wenn der Markt bei diesen Arzneimitteln letztendlich aber ausreichend groß ist, dass sogar Wettbewerb entstehen kann, kann die Förderbedürftigkeit dieser Arzneimittel zumindest im Nachhinein bezweifelt werden.

Gezielte Umwidmung älterer Wirkstoffe für neue Anwendungsgebiete

Dass nicht nur aus Orphan Drugs Generika werden, sondern es auch den umgekehrten Weg gibt, zeigt sich an der Zweitverwendung für alte Arzneimittel als Orphan Drugs in gänzlich anderen Indikationen als denen, für die sie ursprünglich entwickelt wurden. Prinzipiell ist diese Zweitverwertung nicht neu. So ist der Wirkstoff Sildenafil, ursprünglich als Mittel gegen Bluthochdruck geplant, heute besser unter dem Namen Viagra bekannt und als solcher wirksam bei erektiler Dysfunktion. Er ist jedoch auch zur Behandlung des Lungenhochdrucks zugelassen. Ähnliches gilt für Acetylsalicylsäure (beispielsweise Aspirin) als Mittel gegen Schmerzen, das bereits seit langem auch zur Sekundärprophylaxe von Herzinfarkt und Schlaganfall eingesetzt wird. Während die Wissenschaft früher eher zufällig auf alternative Wirkungen von Medikamenten gestoßen ist, gehen Wirkstoffforscher heute deutlich strategischer und systematischer vor. Im Rahmen der gezielten „Umwidmung“ von Medikamenten (drug repurposing, drug repositioning) wird datenbankunterstützt versucht, zu neuen oder bekannten Wirkstoffen weitere passende Krankheiten zu finden. So werden beispielsweise Zusammenhänge zwischen Krankheiten und genetischer Variation gefunden, die dann als neue Angriffspunkte für Therapien genutzt werden können. Optimalerweise ist dazu dann bereits ein passendes Arzneimittel bekannt.

Gerade der Markt für Orphan-Arzneimittel mit einer wachsenden Anzahl an neuen seltenen Leiden, die zu einem großen Anteil durch Gendefekte verursacht werden, und der Tatsache, dass es bisher nur für 5 % der seltenen Erkrankungen ein Arzneimittel gibt, bietet ein großes Feld für das Umwidmen von Medikamenten (Pushpakom et al. 2019). Grundsätzlich ist eine Umwidmung positiv zu bewerten: Die Entwicklungsdauer kann reduziert werden, die Wahrscheinlichkeit des Scheiterns sinkt und insgesamt nehmen die Kosten der Entwicklung nur rund 10 % der „normalen“ Entwicklungskosten ein (Pushpakom et al. 2019) aus gesellschaftlicher Perspektive also durchaus wünschenswert (Davies et al. 2017). Allerdings ist fraglich, ob sich diese enormen Effizienzgewinne in Forschung und Entwicklung auch bei der Preisgestaltung der Hersteller zeigen. So gibt es mehrere Beispiele dafür, dass sich die Preise eher am Preisniveau vergleichbarer Arzneimittel orientieren, wie der ursprünglich als Blutdrucksenker zugelassene und als solcher jahrzehntelang erfolgreich vermarktete Wirkstoff Propranolol, der mittlerweile auch für die seltene Erkrankung infantiles Hämangioblastom zugelassen ist (Zimmermann et al. 2010, Albiñana et al. 2017). Eine Tagesdosis des Blutdrucksenkers kostet im Durchschnitt 0,77 €, während es als Orphan Drug zur Behandlung des Hämangioblastoms 9,14 € je Tagesdosis kostet.

4.2 Wie lassen sich die hohen Preise der Orphan Drugs erklären?

Auf den ersten Blick scheinen hohe Preise bei Arzneimitteln gegen seltene Erkrankungen nachvollziehbar und akzeptabel zu sein, da die Kosten für Forschung und Entwicklung durch den Einsatz in vergleichsweise kleinen Patientenpopulationen refinanziert werden müssen. Trotzdem gibt es einige Gründe, diese Argumentation in Frage zu stellen.

Zunächst einmal spricht der Trend zu einer vermehrten Entwicklung von Arzneimitteln gegen seltene Erkrankungen und ihr dynamisches Umsatzwachstum für ein durchaus profitables Feld (Greiner 2012, Danzon 2018). Die Nettokosten für eine Tagesdosis unter den Top 20 der Orphan-Arzneimittel rangieren zwischen 90 € und 1.250 €, im Durchschnitt liegen sie bei 223,13 € Nettokosten je Tagesdosis (Tabelle 4-1), während sie im Gesamtmarkt bei 1,00 € liegen und im Patentmarkt im Mittel bei 7,36 €. Auch die umsatzstärksten Pharmaunternehmen weltweit forcieren die Entwicklung von Orphan-Arzneimitteln.

Zudem gibt es Hinweise darauf, dass die Kosten für die Entwicklung und Vermarktung der Orphan-Arzneimittel nicht so hoch sind wie angenommen: So konnte gezeigt werden, dass gerade in der letzten Phase der Entwicklung (Phase III) Orphan Drugs deutlich weniger Kosten für die Hersteller verursachen – im Schnitt rund 50 % weniger als Nicht-Orphan Drugs (EvaluatePharma 2015). Insgesamt sei die Rentabilität dieser Phase bei Orphans 1,14-mal größer als bei Nicht-Orphan-Arzneimitteln (Danzon 2018). Zudem wird angesichts der stetig steigenden Anzahl an neuen seltenen Erkrankungen das datengestützte sogenannte „drug repurposing“ (siehe Abschnitt „Gezielte Umwidmung älterer Wirkstoffe für neue Anwendungsgebiete“) immer häufiger genutzt, so dass hier deutliche Effizienzgewinne in den ersten beiden Phasen der Entwicklung möglich sind (Pushpakom et al. 2019).

Auch die Marketingkosten, die einen hohen Anteil an den Kosten haben, können aufgrund der Größe und damit Übersichtlichkeit des Marktes für eine seltene Erkrankung geringer sein als bei Nicht-Orphan Drugs: Der Markt ist informierter, weil er von Spezialisten geprägt ist (Simoens 2011, Danzon 2018). Zudem existieren Patientenregister, die Zulassungsstudien erleichtern und die Einführung in den Markt beschleunigen (van Egmond-Fröhlich/Schmitt 2018).

Der für die Unternehmen aber sicherlich finanziell lohnendste Umstand für die Entwicklung eines neuen Arzneimittels als Orphan Drug ist, dass über die häufig weniger aufwändige Forschung im Rahmen der klinischen Erprobung und den damit meist verbundenen früheren Markteintritt die zur Verfügung stehende Patentlaufzeit länger exklusiv vermarktet werden kann als dies bei konventionell zugelassenen Arzneimitteln der Fall ist. So wurde gezeigt, dass die Zeitspanne von Phase II bis zur Einführung des Medikaments bei Orphan Drugs mit durchschnittlich 3,9 Jahren deutlich kürzer ist als mit 5,4 Jahren bei anderen Arzneimitteln (Meekings et al. 2012).

Die Kostenargumentation „hohe Preise durch niedrige Patientenzahlen“ ist aber vor allen Dingen vor dem Hintergrund konstant hoher Preise für Orphan Drugs bei einer Indikationsausweitung – in der Regel um weitere Orphan-Indikationen – schwer haltbar. Betrachtet man die 20 umsatzstärksten ursprünglich als Orphan Drugs zugelassenen Arzneimittel im Jahr 2019 (Tabelle 4-1) wird deutlich, dass das mögliche Wirkungsspektrum des Arzneimittels oft viel größer ist als das Indikationsspektrum bei Erstzulassung. Sieben der acht nach 2011 zugelassenen Orphan Drugs haben mindestens eine zusätzliche Bewertung aufgrund von Indikationserweiterungen durch den G-BA durchlaufen. Exemplarisch sollen hier die beiden Onkologika Imbruvica und Darzalex, Rang 2 und 4 der Top 20 Orphan Drugs im Jahr 2019 (Tabelle 4-1.) genannt werden. Imbruvica wurde im Jahr 2014 zunächst in den Orphan-Indikationen zur Behandlung des rezidivierten oder refraktären Mantelzell-Lymphoms (MCL) und der chronischen lymphatischen Leukämie zugelassen. Nach mittlerweile fünf Indikationserweiterungen (G-BA Stand: 06/2020) ist es nicht verwunderlich, dass sich dieses Orphan-Arzneimittel zum Blockbuster entwickelt hat und Nettokosten im Jahr 2019 von 306,3 Mio. € verursacht. Auch das umsatzstarke Orphan-Arzneimittel Darzalex kann auf eine Erfolgsgeschichte zurückblicken: Zwar erst 2016 zugelassen gegen das multiple Myelom, gab es bisher drei Indikationserweiterungen (G-BA Stand: 06/2020). Die Nettokosten beliefen sich im Jahr 2019 auf 246,9 Mio. €. Für beide Präparate gab es bereits nach einem Jahr nach Markteintritt vom G-BA ein Nutzenbewertungsverfahren wegen Überschreitung der 50 Mio. €-Grenze für Orphan Drugs, beide Präparate wurden daher vollständig bewertet.

Auch wenn einige Indikationen eine seltene Krankheit gemäß Definition beschreiben, fällt es angesichts der Umsätze und Anzahl der einzelnen Indikationen zumindest bei den nettokostenstärksten dieser Arzneimittel schwer, das Bild förderungsbedürftiger Arzneimittel gegen seltene Erkrankungen aufrechtzuerhalten. Andersherum stellt sich die Frage, warum das pharmakologische Potenzial mancher dieser Arzneimittel nicht gleich zu Beginn ausgeschöpft wird.

Die Frage, wie sich die hohen Preise für Orphan Drugs erklären lassen, kann an dieser Stelle nicht abschließend beantwortet werden. Die genannten Argumente sprechen aber dafür, dass die geforderten Höchstpreise darauf beruhen, dass die Marktchancen, die aus der Sonderstellung als Orphan Drug resultieren, bei der Preisbildung konsequent optimierend genutzt werden.

Wie schneiden Orphan-Arzneimittel in der Nutzenbewertung nach AMNOG ab?

Im Rahmen des AMNOG durchlaufen Orphan-Arzneimittel lediglich eine eingeschränkte Nutzenbewertung. Durch die europäische Zulassung gilt ihr medizinischer Zusatznutzen bereits als belegt. Die Ergebnisse der bisherigen Nutzenbewertungen der Orphan-Arzneimittel insgesamt zeigen, dass für einen Großteil der Präparate das Ausmaß des Zusatznutzens nicht quantifizierbar ist (Ludwig/Schwabe 2019, Ludwig 2019).

Erst bei Erreichen der Umsatzgrenze von 50 Mio. € innerhalb eines Jahres werden die Arzneimittel dann in der Bewertung wie jedes andere Arzneimittel behandelt. Mittlerweile mussten sich bereits elf Arzneimittel (von insgesamt 82 Orphan-Arzneimitteln, die eine Nutzenbewertung durchlaufen haben) einer solchen Bewertung unterziehen. Die Ergebnisse zeigen, dass diese eine reguläre Nutzenbewertung nicht zu scheuen brauchen: Von elf Arzneimitteln, die die volle AMNOG-Nutzenbewertung aufgrund des Überschreitens der Umsatzschwelle durchlaufen haben, können sieben einen Zusatznutzen mindestens in einer Teilindikation aufweisen, sechs davon sogar einen beträchtlichen Zusatznutzen. So zeigt sich erneut, dass eine reguläre Nutzenbewertung

nicht nur machbar ist (Kohzer/Diessel 2019), vielmehr zählt sie sich auch für einige pharmazeutische Unternehmen sogar aus, da die erneuten Nutzenbewertungs-Ergebnisse auch einen Zusatznutzen attestieren. Insofern erscheint die Sonderstellung der Orphan-Arzneimittel in der Nutzenbewertung, die im europäischen Umfeld einzigartig ist (Kohzer/Diessel 2019), nicht gerechtfertigt.

Aus dieser Perspektive stellt die mit dem GSAV erfolgte Festlegung, dass zukünftig nicht nur die ambulanten, sondern auch die vollständigen (stationären) Umsätze für die Initiierung einer regulären Bewertung zu berücksichtigen sind, einen Schritt in die richtige Richtung dar. Trotzdem muss sowohl aus Gründen der evidenzbasierten Therapie als auch im Sinne der Wirtschaftlichkeit hinterfragt werden, dass weiterhin kostenintensive Arzneimittel – dazu häufig auf einer eingeschränkten Datenbasis – den Markt betreten, ohne dass sie einer umfassenden Nutzenbewertung unterliegen.

5 Arzneimittelrabattverträge

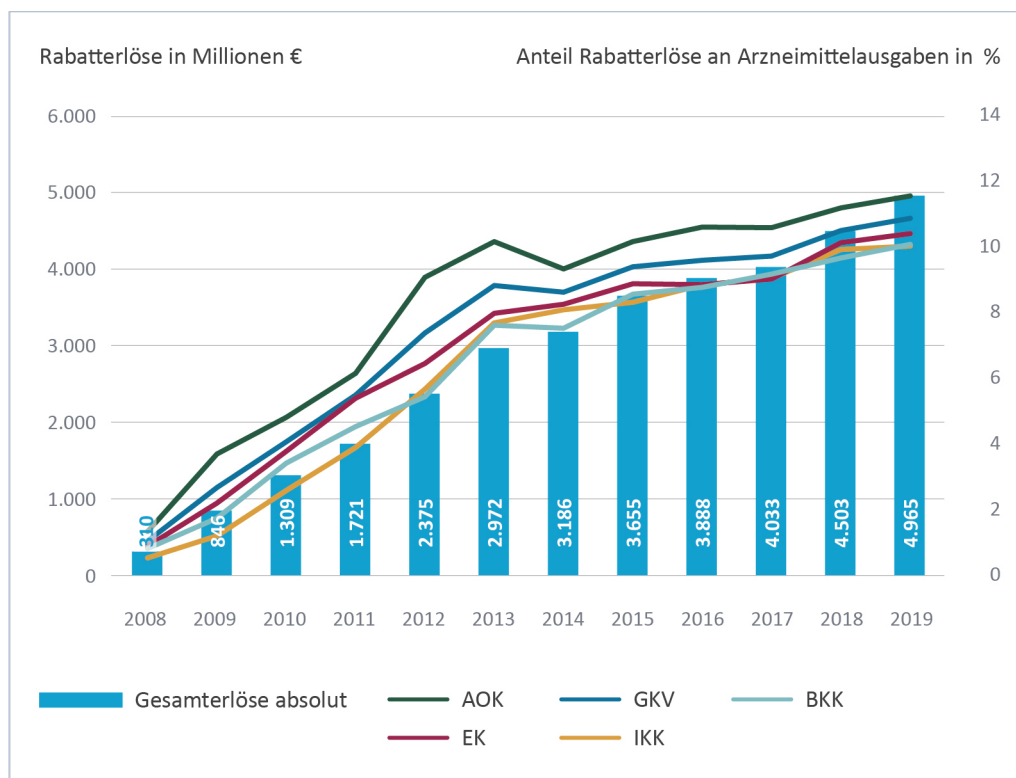
5.1 Die Entwicklung der Arzneimittelrabattverträge

Neben den für alle Krankenkassen gleich wirkenden Steuerungs- und Kostendämpfungs-Instrumenten wie Festbeträgen oder den verschiedenen flächendeckend wirksamen gesetzlichen Abschlägen (Apothekenabschlag, sowie Hersteller-, Preismoratoriums- und Generikaabschlag, vgl. WIdO 2020) haben die Krankenkassen mit dem § 130a Abs. 8 SGB V seit 2003 die Möglichkeit, mit pharmazeutischen Herstellern individuelle Arzneimittelrabattverträge abzuschließen. Dabei schreiben die Krankenkassen auf der Ebene von einzelnen Wirkstoffen gegebenenfalls eingeschränkt auf z. B. einzelne Darreichungsformen öffentlich aus, welcher pharmazeutische Anbieter die Versorgung ihrer Versicherten mit diesem Wirkstoff für einen definierten Zeitraum übernehmen wird. Mit dieser Anbieterfestlegung ist im Gegenzug ein finanzieller Rabatt für die Krankenkasse verbunden. Die Verträge wirken auf diese Weise hauptsächlich ausgaben-senkend. Da die Wirkstoffauswahl selbstverständlich auch weiterhin der behandelnden Ärztin oder dem behandelnden Arzt obliegt, ist mit den Rabattverträgen keine Steuerung der Verordnungen auf bestimmte Wirkstoffe verbunden. Lediglich der Anbieter des verordneten Wirkstoffs wird über den Rabattvertrag bestimmt.

Seit dem 1. April 2007 wurden diese Verträge auch „scharfgestellt“, indem die Apotheken verpflichtet wurden, die kassenspezifischen Rabattverträge bei der Produktauswahl vorrangig zu bedienen, sofern die verordnende Ärztin oder der verordnende Arzt eine Substitution nicht ausgeschlossen hat. Seitdem wird der Wettbewerb von Krankenkassen und pharmazeutischen Herstellern intensiv genutzt und die Krankenkassen erzielen über den Vertragswettbewerb eine relevante Senkung ihrer Ausgaben. Im Jahr 2019 waren unter den insgesamt 2.472 ambulant verordneten Wirkstoffen und Wirkstoffkombinationen 659 bei mindestens einer Krankenkasse rabattiert. Von den im Jahr 2019 für AOK-Versicherte verordneten 280,9 Mio. Arzneimittelpackungen standen 59,0 % zum Zeitpunkt ihrer Verordnung unter einem Rabattvertrag.

Welche Einsparungen werden mit den Rabattverträgen für die GKV erreicht?

Eine Darstellung der finanziellen Auswirkungen erlaubt das seit Mitte 2008 bestehende eigene Haushaltskonto der Krankenkassen in der amtlichen Statistik (KJ 1, seit 2010 ebenfalls in der vorläufigen Statistik KV 45), in dem die Einnahmen aus Rabattverträgen ausgewiesen werden. Für das Jahr 2008 wurde hier im zweiten Halbjahr 2008 erstmals ein Rabattbetrag von 310 Mio. € gebucht. Für das Gesamtjahr 2019 beträgt nach der vorläufigen Statistik die GKV-Rabattsumme 4,96 Mrd. € (2018: 4,50 Mrd. €) und entspricht damit nun 10,9 % der Arzneimittelausgaben (Abbildung 5-1).

Abbildung 5-1: Erlöse aus Rabattverträgen für 2008 bis 2019 nach amtlicher Statistik KJ 1

Quelle: WIdO nach amtlichen Statistiken des Bundesministeriums für Gesundheit (KJ1) für die jeweiligen Jahre

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Dabei unterscheiden sich die Anteile der Rabatteinnahmen an den gesamten Arzneimittelausgaben für die Kassenarten: Während die GKV insgesamt die Ausgaben zu 10,9 % senken konnte, ist eine Spannweite von 10,0 % bei der IKK bis zu 11,6 % bei der AOK zu beobachten.

Die AOKs schreiben seit 2007 die Versorgung für ihre Versicherten wirkstoffbezogen in regionalen Losen aus, seit 2009 erfolgt dies europaweit. Damit bestanden für die AOK im Jahr 2019 Rabattverträge für Arzneimittel mit einem jährlichen AOK-Umsatzvolumen von rund 5,5 Mrd. € (AOK Bundesverband 2019). Die Marktpipeline der Arzneimittel in den Rabattverträgen der AOK belegt beispielhaft die deutliche Marktwirksamkeit dieses Instruments: Seit dem Jahr 2015 wurden konstant durchschnittliche Verordnungsanteile im rabattfähigen Marktsegment von ca. 80 % erreicht (Lohmüller et al. 2019). Dabei ist zu berücksichtigen, dass eine vollständige Umsetzung weder realistisch noch sinnvoll ist: In der Arzneimitteltherapie achten Ärztinnen und Ärzte auf Besonderheiten ihrer Patientinnen und Patienten und geben in begründeten Einzelfällen konkreten Produkten den Vorzug vor Rabattarzneimitteln.

Welche Arten von Rabattverträgen gibt es?

Vorrangig werden Rabattverträge im generikafähigen Marktsegment vereinbart. Hier besteht die Möglichkeit, dass im Rahmen eines Bieterverfahrens von mehreren Herstellern Angebote für einen Wirkstoff abgegeben werden und das wirtschaftlich attraktivste Angebot den Zuschlag erhält. Die Laufzeit der Verträge ist in der Regel auf zwei Jahre begrenzt, danach wird erneut ausgeschrieben.

Die häufigste Art von Rabattverträgen sind Exklusivverträge, die mit nur einem Hersteller vereinbart werden. Mit diesen werden vermutlich auch die höchsten Rabatte erreicht. Bei bestimmten Wirkstoffen kann es aber auch sinnvoll sein, im Rahmen der Ausschreibung Mehrpartner-Modelle vorzusehen, meist werden hier drei Partner gleichberechtigt ausgewählt. Dies kann beispielsweise der Fall sein, wenn eine höhere Anbieterabdeckung erreicht werden soll, da die Umstellungsquoten niedrig sind. Weiterhin sind auch sogenannte Open-House-Verträge möglich, bei denen die Krankenkasse die Konditionen vorgibt und allen interessierten Anbietern den Beitritt zu dem Vertrag gleichberechtigt ermöglicht. Zum 1. September 2019 haben die gesetzlichen Krankenkassen für mehr als die Hälfte (54,5 %) der über 500 verschiedenen generikafähigen und rabattierten Wirkstoffe bzw. Wirkstoffkombinationen mehrere Rabattpartner gemeldet, 45,5 % werden von einem Exklusivpartner bedient. Auch die AOK vergibt in europaweiten Ausschreibungen Aufträge für die Lieferung von Arzneimitteln für ihre Versicherten und entscheidet in jedem Fall, ob die Versorgung von einem Rabattpartner exklusiv oder von mehreren Rabattpartnern übernommen werden soll. Der Blick auf die verordnungsgewichtete Verteilung der Vertragsmodelle zeigt für die AOK, dass 2018 für zwei Drittel der Verordnungen die Versorgung der Versicherten durch einen Exklusivpartner (66,8 %) und bei einem Drittel durch mehrere Rabattpartner (33,2 %) erfolgte (Schröder 2019).

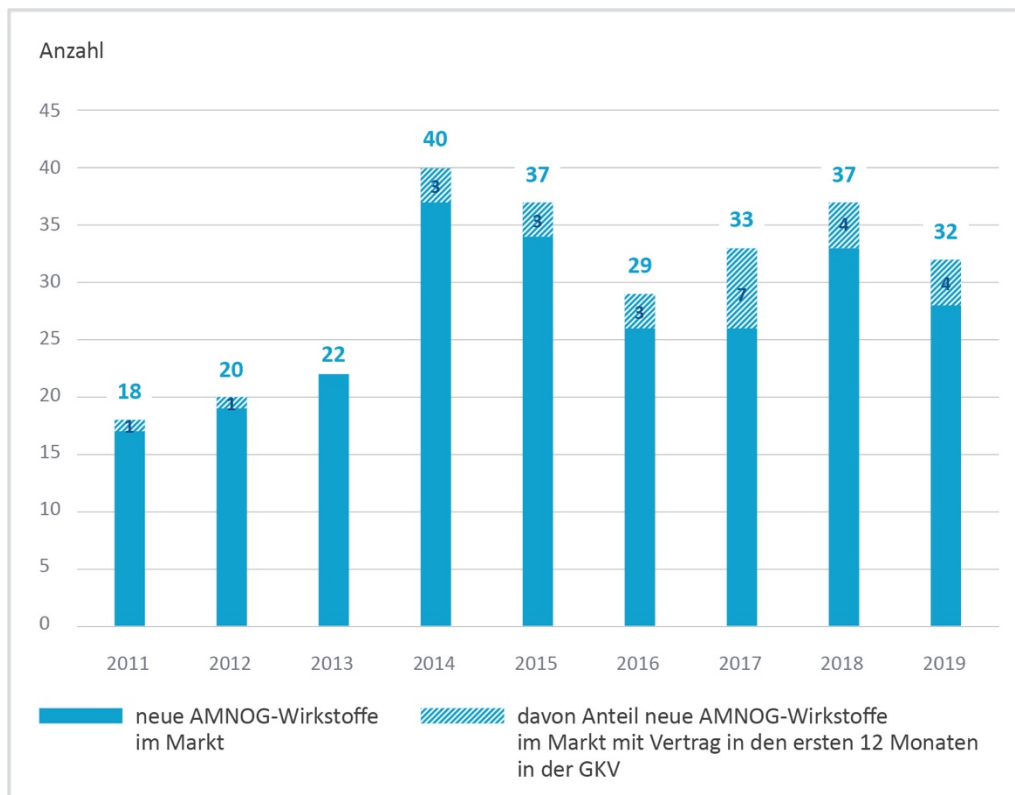
Neben den Verträgen im generikafähigen Marktsegment sind weitere Formen wie Bundling-Verträge (Kombination von Generika und Patentprodukten), Verträge für patentgeschützte Arzneimittel vor Patentauslauf, für patentgeschützte Analogarzneimittel oder für neue patentgeschützte Arzneimittel zu beobachten (Kaesbach 2008, Simoens 2012, Vogler et al. 2012, Schremser et al. 2017). Insbesondere im Patentmarkt existieren Verträge, in denen auch Umsatzobergrenzen oder Rückerstattungen vereinbart werden (siehe Abschnitt „Pay-for-Performance-Verträge“). Systematisch lassen sich derartige Verträge allerdings kaum auswerten, da sie häufig vertraulich und somit nicht öffentlich einsehbar sind. Von den 616 Arzneimitteln, die zum Stichtag 1. April 2019 unter Patentschutz standen, gab es für 111 bei mindestens einer Krankenkasse einen Rabattvertrag. Der Anteil von 18,0 % ist damit höher als in den Vorjahren (2018: 16,4 %, 2017: 17,7 %), jeweils zum Stichtag 1. April.

Wie sind Rabattverträge für neue Patentarzneimittel zu bewerten?

Neue patentgeschützte Arzneimittel, die sich seit 2011 einer Frühen Nutzenbewertung und einer daran anschließenden Preisverhandlung unterziehen müssen, sind immer wieder im Fokus von Rabattverträgen.

Bis zum 31.12.2019 hatte zu 26 von insgesamt 268 verordneten und AMNOG-bewerteten Präparaten bereits in deren ersten Marktjahr mindestens eine gesetzliche Krankenkasse Verträge an die zentrale Meldestelle im GKV-SV gemeldet. Für vier der 32 neuen Präparate, die 2019 in den Markt eintraten und im AMNOG-Verfahren bewertet werden, wurden bis Dezember 2019 Rabattverträge innerhalb der ersten zwölf Monate nach Markteintritt gemeldet (Abbildung 5-2). Die Verträge laufen aber häufig auch darüber hinaus bzw. sind erst später gestartet, sodass inzwischen für 49 der 268 AMNOG-Präparate Rabattverträge gemeldet wurden. Da die Präparate in der Regel nicht in der Apotheke austauschbar sind, besteht keine Verpflichtung zur Meldung der Verträge an den GKV-SV. Insofern kann die tatsächliche Zahl der Vertragsschlüsse bei patentgeschützten Arzneimitteln höher liegen.

Abbildung 5-2: Anzahl Rabattverträge vor vereinbartem Erstattungsbetrag für neue AMNOG-Wirkstoffe nach Jahr des Markteintritts. Angegeben sind die von mindestens einer gesetzlichen Krankenkasse an die zentrale Meldestelle des GKV-Spitzenverbandes gemeldeten Verträge zum Stand 31.12.2019



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Von einzelnen gesetzlichen Krankenkassen werden bereits vor Abschluss der kollektiven Preisverhandlungen des GKV-SV Selektivverträge abgeschlossen. Damit wird zunächst die Regelungslücke überbrückt, dass der verhandelte Erstattungsbetrag erst ab dem 13. Monat nach Markteinführung gültig ist.

Aus ordnungspolitischer Perspektive sind diese Verträge zu diskutieren: Dabei sind die kurzfristig mit dieser Art von Rabattverträgen für einzelne Kassen zu erzielenden Einsparungen gegen längerfristig „vermutlich ungünstigere Ergebnisse“ der zentralen Erstattungsbetragsverhandlungen abzuwägen (Diessel/Focke 2015). So erscheint es plausibel, dass die Verhandlungsmacht des GKV-SV durch Rabattverträge zwischen einzelnen Kassen und dem pharmazeutischen Unternehmen, die vor Abschluss der Erstattungsbetragsverhandlungen geschlossen werden, geschwächt wird.

Besonders problematisch wird es, wenn die Verträge vor der Veröffentlichung der Frühen Nutzenbewertung abgeschlossen werden, da das Informationsdefizit der einzelnen Krankenkasse gegenüber dem pharmazeutischen Unternehmen zu diesem Zeitpunkt groß ist. Diese schlechtere Ausgangsposition schlägt sich dann möglicherweise in höheren Preisen und schlechteren Konditionen für die Krankenkasse nieder. Auch wenn es also für die einzelne vertragsschließende Krankenkasse im Kassenwettbewerb temporär vorteilhaft erscheint, bereits vor Festlegung des kollektiven Erstattungspreises einen Selektivvertrag zu schließen, kann dies möglicherweise für das Kollektiv aller Versicherten mittel- und langfristig zu Nachteilen führen.

Die Neigung einer Krankenkasse, einen solchen Vertrag einzugehen, würde sich jedoch vermutlich reduzieren, wenn gesichert wäre, dass der Erstattungsbetrag rückwirkend zum Markteintritt gilt, was der GKV-SV immer wieder fordert (GKV-Spitzenverband 2015, Stoff-Ahnis 2020). Damit entfielen weitgehend der wirtschaftliche Handlungsdruck, bereits im Jahr der freien Preisbildung die Preise und Kosten selektivvertraglich senken zu müssen. Die Kassen könnten den Abschluss ergänzender Verträge nach § 130c SGB V auf den Zeitpunkt nach der Kollektivverhandlung verschieben, ohne auf den kostensenkenden Effekt im ersten Jahr verzichten zu müssen.

Pay-for-Performance Verträge

Vor dem Hintergrund der besonders hochpreisigen neuen Gentherapeutika wie Yescarta, Kymriah oder das kürzlich zugelassene aktuell teuerste Arzneimittel der Welt Zolgensma und den Unsicherheiten über den Nutzen der Arzneimittel bei Zulassung, werden immer häufiger alternative Erstattungsmodelle vorgeschlagen.

Am häufigsten wird dabei das Modell der erfolgsabhängigen Erstattung auf Basis von Pay-for-Performance-Verträgen diskutiert. Diese existieren bereits in den USA und vereinzelt auch in Deutschland (Der Arzneimittelbrief 2011, Borsch 2018). Hier wird die (Höhe der) Vergütung an den individuellen therapeutischen Erfolg einer Intervention geknüpft. Auf den ersten Blick ist eine solche Herangehensweise positiv zu bewerten, da der eintretende oder nicht eintretende Behandlungserfolg nicht mehr nur den Kostenträger und die Patientinnen und Patienten betrifft (Antonanzas et al. 2019).

Die Umsetzung ist aber in der Praxis eine zentrale Herausforderung und erweist sich als schwierig (Stackelberg et al. 2018 Hecken 2019): Wie ist der Behandlungserfolg definiert? Oder genauer: Wie und zu welchem Zeitpunkt soll der Behandlungserfolg für welche Indikation und für welchen Schweregrad der Erkrankung möglichst objektiv definiert werden? Der als klinischer Endpunkt operationalisierte Erfolg muss in der Praxis einfach, gut und aussagekräftig messbar, der Aufwand zum Nachweis von Erfolg oder Misserfolg kalkulierbar sein. Die obligatorische Generierung von Behandlungsdaten wäre prinzipiell zu begrüßen (Telgheder 2020), jedoch sind damit auch der Zugang zu den und die Verwendung der entscheidungsrelevanten Patientendaten zu klären (von Thiessen 2015). Auch muss festgelegt sein, zu welchen Rückzahlungen ein entsprechender Misserfolg oder gar eine unerwünschte Wirkung des Arzneimittels führt. Damit sind dann auch ethische Fragestellungen verbunden, inwieweit Patientinnen und Patienten mit einer Auseinandersetzung um die Kosten misslungener Therapien tatsächlich belastet werden sollten. Zudem zeigt sich, dass es sich bei den Arzneimittelverträgen bei genauer Betrachtung meist eher um Non-pay-for-non-performance handelt, da nach obligatorischer voller Kostenübernahme erst bei Misserfolgen (Teil-)Rückzahlungen des zuvor voll gezahlten Betrags vereinbart werden (Hecken 2019).

Dass die pharmazeutischen Unternehmen diese Vertragsarten forcieren, überrascht nicht, da sie ihnen eine Reihe von Vorteilen bringen. Zunächst werden sowohl (zunächst) hohe Umsätze als auch Evidenz durch die begleitende Datenerhebung generiert (Hebborn 2019). Angesichts des hohen Einstandspreises, der im Falle Zolgensma jenseits der Millionengrenze liegt, kann vermutet werden, dass das Risiko des Scheiterns zu einem gewissen Grad bereits eingepreist ist. Die unklare Höhe der Rückerstattung bei Nicht-oder Teilerfolg führt zudem zu intransparenten Arzneimittelkosten, die die Transparenzbestrebungen des AMNOG unterwandern. Mit Blick auf die Patientinnen und Patienten bleibt in der jetzigen Situation noch unbeantwortet, ob die Anwendung eines neuen Arzneimittels unter den Bedingungen eines solchen Vertrags unkritischer

erfolgt. Dies wäre jedoch bei einer wirkstoffbezogen unsicheren Evidenzlage vor dem Hintergrund der Patientensicherheit als kritisch zu bewerten.

Folglich ist es nicht verwunderlich, dass das BMG zu dem Schluss kommt, dass Pay-for-Performance-Verträge erst dann gewählt werden sollten, „wenn die Möglichkeiten der vorhandenen anderen Steuerungsinstrumente ausgeschöpft sind und zweifelsfrei die Wirksamkeit von Pay-for-Performance-Projekten nachgewiesen wurde“ (Bundesministerium für Gesundheit 2012). Diese bereits vor Jahren aufgestellte Bedingung ist bislang nicht erfüllt, ob dieser Nachweis je gelingt, bleibt abzuwarten.

Vor dem Hintergrund des Erfolgs der Rabattverträge werden im Folgenden Aussagen, die von Kritikerinnen und Kritikern den Rabattverträgen entgegengehalten werden, einer Analyse unterzogen.

5.2 Wie wirken sich Rabattverträge auf die Anbietervielfalt aus?

Der Wettbewerb der Generikahersteller im Markt der GKV hat sich mit Etablierung der Rabattverträge ab dem Jahr 2007 wesentlich verstärkt. Ob diese Entwicklung, die durch sinkende Preise im Generikamarkt gekennzeichnet ist, auch mit einer Veränderung in der Anbieterstruktur einhergeht, wird im Folgenden thematisiert. Ein stärkerer Preisdruck kann zu einer stärkeren Konzentration der Absätze auf wenige Unternehmen führen, aus der sich möglicherweise eine Marktmacht oder auch eine Marktbereinigung ergibt. Mit einer größeren Zahl an im Wettbewerb stehenden Herstellern sinkt üblicherweise der Preis. Je größer das Marktvolumen ist, desto besser können die Hersteller ihre Fixkosten aufgrund der höheren Mengen verteilen.

Die Betrachtung der Umsatzkonzentration kann auf mehreren Ebenen erfolgen, beispielsweise für alle Arzneimittel, generikafähige Arzneimittel oder Arzneimittel einzelner Wirkstoffe. Im generikafähigen Markt kann davon ausgegangen werden, dass Generikaanbieter die Möglichkeit haben, sich mit entsprechenden Investitionen als Anbieter eines jeglichen Arzneimittels im patentfreien Markt zu betätigen. Die pharmazeutischen Unternehmer sind grundsätzlich in der Wahl der angebotenen Wirkstoffe frei und können ihr Wirkstoffportfolio flexibel und kurzfristig ändern. Die benötigten Grundstoffe und in vielen Fällen auch die einzelnen Schritte der Produktion bis hin zum fertigen Arzneimittel werden häufig von Lohnherstellern übernommen und auf dem Weltmarkt eingekauft (vgl. Kapitel 6). Die notwendigen Investitionen sind dabei – vor allem im Vergleich zur Entwicklung innovativer Arzneimittel – relativ gering: Die Entwicklung eines Generikums erfordert mit 5 Mio. € bei zwei Jahren Entwicklungszeit nur geringe finanzielle und zeitliche Aufwände (Bretthauer 2014). Generika-Anbieter können daher mit vergleichsweise wenig Aufwand flexibel ihr Marktsortiment verändern und nutzen dies rege: Eine Untersuchung der Wirkstoffsortimente der einzelnen ca. 200 marktrelevanten Anbieter im generikafähigen Markt in den Jahren 2012 und 2013 zeigte, dass im Durchschnitt jeweils über 20 % der Wirkstoffsortimente innerhalb dieser Zeit verändert wurden (Schröder et al. 2014). Dies macht deutlich, dass es sich hierbei um einen hoch-dynamischen Markt handelt, was dafürspricht, die Konzentration wirkstoffübergreifend zu messen. Im Folgenden wird daher die Umsatzkonzentration für den Gesamtmarkt und für den gesamten generikafähigen Markt betrachtet.

Zur Beurteilung der Stärke der Anbieterkonzentration in Märkten wird der Herfindahl-Hirschmann-Index (HHI) verwendet, der unter anderem vom Statistischen Bundesamt und der Europäischen Kommission zur Beobachtung der Marktkonzentration herangezogen wird. Gemäß der Europäischen Kommission kennzeichnet ein Wert unterhalb von 1.000 eine niedrige Marktkonzentration, ein Wert bis 1.800 eine mittlere Konzentration und Werte oberhalb 1.800 kennzeichnen eine starke Marktkonzentration. Hier wird die Umsatzkonzentration im Jahr 2006, also vor Einführung der Rabattverträge, der Umsatzkonzentration im Markt im Jahr 2019 gegenübergestellt.

Im Ergebnis ist die Marktkonzentration, die bereits 2006 mit einem Wert von 478 insgesamt niedrig war, 2018 noch weiter auf 277 gesunken (Abbildung 5-1). Im Generikamarkt ist die Umsatzkonzentration ein wenig höher als im Gesamtmarkt. Dies spiegelt wider, dass patentgeschützte Arzneimittel von vielen verschiedenen und nicht nur von einigen wenigen Anbietern entwickelt werden. Betrachtet man den Indexwert des Jahres 2019 für den generikafähigen Markt (277) und vergleicht ihn mit dem Ergebnis für den generikafähigen Rabattvertragsmarkt (297), so sind diese sehr ähnlich. Diese Märkte sind nicht vollständig deckungsgleich, da es auch generikafähige Wirkstoffe gibt, die GKV-weit nicht in Rabattverträgen ausgeschrieben werden. Doch nicht nur an den eher abstrakten Werten des HHI lässt sich ein Rückgang der Anbieterkonzentration ablesen. Auch der Umsatzanteil, der sich auf die zehn oder 20 umsatzstärksten Anbieter konzentriert ist seit 2006 kontinuierlich zurückgegangen. Im Generikamarkt vereinen beispielsweise die zehn stärksten Anbieter nur noch 45 % der Umsätze auf sich, während es 2006 noch 53 % waren (Abbildung 5-1).

Für diese abnehmende Konzentration gibt es mehrere Gründe. So handelt es sich beispielsweise bei den elf AOK-Rabattpartnern der ersten AOK-Rabattwelle 2007 primär um Marktbeteiligte, die bis dahin keine größere Marktbedeutung hatten. Trotzdem kam es in den Jahren 2007 und 2008 zu höheren Werten bei der Branchenkonzentration. Eine Ursache hierfür mag darin liegen, dass zu Beginn die meisten anderen Krankenkassen eher auf Portfolioverträge mit großen Herstellern setzten. Mit den Änderungen der gesetzlichen Rahmenbedingungen 2009 wurden wirkstoffbezogene Ausschreibungen zum Regelfall (s. o.). Mit der Anwendung des Vergaberechts müssen die Ausschreibungen auch beispielsweise durch Losteilungen mittelständischen Unternehmen zugänglich sein. Es zeigt sich, dass in der Folge auch kleinere Anbieter häufiger Zuschläge erhielten, wodurch die Unternehmenskonzentration insgesamt sank.

Tabelle 5-1: Ausgewählte Kennwerte der Bruttoumsatzverteilung nach pharmazeutischen Anbietern in den Jahren 2006 und 2019

	2006	2019
Gesamtmarkt		
Bruttoumsatzanteil der 10 umsatzstärksten Hersteller	44 %	35 %
Bruttoumsatzanteil der 20 umsatzstärksten Hersteller	63 %	55 %
Herfindahl-Hirschman-Index ¹	276	215
Generikamarkt		
Bruttoumsatzanteil der 10 umsatzstärksten Hersteller	53 %	43 %
Bruttoumsatzanteil der 20 umsatzstärksten Hersteller	69 %	62 %
Herfindahl-Hirschman-Index	478	275
Rabattvertragsmarkt (generikafähig)		
Bruttoumsatzanteil der 10 umsatzstärksten Hersteller		45 %
Bruttoumsatzanteil der 20 umsatzstärksten Hersteller		64 %
Herfindahl-Hirschman-Index (HHI)		296

* Der Herfindahl-Hirschman-Index ist die Summe der quadrierten Anteilswerte und kann Werte von 1 bis 10.000 annehmen, wobei der minimale Wert bei Gleichverteilung des Absatzes über alle Anbieter (= minimale Konzentration), der maximale Wert hingegen bei maximaler Konzentration (also wenn der gesamte Absatz auf einen einzigen Anbieter entfällt) erreicht wird. Der ausgewiesene Rückgang beim Herfindahl-Hirschman-Index zwischen 2006 und 2019 zeigt, dass die Marktkonzentration abgenommen hat.

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Bei der Betrachtung einzelner Wirkstoffmärkte zeigt sich, dass es in den letzten Jahren vereinzelt auch zu einer stärkeren Umsatzkonzentration kam (Bauer et al. 2015, Kozińska/Hußmann 2018). Dabei ist die Wirkung von Rabattverträgen in Deutschland auf die Konzentrationsentwicklung nicht so eindeutig wie es scheint, da es sich bei den beteiligten Firmen in der Regel um international tätige Unternehmen handelt. Ein Anstieg der Anbieterkonzentration in Deutschland bei einzelnen Wirkstoffen muss nicht zwingend mit der Steigerung von Marktmacht insgesamt einhergehen. Dies gilt insbesondere, wenn ein Eintritt bzw. Wiedereintritt in Wirkstoffmärkte möglich ist und die Kosten für den Markteintritt infolge der Einführung gemeinsamer europäischer Zulassungsstandards gesunken sind, wie es im Generikamarkt der Fall ist.

Durch die heute üblichen transparenten, europaweiten Ausschreibungen haben auch kleinere und unbekanntere Hersteller eine bessere Möglichkeit, an den Ausschreibungen teilzunehmen. Da das Markenimage eines Anbieters für die Auswahl des Präparats keine Rolle mehr spielt, ermöglichen die Rabattvertragsausschreibungen diesen Herstellern größere Chancen, in den deutschen Markt einzutreten. Zudem wurde mit der Reform der EU-weiten Vergabe von Aufträgen 2016 der Zugang zu öffentlichen Ausschreibungen besonders für kleine und mittlere Unternehmen erleichtert (SIGMA 2016).

Dabei gibt das Vergaberecht vor, dass jeder relevante Wirkstoff heute von den 109 einzelnen Krankenkassen getrennt beziehungsweise in kleineren Verbünden oder unter Einschränkung auf Regionallose ausgeschrieben wird. Jede Kasse bzw. jeder Verbund handelt mit dem Start der Vertragslaufzeit voneinander unabhängig. Aus Anbietersicht ergeben sich also für jeden einzelnen Wirkstoff laufend neue Möglichkeiten zur Teilnahme an einer Ausschreibung. Durch die gesetzliche Befristung der Laufzeit von Rabattverträgen auf höchstens zwei Jahre ist zudem gewährleistet, dass die Krankenkassen einen Wirkstoff nur für eine begrenzte Dauer vergeben. Durch die Neuausschreibung kann es stets Wechsel zwischen Herstellern geben. Dies lässt sich für eine Reihe von Wirkstoffen wie Metoprolol, Omeprazol oder Simvastatin immer wieder beobachten (Bauer et al. 2015). Auch wenn Wechsel in manchen Märkten weniger häufig auftreten, so ist die Marktmacht der bestehenden Anbieter durch die Möglichkeit eines Wiedereintritts der Wettbewerbenden restringiert. Ein Rückzug der potenziellen Anbieter vom europäischen Markt ist nicht plausibel.

Eine Gefahr für den Wettbewerb kann hingegen durch die zunehmende Verflechtung von Generikaanbietern untereinander und insbesondere mit Originalanbietern bestehen: Eine Untersuchung im amerikanischen Markt zeigt, dass die Wahrscheinlichkeit, ein Nachahmerpräparat auf den Markt zu bringen, geringer ist, wenn ein Generikahersteller und der Hersteller des Originalpräparats finanziell verflochten sind. Der dadurch verringerte Wettbewerb kann letztlich auch zu höheren Preisen bzw. geringeren Rabatten der anderen Anbieter führen (Newham et al. 2018).

5.3 Wie beeinflussen Rabattverträge die Versorgung der Versicherten?

Als Maß für die Versorgungsqualität der Patientinnen und Patienten lässt sich die Häufigkeit von Anbieterwechseln für die Arzneimittelpatientinnen und -patienten unter Dauertherapie heranziehen, da diese sich dann seltener an ein neues Erscheinungsbild der Verpackung oder der einzunehmenden Arzneimittel gewöhnen müssen. Zwar haben zahlreiche Untersuchungen beispielsweise des Zentrallaboratoriums der Apotheker belegt, dass die pharmazeutische Qualität sich zwischen den Produkten der Anbieter kaum unterscheidet und in jedem Fall den geforderten Spezifikationen entspricht (beispielsweise Abdel-Tawab et al. 2014a, Abdel-Tawab et al. 2014b), jedoch ist ebenso bekannt, dass psychologische Effekte einer kontinuierlich gleichen Versorgung zu einer besseren Therapieadhärenz der Patientinnen und Patienten beitragen (Esberger-Chowdhury 2015, AOK Bundesverband 2017) und damit die Qualität der Versorgung erhöhen.

Die Analyse von 44,2 Mio. wirkstoffbezogenen Patientenprofilen der AOK zeigt, dass im Jahr 2018 unter den Bedingungen der Rabattverträge deutlich weniger Medikamentenwechsel stattfanden als noch 2006 ohne den Einfluss von Rabattverträgen. Untersucht wurden 208 dauerhaft generikafähige Wirkstoffe, die 2018 unter Rabattvertrag standen und bereits 2006 generikafähig waren. Während im Jahr 2006 lediglich 73,4 % der Patientinnen und Patienten während des gesamten Jahres das gleiche Arzneimittel des jeweiligen Wirkstoffs innerhalb des Betrachtungsjahres erhalten hatten, lag dieser Anteil im Jahr 2018 mit 79,1 % deutlich höher (Abbildung 5-3). Nur 2 % der Patientinnen und Patienten erhielten 2018 ihr Arzneimittel von drei oder mehr Anbietern, 2006 waren es dagegen noch 5 %.

Bei dem nach Tagesdosen GKV-weit am meisten verordneten Wirkstoff Ramipril, für den allein zwei Mio. Patientenprofile der AOK-Versicherten ausgewertet werden konnten, erhielten 2006 noch über 35 % der Patientinnen und Patienten den Wirkstoff innerhalb des Jahres von mehreren Herstellern, 2018 waren es nur noch 14 %. Damit ist die Rate an unnötigen Medikamentenwechseln deutlich zurückgegangen (WIdO 2018). Die Patientinnen und Patienten werden also insgesamt unter den aktuellen Bedingungen der Rabattverträge deutlich stabiler mit Arzneimitteln versorgt. Diese Erkenntnisse bezüglich der Patientinnen und Patienten der AOK stehen damit der häufig geäußerten Kritik entgegen, dass Rabattverträge zu mehr Umstellungen führen würden (beispielsweise BAH 2010, BPI 2015).

Neben der höheren Kontinuität der Versorgung mit dem Arzneimittel des gleichen Herstellers haben die Versicherten auch einen finanziellen Vorteil aus den Rabattverträgen, wenn die Krankenkassen auf die Zuzahlung für die Rabattarzneimittel verzichten und die Versicherten so unmittelbar an den Einsparungen der Verträge beteiligen (vgl. Kapitel 7). Für 21,8 % der Vertragsarzneimittel in der GKV war dies im Laufe des Jahres 2019 der Fall. Sogar für 41,9 % ihrer Rabattarzneimittel haben die AOKs auf die Zuzahlung verzichtet, womit die AOK-Versicherten im Vergleich zur regulären Zuzahlung im Jahr 2019 direkt um 96,0 Mio. €¹ entlastet wurden.

5.4 Welche Vorteile ergeben sich aus den verschiedenen Vertragsarten?

Die Frage nach den Vorteilen von Exklusiv- oder Mehrpartnerverträgen muss zunächst getrennt für die unterschiedlichen Perspektiven untersucht und beantwortet werden. Für die Krankenkassen stehen zunächst die zu erzielenden Einsparungen für die Versicherten im Vordergrund, jedoch müssen auch die Auswirkungen auf die Anbieterstruktur und damit den Wettbewerb sowie die Versorgung der Arzneimittelpatientinnen und -patienten betrachtet werden.

Die Bezifferung der Einsparungen, die sich über eine exklusive, auf mehrere Anbieter bezogene oder völlig offene Vergabe für eine Krankenkasse ergeben, ist nur im Rahmen von Abschätzungen möglich. Die Verträge und insbesondere die produktbezogenen Rabatte sind vertraulich und somit nicht miteinander vergleichbar. Die Höhe der Rabatte hängt neben der Art der Ausschreibung auch von vielen weiteren Faktoren wie der Anzahl der zu versorgenden Arzneimittelpatientinnen und -patienten, der Zahl der Anbieter im Markt oder dem Umsatzvolumen ab. Grundsätzlich kann davon ausgegangen werden, dass durch die höhere Absatzmenge für einen pharmazeutischen Hersteller im Falle eines Exklusivvertrages gegenüber einem Vertrag im Rahmen des Mehrpartnernetzmodells die erzielbare Rabatthöhe und damit die Kostenersparnis für die Krankenkasse höher ausfallen können. Der Hersteller kann sich sicherer sein, einen geplanten bzw. hohen Marktanteil zu erreichen, wenn er allein den Zuschlag erhält und entsprechend günstigere Konditionen anbietet. Dass der zu erzielende Marktanteil bei einer Vergabe im Dreipartnermodell für einen Anbieter nur schwer vorherzusehen ist, zeigt die Analyse der Verteilung der Herstelleranteile bei den Dreipartnerverträgen der AOK: Anders als man vielleicht vermuten würde, verteilen sich die Verordnungsanteile

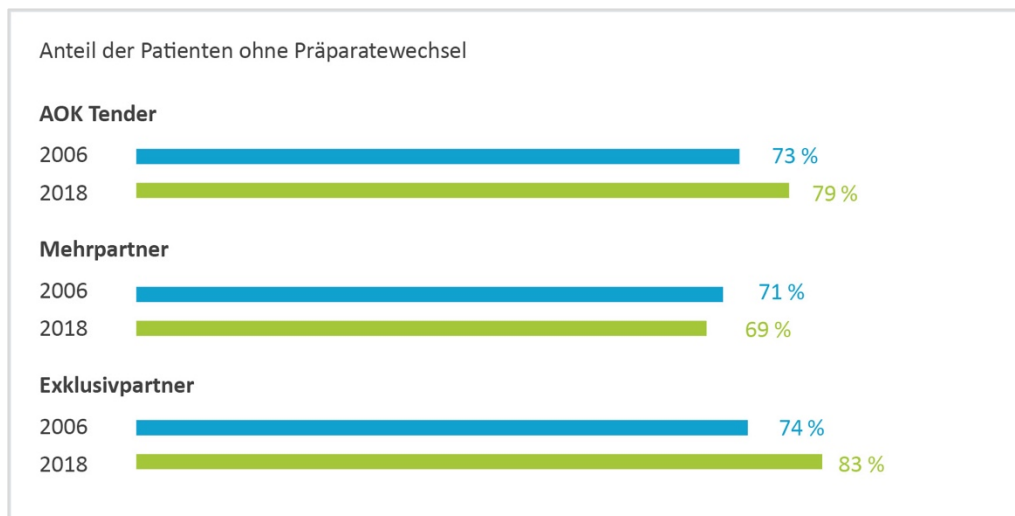
¹ In dieser Berechnung sind bereits die Verordnungen an Versicherte, die wegen individueller wirtschaftlicher Gründe von der Zuzahlung befreit sind, berücksichtigt. Ohne deren Einberechnung liegt das Potenzial der verzichteten Zuzahlungen sogar bei 140,7 Mio. € im Jahr 2019.

nämlich nicht relativ gleich über alle einbezogenen Unternehmen. So entfallen im Schnitt je Wirkstoff rund 60,2 % der Verordnungen auf den verordnungstärksten Partner, 27,6 % auf den zweiten und lediglich 12,2 % auf den dritten Partner. Bei einzelnen Wirkstoffen übernahm im Jahr 2018 der verordnungstärkste Rabattpartner sogar 93,0 % der Verordnungen (z. B. Morphin), für einen anderen Rabattpartner blieb beispielsweise beim Wirkstoff Losartan nur 0,2 % der Versorgung übrig (WIdO, 2019). Die Kalkulation ist für die Anbieter bei Ausschreibung im Mehrpartnermodus deutlich erschwert. Diese Unsicherheit schlägt sich zwangsläufig in der Rabatthöhe nieder. Da in den nicht exklusiv vergebenen Verträgen das gesamte Marktvolumen zwischen den Anbietern aufgeteilt wird und diese außerdem im Vorhinein keine absolute Sicherheit über die tatsächlich zu erzielenden Marktanteile haben, liegt es nahe, dass diese Vertragstypen letztlich finanziell weniger attraktiv für die Krankenkassen sind.

Bei der ausschließlichen Nutzung von Mehrpartner- oder Open-House-Verträgen besteht die Gefahr, dass über den gesamten Markt gesehen vor allem große Anbieter größere Marktanteile erzielen könnten, da diese die Kapazitäten haben, ein breites Produktsortiment anzubieten und sich gegenüber kleineren Nischenanbietern durchzusetzen. Da die Auswahl des abgegebenen Arzneimittels in der Apotheke erfolgt, ist damit zu rechnen, dass diese sich eher mit den Sortimenten der großen und bekannteren Anbieter bevorraten, mit denen dann die meisten Verträge bedient werden können. Kleinere Anbieter hätten das Nachsehen und die gewünschte Anbietervielfalt würde reduziert (Tabelle 5-1).

Wie gezeigt, können Rabattverträge durch die grundsätzliche Abgabe des Vertragsmedikaments dazu führen, dass die Patientinnen und Patienten – zumindest während der Vertragslaufzeit – stabiler mit dem immer gleichen Arzneimittelpräparat versorgt werden (Abbildung 5-3). Betrachtet man dies getrennt nach der Anzahl der Rabattpartner der verschiedenen Vertragsarten, so ergibt sich für die Arzneimittelpatientinnen und -patienten der AOK im Verordnungsjahr 2018, dass 82,7 % der Patientinnen und Patienten, die ihren rabattierten Wirkstoff von einem exklusiven Rabattpartner über einen längeren Zeitraum einnahmen, ihr Medikament dauerhaft von demselben Hersteller erhielten. Vor Einführung der Rabattverträge 2006 lag der Vergleichswert bei diesen Wirkstoffen noch bei 73,6 %. Bei den Wirkstoffen, bei denen sich 2018 zwei und mehr Rabattpartner die Versorgung teilten, erhielten nur 69,1 % der Arzneimittelpatientinnen und -patienten das Arzneimittel immer vom selben Hersteller. Im Umkehrschluss fand bei 30,9 % der Patientinnen und Patienten im Jahresverlauf mindestens ein Wechsel statt, kaum verändert im Vergleich mit 2006 (29,5 %). Rabattverträge mit Exklusivpartnern tragen somit dazu bei, unnötige Medikamentenwechsel zu vermeiden und leisten somit einen Beitrag zum Erfolg der Therapie (Abbildung 5-3).

Abbildung 5-3: Anteil der Patienten ohne Präparatewechsel insgesamt und nach Wirkstoffen in den verschiedenen Vertragsmodellen der AOK Gemeinschaft



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Ein weiterer Aspekt zur Bewertung von Ein- und Mehrpartnerverträgen ist die Liefersicherheit (siehe Kapitel 6). Um diese zu erhöhen, müssen die Vertragspartner der AOK einen ausreichenden Arzneimittelbestand vorhalten, sowohl während der gesamten Vertragslaufzeit als auch bereits vor Vertragsstart. Insbesondere Exklusivverträge sind hierbei im Vorteil, da pharmazeutische Unternehmen damit ihre Absatzmengen besser kalkulieren können, als wenn sie bei Mehrpartnerverträgen mit mehreren Anbietern konkurrieren müssen.

Wie oben dargestellt, erschwert die Ausschreibung in Mehrpartnermodus die Kalkulation für die Anbieter deutlich. Diese Unsicherheit kann Lieferengpässen sogar Vorschub leisten, wenn in den Apotheken einzelne der möglichen Rabattpartner bevorzugt werden und die Hersteller die dadurch höheren Verordnungsmengen nicht eingeplant haben. Auch wenn Exklusivverträge die kontinuierliche Lieferfähigkeit nicht garantieren, bieten sie auch in dieser Hinsicht sowohl Vorteile für die Anbieter als auch für die Versorgung der Patientinnen und Patienten.

Somit kann resümiert werden, dass sich durch Exklusivverträge erstens höhere Einsparungen für die Krankenkassen erreichen lassen, zweitens Exklusivverträge die Anbietervielfalt fördern und drittens auch Vorteile für die Patientinnen und Patienten in Form einer stabileren Versorgung bringen. Darüber hinaus kann auch eine höhere Liefersicherheit erreicht werden.

5.5 Sind die Rabattverträge der Krankenkassen dafür verantwortlich, dass Arzneimittel nur noch im Ausland produziert werden?

Wurden in den 1990er Jahren noch 80 % aller Wirkstoffe in Europa hergestellt, wird heute geschätzt, dass bereits 80 % der Wirkstoffe aus Indien oder China kommen und zwischenzeitlich vielfach auch die gesamte Produktion in weitere Länder ausgelagert wird (Deutsche Pharmazeutische Gesellschaft/Zentrallaboratorium Deutscher Apotheker 2011, Wallet 2017). Auch wenn diese allgemeinen Aussagen dem öffentlich wahrgenommenen Bild der globalisierten Welt entsprechen, zeigt eine aktuelle Untersuchung, dass die Abhängigkeit des deutschen Arzneimittelmarktes von China nicht annähernd so groß ist, wie gemeinhin vermutet wird.

So zeigen Braml et al. (2020) auf Basis der Handelssalden von Arzneimitteln und medizinischer Ausrüstung im Jahr 2019, dass Deutschland zunächst einmal insgesamt einen Handelsbilanzüberschuss bei diesen Produkten aufweist: Tatsächlich liegt der Wert der Importe von Arzneien und medizinischer Ausrüstung also niedriger als der Wert für Exporte. Zudem bezieht Deutschland rund 72 % seiner Arzneimittelimporte aus den Mitgliedsstaaten der EU und nur 0,8 % aus Indien und China. Insofern kann nicht davon ausgegangen werden, dass Deutschlands Arzneimittelmarkt insgesamt „am Tropf der Globalisierung“ hänge (Braml et al. 2020). Dabei ist aber zu berücksichtigen, dass bei der Analyse nicht nach Prozess- oder Produktstadium unterschieden wird.

Ob dies auch für einzelne bestimmte Wirkstoffe im Generikamarkt oder im Rabattmarkt gilt, kann hierbei nicht geklärt werden, da die Produktcodes, die für die Auswertung zentral sind, kaum weitere Differenzierung erlauben. Grundsätzlich kann aber davon ausgegangen werden, dass der Anteil der Produktion in China und Indien bei generika-fähigen Wirkstoffen erheblich höher ist als bei Patentarzneimitteln, da Originalhersteller in der Regel aus patentrechtlichen Gründen ihre Wirkstoffe selbst produzieren.

Abgesehen davon werden Rabattverträge immer wieder als die Ursache dafür angeführt, dass die Produktion gerade generikafähiger Wirkstoffe in Ländern wie China oder Indien verlagert wurde. Daraus wird dann die Forderung abgeleitet, die Rabattverträge abzuschaffen, um die Generikaproduktion im Inland zu erhalten bzw. wieder zurück zu holen (BPI 2015, Kozianka/Hußmann 2018, Sträter 2020). Wenn nun von einer Verlagerung der Produktionstätigkeit ausgegangen wird, so entsteht dies durch die Entscheidung eines international agierenden Unternehmens, das nicht nur den deutschen Absatzmarkt beliefert. Die weltweiten Arzneimittelausgaben betrugen im Jahr 2018 ca. 1,205 Billionen \$ (IQVIA 2020), der deutsche GKV-Markt hat demnach lediglich einen Anteil von ca. 3,6 % am weltweiten Arzneimittelmarkt. Angesichts dieser relativ geringen Bedeutung ist die Argumentation gegen die Rabattverträge sicher nicht haltbar.

Auch ein weniger intensiver Wettbewerb bei Abschaffung der Rabattverträge oder vergleichbarer Instrumente – stellt eine konkurrenzfähige Generikaproduktion in Deutschland keinesfalls sicher. Wenn die Produktion im Ausland in der international kalkulierenden Perspektive günstiger ist, werden die gewinnmaximierenden Unternehmen die Produktion mittelfristig immer dorthin verlagern, sofern ihnen nicht die Produktion an nationalen oder europäischen Standorten verpflichtend vorgeschrieben wird. Mit Blick auf die unternehmerische Freiheit darf die Akzeptanz einer solchen Verpflichtung jedoch bezweifelt werden.

Auch ist der strategische Wert einer Generikaproduktion im Inland, beispielsweise in Krisenzeiten, nicht erkennbar, zumindest wäre es kein ökonomisch plausibles Argument gegen Rabattverträge oder Generikawettbewerb im Allgemeinen. So birgt gerade die globalisierte Produktion ein geringeres Risiko eines kompletten Produktionsausfalls (siehe auch Kapitel 6, sowie Braml et al. 2020). Es bleibt abzuwarten, wie sich die durch die Coronavirus-Pandemie bedingten Bestrebungen nach einer nationalen Herstellung oder Bevorratung auswirken werden, zu der die EU-Kommission die Mitgliedsstaaten aufgerufen hat (Europäische Kommission 2020). Mit dem Konjunkturpaket zur Bekämpfung der Pandemiefolgen soll dieses Vorhaben auch in Deutschland umgesetzt werden (Bundesregierung 2020).

6 Sicherheit in der Arzneimittelversorgung

Zusammenhang zwischen Lieferausfällen, Lieferengpässen und Versorgungsengpässen

Im Laufe des Jahres 2019 wurden Stimmen zunehmend lauter, die eine steigende Häufigkeit von Lieferschwierigkeiten bei Arzneimitteln in Deutschland beklagten. Die daraus erwachsenden Gefahren für die Versorgungssicherheit der Patientinnen und Patienten wurden kontrovers diskutiert (Sucker-Sket 2015, WIdO 2019a, Müller 2020, Pro Generika 2020). Doch wie hängen Lieferausfälle und -engpässe zusammen und was bedeuten sie für die Versorgung der Versicherten? Wie ist ein Lieferengpass von einem Versorgungsengpass abzugrenzen?

Aufgrund der Vielzahl an weltweit vernetzten Produktionsschritten und beteiligten Akteuren kann es während des gesamten Herstellungsprozesses eines Arzneimittels zu Unterbrechungen oder Störungen kommen. So kann es Verzögerungen oder Qualitätsprobleme bei den Wirkstoffherstellern geben, die Produktionsanlagen können beeinträchtigt sein oder ganze Regionen durch außergewöhnliche Ereignisse verhindert sein zu produzieren (BAH et al. 2019). Selbst ein Druckfehler in der Packungsbeilage kann dazu führen, dass eine gesamte Produktionscharge nicht freigegeben wird oder zurückgerufen werden muss und es dadurch zu Verzögerungen oder Lieferausfällen kommt (Deutsche Apothekerzeitung 2018, Deutsche Apothekerzeitung 2020).

Zunächst soll eine begriffliche Definition vorangestellt werden. Liefersicherheit bei Arzneimitteln besteht, wenn das verordnete bzw. aufgrund vertraglicher Verpflichtungen abzugebende Arzneimittel in der Apotheke an die Patientinnen und Patienten ausgehändigt werden kann. Lieferengpässe entstehen dann, wenn die Nachfrage nach einem bestimmten Arzneimittel das verfügbare Angebot, das möglicherweise durch einen Lieferausfall reduziert ist, überschreitet und letztlich den Patientinnen und Patienten dieses Arzneimittel nicht zur Verfügung gestellt werden kann (Kirchhoff 2020). Sofern die Therapie mit einem vergleichbaren Medikament fortgeführt werden kann, ergibt sich aus dem Lieferengpass erst einmal kein Versorgungsengpass. Die Versorgung ist dann nicht gefährdet und es besteht weiterhin Versorgungssicherheit, da Arzneimittel den Patienten in der Apotheke zur Verfügung stehen. Erst wenn auch kein vergleichbares Arzneimittel eines anderen Herstellers abgegeben werden kann, spricht man von einem Versorgungsengpass (Kirchhoff 2020). In diesen Fällen sind Ärztinnen und Ärzte und Apotheken gefragt, eine ggf. wirkstoffübergreifende therapeutische Alternative zu suchen.

In vielen Fällen kann ein Engpass mit einer ausreichenden und vorausschauenden Lagerplanung vermieden werden. Zudem gibt es für generische Wirkstoffe in der Regel mehrere Hersteller, die nach Wirkstoff, Darreichungsform, Stärke und Packungsgröße gleiche Arzneimittel im Markt anbieten. Hier kann meist problemlos ein Wechsel von einem Produkt auf das andere stattfinden, sodass die Patientinnen und Patienten in der Apotheke durch einen Ausfall in der Regel keine Nachteile erfahren.

Kritisch kann es jedoch werden, wenn flächendeckend ein Wirkstoff nicht mehr zur Verfügung steht, weil dieser beispielsweise nur von einem Produzenten hergestellt wird, wie es in der Patentsituation meist der Fall ist. Dann kann aus einem Lieferausfall tatsächlich ein Versorgungsengpass entstehen, der meist nur durch eine individuelle Therapieumstellung der Patientinnen und Patienten auf einen anderen Wirkstoff kompensiert werden kann und mit entsprechenden Aufwänden verbunden ist.

6.1 Wie ausgeprägt sind Lieferengpässe in Deutschland?

Um diese Frage zu beantworten, werden verschiedene Ansätze verfolgt, in denen unterschiedliche Datenquellen verwendet werden.

So kann man zum einen das zentrale Register „Lieferengpässe für Humanarzneimittel in Deutschland“, das beim BfArM geführt wird, für Analysen heranziehen. Hier können pharmazeutische Hersteller auf freiwilliger Basis ihre Lieferausfälle mit Angabe der Dauer des Engpasses eintragen. Dabei wird ein Lieferengpass als eine „über voraussichtlich zwei Wochen hinausgehende Unterbrechung einer Auslieferung im üblichen Umfang oder eine deutlich vermehrte Nachfrage, der nicht angemessen nachgekommen werden kann“ (BfArM), definiert. Auf Basis dieser Liste zeigt sich in Deutschland eine hohe Lieferfähigkeit: Von den im September 2019 am Markt befindlichen und zu Lasten der GKV verordneten über 66.000 Arzneimitteln waren lediglich 461 Arzneimittel als vorübergehend nicht verfügbar gelistet. Das entspricht einer Liefersicherheit von 99,3 % (WIdO 2019a).

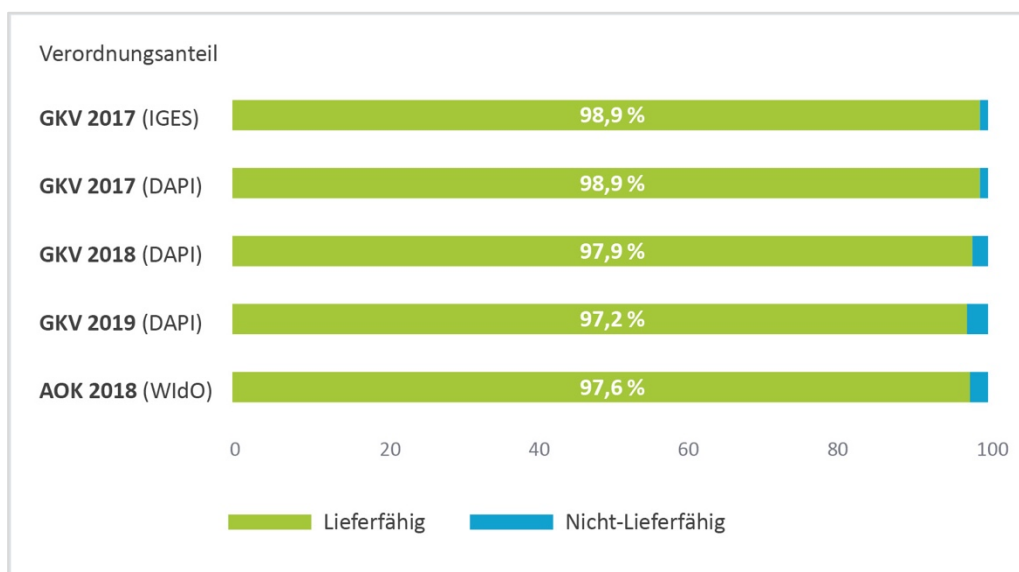
Ein aktuelles Gutachten für den GKV-SV vergleicht die Lieferunfähigkeitssituation in Deutschland mit der in Finnland, Schweden, Italien und den Niederlanden auf Basis von Melderegisterdaten der jeweiligen Länder. Es zeigt sich, dass Lieferunfähigkeitsmeldungen in allen Ländern zunehmen, jedoch in unterschiedlichen Ausprägungen (Vogler/Fischer 2020). Im Vergleich zu den Angaben des BfArM-Registers (zum Untersuchungszeitpunkt 320 Meldungen) lag der Wert in Finnland für das gesamte Jahr 2019 mit ca. 1.700 Meldungen deutlich höher, im Nachbarland Schweden für den gleichen Zeitraum mit 678 immer noch mehr als doppelt so hoch. Die Autorinnen verdeutlichen, dass die Ergebnisse in einem solchen Ansatz auch durch Unterschiede in der Meldemoral oder in der Sanktionierungsmöglichkeit bei Nichtmeldungen (diese existiert beispielsweise in Finnland) getrieben sein können. Grundsätzlich weisen sie auf das Problem der Untererfassung hin, das bei der Nutzung von Melderegisterdaten existiert (Vogler/Fischer 2020).

Zum anderen besteht die Möglichkeit, Routinedaten der gesetzlichen Krankenkassen auszuwerten. Diese Abrechnungsdaten beinhalten eine Kennzeichnung für ein ersatzweise in der Apotheke abgegebenes Arzneimittel, wenn das verordnete aufgrund einer aktuellen Lieferunfähigkeit nicht verfügbar war. Mit dieser Kennzeichnung stellt sich die Apotheke frei von Ersatzansprüchen, die aufgrund von Lieferverpflichtungen aus Festbetragsregelungen oder Rabattverträgen bestehen. Die Auswertung dieses Nichtverfügbarkeitskennzeichens weist den Vorteil einer verordnungsgewichteten Quantifizierung der Nicht-Lieferbarkeit (und Alternativversorgung) auf, die die Versorgungsrealität mit festbetragsgebundenen und rabattierten Arzneimitteln in Deutschland besser widerspiegelt.

Auch dieser Ansatz ließ für die Jahre 2017 und 2018 keine ungewöhnlich hohen Ausfälle erkennen. Wie gleich mehrere Auswertungen des Deutschen Arzneiprüfungsinstituts (DAPI), des IGES Instituts und des WIdO zeigen, lag die Liefersicherheit im Gesamtmarkt in den Jahren 2017 und 2018 bei ca. 99 % (WIdO 2019a). Da die Nichtverfügbarkeitskennzeichnung insbesondere im Rabattvertragsmarkt eingesetzt wird, ist es sinnvoll den Anteil auf dieses Segment zu beziehen. So zeigt das DAPI für das Rabattvertragssegment, dass es 2018 zwar einen Zuwachs gegenüber 2017 gab, die Liefersicherheit aber mit 98,9 % 2017 und 97,9 % 2018 hoch lag (ABDA 2019). Das IGES Institut hat mit 98,9 % Liefersicherheit für 2017 einen vergleichbaren Wert ermittelt (Höer/Maag 2019). Das WIdO bestätigt diesen Eindruck ebenfalls mit einem Verfügbarkeitsanteil

von 97,6 % für das Jahr 2018 (WIdO 2019a). Eine neuere Auswertung des DAPI zeigt, dass sich die Nichtverfügbarkeitsproblematik 2019 verschärft hat und auf einen Anteil von 2,8 % angewachsen ist (Gradl 2020). Getrieben wurde dies vor allen Dingen durch die Wirkstoffgruppe der Sartane, die 2019 von massiven Lieferausfällen durch den Valsartan-Skandal (siehe unten) betroffen waren. Rund 34 % der Valsartan-Verordnungen weisen ein Nicht-Verfügbarkeitskennzeichen auf. Trotzdem sind laut DAPI 2019 rund 97,2 % der Arzneimittelverordnungen im rabattfähigen Markt verfügbar gewesen (Abbildung 6-1).

Abbildung 6-1: Liefersicherheit im Rabattvertragsmarkt in den angegebenen Jahren für verschiedene Studien



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Die auf Basis der Abrechnungsdaten ermittelten Nichtverfügbarkeitskennziffern allein zeigen aber auch kein abschließendes Bild der Versorgungssituation in Deutschland. So kann man mit den Abrechnungsdaten der in Apotheken abgegebenen Arzneimittelrezepte zwar ermitteln, welche Arzneimittel in welchen Zeiträumen abgegeben wurden. Verordnungen, die nicht beliefert werden konnten, tauchen aber in den Abrechnungsdaten nachvollziehbarerweise nicht auf. Folglich bilden diese Daten nur die Situation ab, in der eine entsprechende Ersatzbelieferung erfolgt ist und Patientinnen und Patienten also alternativ versorgt wurden. Nicht erkannt werden dadurch jedoch die Fälle, in denen in Absprache mit der verordnenden Ärztin oder dem verordnenden Arzt die Therapie umgestellt wurde auf Arzneimittel mit anderen Wirkstoffen, die dann regulär beliefert werden konnten. Dies könnte nur mit patientenbezogenen Analysen untersucht werden, wobei auch dann mit Hilfe dieser Ergebnisse nicht abschließend geklärt werden kann, ob eine Umstellung aus therapeutischen Gründen oder wegen Versorgungsproblemen erfolgte. Für die genannten Konstellationen gilt jedoch, dass es sich dabei nicht um Versorgungsengpässe handelt, da die Patientinnen und Patienten mit einem vergleichbaren Arzneimittel versorgt wurden. Die Fälle, bei denen Personen gar kein Arzneimittel erhalten, da es keine adäquate Alternative zum nichtverfügbaren Arzneimittel gibt, werden nicht dokumentiert. So können mit Routinedaten lediglich Anhaltspunkte für bestimmte Lieferengpässe gefunden werden, Versorgungsengpässe jedoch sind nicht detektierbar. Eine Versachlichung der Diskussion kann nur erreicht

werden, wenn die pharmazeutischen Hersteller in Deutschland verpflichtet werden, alle Lieferschwierigkeiten ihrer Arzneimittel unmittelbar zu melden. Ein solches Meldesystem wird beispielsweise bereits in Schweden und Finnland erfolgreich eingesetzt (WiDO 2019a). Wenn mit einem solchen verpflichtenden System auch in Deutschland frühzeitig transparent wäre, dass für ein bestimmtes Arzneimittel keine ausreichende Liefersicherheit im Folgemonat gewährleistet werden kann, könnten Zulassungsbehörden, ärztliche Fachgesellschaften und andere Akteure Hinweise geben, wie weiterhin eine qualitativ hochwertige Versorgung der Patientinnen und Patienten sichergestellt werden kann.

Auf Basis beider Ansätze – Melderegister oder Routinedaten – zeigt sich die Existenz und die Zunahme von Lieferengpässen über die letzten Jahre, wobei ihre Ausprägung über den gesamten Markt in Deutschland immer noch relativ gering ist und man insgesamt von einer hohen Liefersicherheit sprechen kann. Bei einzelnen Wirkstoffen kann die Situation dagegen anders aussehen (siehe Gradl 2020).

Eingeschränkte Liefersicherheit für Valsartan

Mitte des Jahres 2018 hat die Diskussion um Versorgungssicherheit und die globalisierte Wirkstoffproduktion aus Anlass des sogenannten Valsartan-Skandals erneut Auftrieb erfahren. Was war passiert?

Der Wirkstoff Valsartan wurde seit längerem im Auftrag zahlreicher Anbieter bei einem – offenbar nur bedingt überprüften – chinesischen Lohnhersteller produziert. Nach einer Umstellung im Syntheseverfahren des Wirkstoffs wurden 2018 eher zufällig krebserzeugende Verunreinigungen in einzelnen Herstellungschargen entdeckt. In der Folge wurden diese auch bei weiteren Produzenten nachgewiesen, was zu einem nahezu kompletten Ausfall der Produktion dieses Wirkstoffs und dem Rückruf unzähliger Chargen der betroffenen Arzneimittel führte. Hiervon waren jedoch nicht nur die Produkte der im deutschen Markt aktiven Anbieter betroffen, die den Wirkstoff meist im außereuropäischen Ausland auf wenige Produktionsstandorte konzentriert herstellen ließen. Vielmehr kam es weltweit zu Lieferengpässen und Marktrückrufen, sodass nach Aussage des BfArM 50 % des Weltmarktes dieser Präparate betroffen waren (Horn 2019).

Es handelte sich hier also um ein Problem, das nicht nur im deutschen Markt auftrat. Zudem ist fraglich, ob es bei einer ausschließlich europäischen Wirkstoff- und Arzneimittelproduktion zu einer anderen Situation gekommen wäre. So garantiert eine europäische Wirkstoffproduktion allein keine Freiheit von problematischen Verunreinigungen. Die Arzneimittelqualität müssen die Hersteller für die von ihnen angebotenen Arzneimittel über die gesamte Produktionskette sicherstellen und für ihre Produkte umfänglich haften. Die aktuellen Prüfvorschriften scheinen jedoch nicht immer auszureichen, um die Produktqualität zu gewährleisten. Denn nach Entdeckung der Valsartan-Verunreinigungen wurden bei anderen Sartanen und zuletzt auch bei den nicht verwandten Wirkstoffen Metformin und Ranitidin ebenfalls Verunreinigungen entdeckt (Arznei-Telegramm 2019, European Medicines Agency 2019b, Hüttemann 2019, Sörgel et al. 2019). Die EMA hat daraufhin im September 2019 für alle potentiell betroffenen Wirkstoffe ein dreijähriges Review-Verfahren mit den Herstellern begonnen, wie Nitrosamin-Verunreinigungen in Arzneimitteln zukünftig vermieden werden können (European Medicines Agency 2019a). Im April 2020 hat die EMA zudem empfohlen, die Zulassung aller Ranitidin-Arzneimittel zu widerrufen (European Medicines Agency 2020).

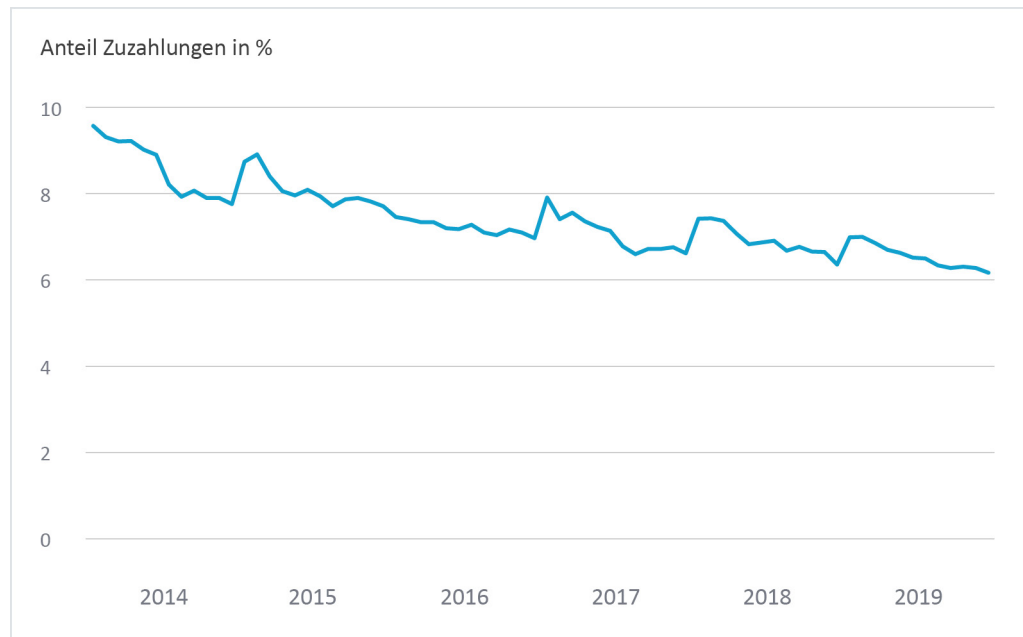
Hier könnten routinemäßig durchgeführte Qualitätskontrollen bei Arzneimitteln heute noch nicht bekannte Verunreinigungen aufdecken. Die technischen Voraussetzungen für solche Untersuchungen, mit denen auch nicht zielgerichtet auf Verunreinigungen gescreent und diese entdeckt werden können, sind vorhanden, ihr Einsatz ist aber derzeit nicht verpflichtend (Scherf-Clavel et al. 2019).

Welche Auswirkungen haben Lieferengpässe für Patientinnen und Patienten?

Sofern es mehrere pharmazeutische Unternehmen gibt, die einen generischen Wirkstoff in Arzneimitteln mit gleicher Darreichungsform, Stärke und Packungsgröße anbieten, kann meist ein problemloser Wechsel von einem Produkt auf das andere stattfinden, sodass die Patientinnen und Patienten in der Regel keine Nachteile erfahren. Im Falle einer Dauertherapie können häufige Anbieterwechsel jedoch zu einer schlechteren Therapietreue führen, da sich die Patientinnen und Patienten bei Wechsel auf ein Arzneimittel eines anderen Anbieters an ein neues Erscheinungsbild der Verpackung oder der einzunehmenden Arzneimittel oder eine unter Umständen neue Darreichungsform gewöhnen müssen (AOK Bundesverband 2017).

Ebenso kann sich eine finanzielle Belastung für die Patientin oder den Patienten dadurch ergeben, dass bei Ausfall eines besonders günstigen bzw. eines Rabattvertragsarzneimittels auf ein höherpreisiges Präparat umgestellt werden muss, was auch zu einer höheren Zuzahlung der Patientinnen und Patienten führen kann. In den letzten Jahren sind die Lieferunfähigkeitsmeldungen und die Nichtverfügbarkeitsangaben in den Verordnungen insgesamt gestiegen (Gradl 2020, Vogler/Fischer 2020). Ob durch Liefereinschränkungen die Belastung gestiegen ist, lässt sich nicht in jedem Einzelfall nachvollziehen, da bei einer eventuellen Ersatzbelieferung nicht bekannt ist, gegen welches Arzneimittel – mit gegebenenfalls geringerer Zuzahlung – substituiert wurde. Die Zuzahlungssituation kann daher nicht im Kausalzusammenhang, sondern nur global betrachtet werden. Für die AOK-Versicherten ist der Anteil der Zuzahlungen und Aufzahlungen an den Nettokosten zwischen 2014 und 2019 insgesamt gesunken: Lag der Anteil im Dezember 2014 noch bei 7,8 % waren es fünf Jahre später noch 6,2 % (Abbildung 6-2). Auch absolut sind die geleisteten Zu- und Aufzahlungen von 77,44 Mio. € auf 70,08 Mio. € gesunken. Eine Gesamtbetrachtung der Zuzahlungssituation der GKV-Versicherten findet sich im Kapitel 7. Insgesamt ist also eine geringere Belastung der AOK-versicherten Arzneimittelpatientinnen und -patienten trotz gleichzeitig steigender Lieferunfähigkeiten zu erkennen.

Abbildung 6-2: Anteil der Zuzahlungen und Mehrkosten an den gesamten Arzneimittel-Nettokosten der AOK-Versicherten in den Jahren 2014 bis 2019



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6.2 Beeinflussen Rabattverträge die Lieferfähigkeit von Arzneimitteln?

Auch wenn immer wieder argumentiert wird, dass das deutsche System der Rabattverträge die Ursache für eine Verschärfung der Lieferengpässe darstellt (BAH et al. 2019, Deutsche Apothekerzeitung 2020, Pro Generika 2020), so ist dieser Zusammenhang bei näherer Betrachtung weder einleuchtend noch belegbar.

Wie bereits in Kapitel 5 dargelegt, sind pharmazeutische Unternehmen global agierende, meist börsennotierte Unternehmen. Die weltweiten Arzneimittelausgaben betrugen im Jahr 2018 ca. 1,205 Billionen \$ (IQVIA 2020). Der deutsche Markt stellt für die Unternehmen zwar einen der relevantesten in Europa dar, global betrachtet besitzt er aber nur einen Anteil von ca. 3,6 % am weltweiten Arzneimittelmarkt. Deswegen erscheint es wenig plausibel, dass die deutschen Rabattverträge im Generikamarkt, der dann nur noch einen Umsatzanteil von 1,8 % des Weltmarktes darstellt, für weltweit auftretende Lieferengpässe verantwortlich sein könnten.

In einem Gutachten für den GKV-SV zeigen Vogler/Fischer (2020), dass es keinen Zusammenhang zwischen Lieferengpässen und Rabattverträgen und vergleichbaren Instrumenten in den betrachteten Ländern gibt. Lieferengpässe werden sowohl für Produkte mit Rabattvertrag als auch für Produkte ohne Rabattvertrag gemeldet. Betrachtet man die Arzneimittelrabattverträge der AOK, so zeigt sich, dass lediglich für rund 0,3 % der im September 2019 als lieferunfähig gemeldeten Arzneimittel zu diesem Zeitpunkt ein Rabattvertrag mit der AOK bestand.

Vielmehr argumentieren Vogler/Fischer (2020), dass Rabattverträge sogar eine Chance zur Vermeidung von Lieferengpässen darstellen, da sie eine Verpflichtung zur Lieferfähigkeit der Anbieter, eine Sanktionierung im Falle von Lieferausfällen sowie eine ausgeprägte Informationspflicht vorsehen. Auch der Sachverständigenrat Gesundheit stellt die „präventive Wirkung“ dieser Konventionalstrafen in seinem Gutachten heraus (Sachverständigenrat zur Begutachtung der Entwicklung im Gesundheitswesen 2014). Darüber hinaus müssen Rabattvertragspartner (zumindest bei den Rabattvertragsausschreibungen der AOK) einen ausreichenden Arzneimittelbestand bereits vor Vertragsstart vorhalten. Für die Anbieter ist ihre Absatzmenge besser kalkulierbar, als wenn sie bei Mehrpartnerverträgen mit mehreren Anbietern konkurrieren müssen (vgl. Kapitel 5). Insofern stellen Rabattverträge eher eine Möglichkeit dar, das Problem der Lieferengpässe zu reduzieren, als dass sie deren Ursache wären.

Zudem sind die meisten gemeldeten Lieferengpassarzneimittel als krankenhausrelevant gekennzeichnet und werden vorwiegend in der stationären Versorgung eingesetzt. Von den 461 im September 2019 gemeldeten Arzneimitteln waren 429 als krankenhausrelevant gekennzeichnet, was einem Anteil von 93,1 % entspricht. Da der Arzneimittelbedarf der Krankenhäuser von diesen selbst eingekauft wird, existieren für diesen Bereich in der Regel gar keine Rabattverträge.

Welche Maßnahmen zur Vermeidung von Lieferengpässen werden diskutiert und umgesetzt?

Um die Lieferfähigkeit von Arzneimitteln zu erhöhen, sind verschiedene Maßnahmen denkbar, die auf allen Stufen von der Produktion bis zu den Modalitäten der Abgabe an die Patientin oder den Patienten ansetzen können. Nach regen Diskussionen konnte sich die Bundesregierung Ende des Jahres 2019 auf einige gesetzliche Neuregelungen zur Minderung von Lieferengpässen einigen, die am 13. März 2020 mit dem Fairer-Kassenwettbewerb-Gesetz (FKG) verabschiedet wurden.

Um die Versorgungslage besser einschätzen zu können, wurde die Meldepflicht für drohende und bestehende Lieferengpässe zu versorgungsrelevanten Arzneimitteln für pharmazeutische Unternehmer und Arzneimittelgroßhändler gegenüber dem BfArM eingeführt. Darüber hinaus müssen pharmazeutische Unternehmer nun Daten zu den verfügbaren Lagerbeständen sowie zur Produktions- und Absatzmenge offenlegen. Auch wenn die Herstellung von Transparenz ein notwendiger Schritt zur Bewältigung und Verringerung von Lieferengpässen ist, so fehlt doch ein wirksamer Sanktionsmechanismus, der in diesem Zusammenhang bereits seit langem diskutiert wird (Sachverständigenrat zur Begutachtung der Entwicklung im Gesundheitswesen 2014, Vogler/Fischer 2020).

Zudem wird ein Beirat, bestehend aus unterschiedlichen Stakeholdern (Vertreter der Ärzte- und Apothekerschaft, der pharmazeutischen Industrie, der Patienteninteressen und der Kassen) im BfArM die Versorgungslage mit Arzneimitteln kontinuierlich beobachten, bewerten und das BMG beraten. Im Falle eines existierenden oder drohenden Lieferengpasses können dann für versorgungskritische Arzneimittel Vorgaben zur Lagerhaltung gegenüber den pharmazeutischen Unternehmen und Arzneimittelgroßhändlern durch die Bundesoberbehörde erteilt werden. Somit übernimmt die Behörde nicht nur das Monitoring, sondern kann in die Lagerhaltung der Unternehmen und Großhändler eingreifen – sofern es notwendig ist.

Dass eine Vorratshaltung von Arzneimittelreserven ein geeignetes Instrument für die Versorgungssicherheit darstellt, argumentieren Braml et al. (2020). Vogler/Fischer (2020) befürworten dies ebenfalls, allerdings weisen sie auf die hohen Kosten der Lagerhaltung von Arzneimitteln hin und empfehlen eine begründete Auswahl von Arzneimitteln. Außerdem weisen sie auf drohende Marktaustritte hin, sofern die Lagerhaltung bei pharmazeutischen Unternehmen angesiedelt sein soll (Vogler und Fischer, 2020). Insofern ist es nicht verwunderlich, dass die pharmazeutische Industrie diese Maßnahme als „Tabubruch“ kritisiert (BAH et al. 2019).

Um im Falle eines existierenden oder drohenden Lieferengpasses das Angebot an Arzneimitteln, die auf dem deutschen Markt abgegeben werden können, zu erhöhen, wurde die Pflicht zur Kennzeichnung in deutscher Sprache eingeschränkt. So dürfen im Ausnahmefall künftig auch Arzneimittel abgegeben werden, die in einer anderen Sprache gekennzeichnet sind. Um die Arzneimittelsicherheit nicht zu beeinträchtigen sind die Ausnahmen beschränkt auf versorgungsrelevante Arzneimittel, die unmittelbar von der Ärztin oder vom Arzt bei der Patientin oder dem Patienten angewendet werden. Diese regulatorische Maßnahme wird auch in anderen Ländern genutzt (Vogler/Fischer 2020).

Eine weitere Maßnahme zur Erhöhung des Angebotes an Arzneimitteln, die auf dem deutschen Markt abgegeben werden können, wurde mit der Veränderung der Abgaberegulungen im Rabattvertragmarkt geschaffen. Sollte in der Apotheke ein rabattiertes Arzneimittel nicht zur Verfügung stehen, kann zukünftig bereits früher und mit erheblich weniger Dokumentationspflichten als bisher ein alternatives Arzneimittel abgegeben werden, wobei etwaige Mehrkosten (Zuzahlungen) nicht unmittelbar von der Patientin oder dem Patienten, sondern von der Krankenkasse zu tragen sind. Von der – vor allen Dingen von den pharmazeutischen Unternehmen geforderten – Verpflichtung zur Mehrfachvergabe bei Rabattverträgen¹ oder gar einem grundsätzlichen Verzicht von Ausschreibungen (BAH et al. 2019) wurde im FKG abgesehen.

Weitere Maßnahmen, die im Gutachten für den GKV-SV (Vogler und Fischer, 2020) empfohlen werden, sind Sondergenehmigungen zum leichteren Import betroffener Arzneimittel aus dem Ausland sowie Exportverbote. Dies kann eine Möglichkeit darstellen kurzfristige Versorgungslücken zu schließen, allerdings sollten Handelsbeschränkungen aus handels- und wettbewerbspolitischer Sicht im Verbund mit den anderen EU-Staaten erfolgen (Braml et al., 2020).

In diesem Zusammenhang wird auch in der deutschen Politik immer wieder die Rückverlagerung der Medikamentenproduktion nach Europa oder Deutschland als Lösung gefordert. Braml et al. (2020) argumentieren hier aber, dass dies eine Abkehr vom Freihandelsoptimum bedeuten würde, die mit höheren Kosten einherginge. Aus ökonomischer Perspektive wäre eine Bevorratung gegenüber einer solchen Rückverlagerung der Produktion zu bevorzugen.

¹ Zur Diskussion „Exklusivvertrag versus Mehrpartnermodelle“ siehe Kapitel 5.

Zudem übernehme die internationale Arbeitsteilung im globalen Handel auch die Funktion der Produktionsausfallversicherung, wie am Beispiel der COVID-19-Pandemie deutlich wird. So konnten, während in Europa und Nordamerika erst im zweiten Quartal 2020 starke Ausbrüche und somit Produktionsausfälle stattfanden, die Kapazitäten in China wieder hochgefahren werden, wo die Produktion bereits im ersten Quartal betroffen war (Braml et al. 2020). In einem Szenario, in dem bei vorwiegend national organisierter Wirkstoffproduktion in Deutschland diese auch nur teilweise eingestellt werden müsste, wäre denkbar, dass innerhalb kürzester Zeit Abnahmeverträge oder Handelsabkommen mit Staaten mit intakter Produktion abgeschlossen werden müssten. Diese Notwendigkeit besteht in der globalisierten Produktion nicht in dem Maße, sodass eine nationale Wirkstoffproduktion nicht vor allen Ursachen von Liefer- oder Versorgungsengpässen schützt. Es bleibt abzuwarten, wie sich die COVID-19-bedingten nationalen Bestrebungen einer nationalen oder europäischen Herstellung oder ggf. erweiterten Bevorratungsverpflichtung der pharmazeutischen Hersteller auswirken werden (Bundesregierung 2020, Europäische Kommission 2020).

7 Hersteller, Distribution und Zuzahlung der Patientinnen und Patienten im Arzneimittelmarkt

Die Nettokosten im GKV-Arzneimittelmarkt des Jahres 2019 von 43,86 Mrd. € wurden für 690 Mio. verordnete Arzneimittelpackungen aufgewendet, die von rund 149.000 Vertragsärztinnen und -ärzten und 63.000 Vertragszahnärztinnen und -ärzten an die ca. 73 Mio. GKV-Versicherten verordnet und in rund 19.500 öffentlichen Apotheken zu Lasten der 109 gesetzlichen Krankenkassen abgegeben wurden. Verschiedene Auswertungen, wie sich die Arzneimittelverordnungen und die damit verbundenen Kosten für die GKV nach Fachgruppe der verordnenden Ärzte sowie nach Alter und Geschlecht der Versicherten verteilen, finden sich in den methodischen Erläuterungen des WIdO (WIdO 2020). Der Weg eines Arzneimittels vom Hersteller zur Patientin oder zum Patienten erfolgt über mehrere Distributionsstufen, die den Preis des Arzneimittels und damit die Ausgaben der GKV bestimmen. Der pharmazeutische Großhandel übernimmt als Zwischenhändler die Hauptlagerhaltung und regionale Verteilung der Arzneimittel an die Apotheken. Von letzteren erhalten die Patientinnen und Patienten die von der Ärztin oder vom Arzt verordneten Arzneimittel. Die zulässigen Aufschläge dieser Distributionsstufen auf die Abgabepreise der pharmazeutischen Unternehmen sind in der Arzneimittelpreisverordnung gesetzlich festgeschrieben und dürfen weder unter- noch überschritten werden. Durch diese Aufschläge sowie die Mehrwertsteuer erhöht sich der Arzneimittelpreis gerade bei geringen Herstellerabgabepreisen anteilmäßig relativ stark. Bei dem mittleren Preis eines Arzneimittels (Medianpreis) von 46,63 € (Dezember 2019) liegt dieser Aufschlag bei rund 50 %. Zurückzuführen ist dieser hohe Anteil der Distributionskosten insbesondere auf die starke Belastung der Arzneimittelausgaben durch die Erhebung des vollen Mehrwertsteuersatzes, während in anderen europäischen Ländern ein reduzierter Steuersatz gilt oder sogar Steueranteile aus anderen Steuerquellen bezogen werden (ABDA 2020).

Die verschiedenen, teils fixierten, teils prozentualen und teils gedeckelten Aufschläge führen basierend auf dem APU zum gesetzlich festgelegten AVP, der für alle Arzneimittel maßgeblich für die Bruttoumsätze ist. Die gesetzlichen Krankenkassen erhalten von den Apotheken wie von den Herstellern gesetzlich festgelegte Abschläge, die den zu zahlenden Preis reduzieren. Unter Berücksichtigung dieser Abschläge ergeben sich als Umsatzgröße die Nettokosten. Im Rahmen der Zuzahlung ist ein Teil des Preises zudem direkt von den Patientinnen und Patienten zu zahlen, der Rest wird von der Krankenkasse der oder des Versicherten erstattet. Ausgehend von einem beispielhaften APU von 100,00 € ergibt sich ein Brutto-AVP von 137,48 €. Für eine Packung dieses Arzneimittels entstehen nach Abzug der gesetzlichen Abschläge Nettokosten in Höhe von 128,71 €, von denen nach Abzug der Zuzahlung 118,71 € von der Krankenkasse erstattet werden (Tabelle 7-1).

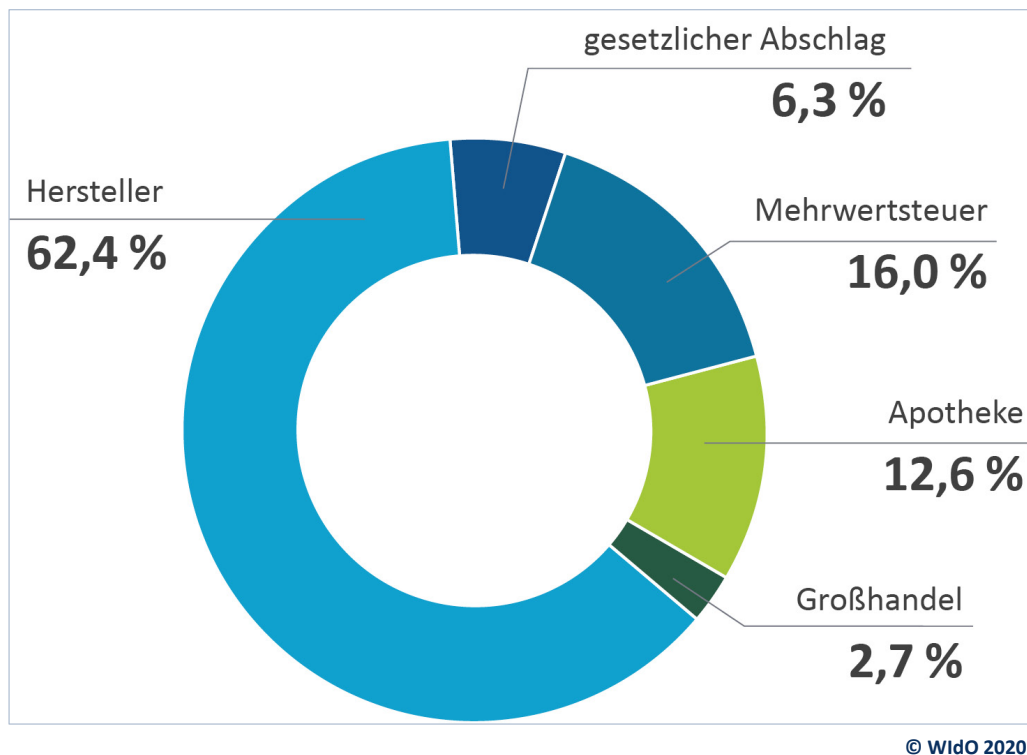
Tabelle 7-1: Beispielhafte Zusammensetzung des Apothekenverkaufspreises, der Nettokosten und Zuzahlung, Stand Dezember 2019. In Anlehnung an ABDA (2017)

APU (Herstellerabgabepreis)	100,00 €
+ Großhandelszuschlag (3,15 % (maximal: 37,80) + 0,70 €)	3,85 €
AEP (Apothekeneinkaufspreis)	103,85 €
+ Apothekenzuschlag (3 %) + 8,35 €	11,47 €
+ Notdienstzuschlag (0,21 €)	0,21 €
AVP (Netto-Apothekenverkaufspreis)	115,53 €
+ Umsatzsteuer (19 %)	21,95 €
AVP (Brutto-Apothekenverkaufspreis)	137,48 €
- Gesetzlicher Apothekenabschlag (1,77 €)	1,77 €
- Gesetzlicher Herstellerabschlag (7 % APU)	7,00 €
Nettokosten	128,71 €
- Gesetzliche Zuzahlung (10 %, min 5 €, max 10 €)	10,00 €
Effektive Ausgaben der GKV (evtl. Rabattvertrag unberücksichtigt)	118,71 €

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Ausgehend vom GKV-Fertigarzneimittelumsatz des Jahres 2019 ist der Umsatzanteil der Hersteller mit 62,4 % im Vergleich zum Vorjahr (61,8 %) leicht gestiegen, während die gesetzlichen Abschläge mit einem Anteil von 6,6 % auf 6,3 % leicht zurückgegangen sind. Bei den Herstellern sind damit insgesamt 0,6 % mehr Umsatzanteile verblieben. Auf die Distribution entfallen 15,3 %. Dabei sinkt der Umsatzanteil der Apotheken im Jahr 2019 leicht von 13,0 % auf 12,6 %. Der Rohertrag in den Apotheken (GKV-Rezeptumsatz ohne gesetzliche Abschläge und Steuern) liegt damit insgesamt bei rund 5,2 Mrd. €. Auf die Mehrwertsteuer entfallen 16,0 % des Gesamtumsatzes (Abbildung 7-1). Die Belastung der Arzneimittelausgaben durch die Mehrwertsteuer ist in Deutschland im internationalen Vergleich nach wie vor hoch. Zwar liegt in Deutschland seit 2007 das Umsatzsteuerniveau mit 19 % innerhalb der EU im Mittelfeld, aber anders als in den meisten europäischen Ländern wird in Deutschland der volle Mehrwertsteuersatz auf Arzneimittel erhoben.

Abbildung 7-1: Verteilung des Fertigarzneimittelumsatzes nach Distributionsstufen 2019



7.1 Welchen Anteil haben die Zuzahlungen, die die Arzneimittelpatientinnen und -patienten leisten?

Ein Teil des Umsatzes wird nicht von den Krankenkassen übernommen, sondern ist anteilig von den Versicherten für die für sie verordneten Arzneimittel als Zuzahlung bzw. Eigenanteil zu leisten.

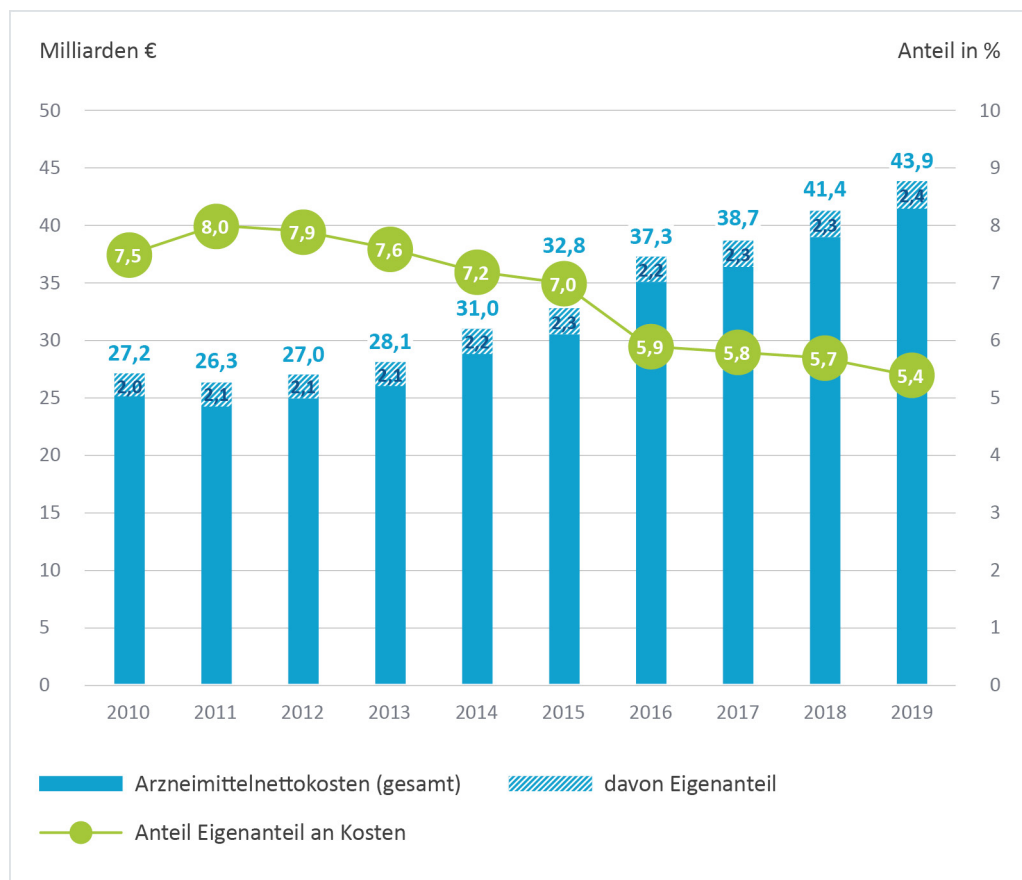
Die Zuzahlung von verschreibungspflichtigen Arzneimitteln wird in § 61-62a SGB V geregelt. So beträgt die Zuzahlung üblicherweise 10 % des Abgabepreises, mindestens aber 5 € und höchstens 10 €. Die Zuzahlung darf nicht höher als die Kosten des Mittels selbst sein. Bestimmte Personengruppen sind von der Zuzahlung ausgenommen, wie Kinder und Jugendliche unter 18 Jahren. Zudem gibt es eine jährliche Belastungsgrenze, die bei 2 % des Bruttoeinkommens liegt, bei chronisch Kranken liegt diese bei 1 %. Wenn die Belastungsgrenze durch Kosten der Zuzahlungen für Arzneimittel oder weitere Eigenanteile erreicht ist, so ist die oder der Versicherte von allen weiteren Zuzahlungen befreit (Bundesministerium für Gesundheit 2020b).

Bei Festbetragsarzneimitteln können Zuzahlungen entfallen, wenn der Hersteller das Arzneimittel zu einem Preis anbietet, der mindestens 30 % unterhalb des Festbetrags liegt. Liegt der Preis des Arzneimittels hingegen über dem Festbetrag, trägt die Patientin oder der Patient die Mehrkosten allein, solange er sich nicht für eine preisgünstigere Alternative ohne Mehrkosten oder gar eine zuzahlungsfreie entscheidet.

Ist im Rahmen eines Rabattvertrags ein Arzneimittel abzugeben, das mehrkostenpflichtig ist, so dürfen diese Mehrkosten oberhalb des Festbetrags nicht den Patientinnen und Patienten berechnet werden. Die Krankenkassen können zudem Ersparnisse durch Rabattverträge an die Versicherten weitergeben und die Zuzahlung rabattierter Produkte (Vertragsmedikament) mindern oder sogar erlassen. Entscheidet sich die Patientin oder der Patient gegen ein Vertragsmedikament und für ein teureres Wunschmedikament, wird der Listenpreis des Rabatt-begünstigten Arzneimittels maximal bis zum geltenden Festbetrag erstattet (BMG 2019).

Nicht verschreibungspflichtige Arzneimittel werden von den gesetzlichen Krankenkassen nicht erstattet. Aber auch hier gibt es Ausnahmen: Jugendliche mit Entwicklungsstörungen und Kinder unter zwölf Jahren bekommen nicht verschreibungspflichtige Arzneimittel erstattet, wenn sie ärztlich verordnet wurden. Zählen nicht verschreibungspflichtige Arzneimittel zu einer Standardtherapie bei schweren Erkrankungen und sind als Begleitmedikation zwingend erforderlich, werden diese ebenfalls erstattet. Bei der Zuzahlung gelten dieselben Regeln wie bei den verschreibungspflichtigen Arzneimitteln (Bundesministerium für Gesundheit 2020b).

Abbildung 7-2: Gesamtnettokosten und Eigenanteile (Zuzahlungen und Mehrkosten) für Arzneimittel und deren Verhältnis seit 2010




In den vergangenen Jahren ist der Anteil der Zuzahlungen an den Gesamtnettokosten deutlich gesunken. Auch wenn die absoluten Zuzahlungssummen im Zeitverlauf leicht gestiegen sind, so lag der Anteil an den Gesamtkosten mit 5,4 % 2019 deutlich unter dem Anteil 2010 mit 7,5 % (Abbildung 7-2). Zum einen wird hier deutlich, dass die Zuzahlungen der Versicherten einen nicht unerheblichen Anteil an den Gesamtkosten der GKV-Arzneimittelversorgung ausmachen. Zum anderen zeigt sich jedoch, dass der Anteil an den Ausgaben zurückgeht und die Patientinnen und Patienten relativ weniger Zuzahlung leisten.

7.2 Hersteller im deutschen Arzneimittelmarkt

Die Nettokosten im GKV-Arzneimittelmarkt in Höhe von 43,86 Mrd. € entsprechen einem Umsatz der pharmazeutischen Industrie nach Herstellerabgabepreisen ohne Mehrwertsteuer von insgesamt 31,26 Mrd. €.

Die zehn Hersteller im gesamten Arzneimittelmarkt der GKV, auf die die höchsten Nettokosten im Jahr 2019 entfielen, vereinen auf sich einen Anteil von 33,5 % des Gesamtmarkts. In Tabelle 7-2 sind die laut der Wirtschaftsprüfungsgesellschaft Ernst & Young 21 weltweit umsatzstärksten Pharmaunternehmen aufgeführt (Ernst & Young 2020). Bei diesen Unternehmen handelt es sich eher um Hersteller, die das Gros ihrer Umsätze mit Patentarzneimitteln erzielen. Wie für den Patentmarkt typisch (siehe Kapitel 2), sind die Versorgungsanteile – gemessen in Tagesdosen – bei Patentarzneimitteln sehr gering. So entstehen die Nettokosten von 2,8 Mrd. € für Arzneimittel des Herstellers Novartis im Jahr 2019 zu 86 % durch Patentarzneimittel. Allein die Arzneimittel dieses Herstellers sind damit für 6,3 % der gesamten Nettokosten im Markt verantwortlich. Die damit verordneten etwa 390 Mio. Tagesdosen hingegen entsprechen einem Versorgungsanteil von gerade einmal 0,9 % des Gesamtmarktes. Gemeinsam erreichen die Arzneimittel der drei Hersteller mit den höchsten Umsätzen im Jahr 2019 einen Nettokostenanteil von 13,9 % bei einem Versorgungsanteil in Tagesdosen von nur 1,1 %. Die Nettokosten aller 21 Unternehmen dieser Liste ergeben mit 19,93 Mrd. € einen Anteil von 45,4 % am Gesamtmarkt, nach Tagesdosen liegt der Anteil lediglich bei 11,6 %.

Tabelle 7-2: Nettokosten, verordnete Tagesdosen und umsatzstärkstes Arzneimittel im GKV-Arzneimittelmarkt 2019 sowie EBIT-Margen der 21 Top-Pharmafirmen

Rang	Hersteller*	Konzernsitz	EBIT-Margen** in %	Nettokosten in Mrd. €	Kostenanteil in %	DDD in Mrd.	Versorgungsanteil in %	Blockbuster Arzneimittel
1	Novartis		23,4	2,77	6,3	0,39	0,9	Lucentis
2	Johnson & Johnson		25,7	1,70	3,9	0,06	0,1	Zytiga
3	Roche		34,0	1,62	3,7	0,03	0,1	Avastin
4	Merck & Co.		31,0	1,52	3,5	0,30	0,7	Keytruda
5	Sanofi		7,9	1,49	3,4	1,34	3,0	Lantus
6	Bristol-Myers Squibb		27,0	1,46	3,3	0,26	0,6	Eliquis
7	Biogen		50,6	0,98	2,2	0,03	0,1	Tecfidera
8	Pfizer		25,7	0,97	2,2	0,19	0,4	Ibrance
9	Bayer		14,8	0,94	2,1	0,18	0,4	Xarelto
10	Amgen		41,6	0,84	1,9	0,06	0,1	Kanjinti
11	Eli Lilly		20,4	0,74	1,7	0,24	0,5	Trulicity
12	Astra Zeneca		12,8	0,73	1,7	0,27	0,6	Symbicort
13	AbbVie		41,2	0,72	1,6	0,01	0,0	Humira
14	Novo Nordisk		43,4	0,62	1,4	0,34	0,8	Novorapid
15	Boehringer Ingelheim		18,8	0,62	1,4	0,32	0,7	Jardiance
16	Astellas		24,2	0,48	1,1	0,07	0,2	Xtandi
17	Merck KGaA		15,7	0,43	1,0	0,62	1,4	Rebif
18	Gilead Sciences		22,7	0,42	1,0	0,01	0,0	Biktarvy
19	GlaxoSmithKline		24,6	0,41	0,9	0,29	0,7	Viani
20	Takeda		5,3	0,37	0,8	0,08	0,2	Entyvio
21	Otsuka		13,6	0,07	0,2	0,00	0,0	Abilify
Top 21				19,93	45,4	5,09	11,6	
Gesamt				43,86		43,93		

* Bei der Berechnung der Nettokosten und Verordnungen nach Tagesdosen bleiben Unternehmensverflechtungen unberücksichtigt

** EBIT-Margen gemäß Ernst & Young (2020): Die größten Pharmafirmen weltweit – Analyse der wichtigsten Finanzkennzahlen der Geschäftsjahre 2017, 2018 und 2019, https://assets.ey.com/content/dam/ey-sites/ey-com/de_de/news/2020/06/ey-studie-pharmabilanzen-top21-2020.pdf

Gewinne der Arzneimittelhersteller

Nach Gewinnrückgängen im Jahr 2018 bei mehreren großen Pharmakonzernen konnten fast alle im Jahr 2019 wieder positive Ergebnisse vermelden. Spitzenreiter ist hier die Firma AstraZeneca, die ihr EBIT¹ um 77 % auf nun 12,8 % steigern konnte. Die absolut höchsten Gewinne konnte Roche mit 19,8 Mrd. € erwirtschaften. Gesamtwirtschaftlich betrachtet werden in der Branche Pharma und Biotechnologie die mit Abstand höchsten EBIT-Margen sowohl in Europa als auch in den Vereinigten Staaten erzielt: Im Jahr 2019 lag das durchschnittliche weltweit erwirtschaftete Betriebsergebnis der umsatzstärksten 21 Unternehmen bei 24,7 % (Ernst & Young 2020). Einzelne Biotechnologieunternehmen weisen noch viel größere EBIT-Margen auf, wie Biogen mit 50,6 % und Amgen mit 41,6 %, aber auch Novo Nordisk mit 43,4 %. Im Vergleich dazu lag diese Kennzahl für das Jahr 2018 in der ebenfalls finanzkräftigen Branche der Informationstechnologie und Telekommunikation bei lediglich bei 14,0 % (Ernst & Young 2017b, Ernst & Young 2017a, Ernst & Young 2019, Ledley et al. 2020). Auch hier gibt es durchaus erfolgreiche Unternehmen mit Apple, Microsoft und Google, die aber in ihren EBIT-Margen bei weitem nicht an die der oben genannten Biotechnologieunternehmen herankommen.

Diese Beobachtung wird auch durch die Studie von Ledley et al. (2020) unterstützt, die zeigen konnten, dass die Rentabilität der großen pharmazeutischen Unternehmen in den Jahren 2000 bis 2018 signifikant höher war als von großen Unternehmen aus anderen Branchen: So lag die durchschnittliche internationale EBITDA-Marge² der untersuchten pharmazeutischen Unternehmen bei 29,4 %, während sie bei den betrachteten Großunternehmen aus anderen Branchen bei 19,0 % lag.

¹ Earnings Before Interest and Taxes; Gewinn vor Zinsen und Steuern

² Earnings Before Interest, Taxes, Depreciation and Amortization; Gewinn vor Zinsen, Steuern, Abschreibungen auf Sachanlagen und Abschreibungen auf immaterielle Vermögensgegenstände

Abkürzungsverzeichnis

AKdÄ	Arzneimittelkommission der deutschen Ärzteschaft
AMNOG	Arzneimittelmarktneuordnungsgesetz
AMVSG	Gesetz zur Stärkung der Arzneimittelversorgung in der GKV
AOK-BV	AOK-Bundesverband
APU	Abgabepreis des pharmazeutischen Unternehmens
ATMP	Arzneimittel für neuartige Therapien
AVP	Apothekenverkaufspreis
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte
BMG	Bundesministerium für Gesundheit
DAPI	Deutsches Arzneiprüfungsinstitut
DDD	Defined Daily Dose (Definierte Tagesdosis)
DOAK	Direkte orale Antikoagulantien
EBIT	Earnings Before Interest and Taxes (Gewinn vor Zinsen und Steuern)
EBITDA	Earnings Before Interest, Taxes, Depreciation and Amortization (Gewinn vor Zinsen, Steuern, Abschreibungen auf Sachanlagen und Abschreibungen auf immaterielle Vermögensgegenstände)
EMA	Europäische Arzneimittel-Agentur
EPAR	European Public Assessment Report
EU	Europäische Union
FKG	Fairer-Kassenwettbewerb-Gesetz
G-BA	Gemeinsamer Bundesausschuss
GKV	Gesetzliche Krankenversicherung
GKV-SV	GKV-Spitzenverband
GSav	Gesetz für mehr Sicherheit in der Arzneimittelversorgung
GvHD	graft-versus-host disease
HHI	Herfindahl-Hirschman-Index
KBV	Kassenärztliche Bundesvereinigung
KEP	Krankenhauseinkaufspreis
KV	Kassenärztliche Vereinigung
MCL	Mantelzell-Lymphom
PEI	Paul-Ehrlich-Institut
PPU	Preis des pharmazeutischen Unternehmers
WiDO	Wissenschaftliches Institut der AOK

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Parallelhandel mit Arzneimitteln: Kommission stellt Vertragsverletzungsverfahren und Beschwerden gegen Polen, Rumänien und die Slowakei ein

Brüssel, 17. Mai 2018

Von Beginn an hat die Kommission Juncker ihre [politischen Prioritäten](#) in den Mittelpunkt gestellt und sie energisch verfolgt. Diese Vorgehensweise spiegelt sich auch im Umgang der Kommission mit Vertragsverletzungsverfahren wider. In der Mitteilung „[EU-Recht: Bessere Ergebnisse durch bessere Anwendung](#)“ wird der Ansatz der Kommission dargelegt: Sie geht bei der Prioritätensetzung strategisch vor und wägt die jeweiligen unterschiedlichen öffentlichen und privaten Interessen sorgfältig ab.

Der Parallelimport- bzw. -export von Arzneimitteln ist eine legale Form des Handels im Binnenmarkt. Die Mitgliedstaaten können jedoch in bestimmten Fällen den Parallelhandel beschränken, um einem berechtigten öffentlichen Interesse zu entsprechen, wenn die Maßnahmen gerechtfertigt, sinnvoll und verhältnismäßig sind – beispielsweise, um eine angemessene und kontinuierliche Versorgung der Bevölkerung mit Arzneimitteln zu gewährleisten.

In den letzten Jahren ist es in einer Reihe von Mitgliedstaaten zunehmend zu Engpässen bei der angemessenen und kontinuierlichen Versorgung von Apotheken mit Humanarzneimitteln gekommen. Dies ist ein ernstes Problem, das die Behandlung von Patienten schwerwiegend beeinträchtigen kann. Der Kommission ist bewusst, dass einer der Gründe für Lieferengpässe bei einer Reihe von Humanarzneimitteln im Parallelhandel mit Arzneimitteln liegen kann.

Um den Grundsatz des freien Warenverkehrs mit dem Recht des Patienten auf Zugang zur Gesundheitsversorgung in Einklang zu bringen, muss sorgsam abgewogen werden. Nach sorgfältiger Prüfung kam die Kommission zu dem Schluss, dass es besser ist, nicht auf Vertragsverletzungsverfahren zu setzen, um dieses komplexe Problem, das sich negativ auf die Gesundheit der europäischen Bürger auswirken könnte, schnell und effizient zu lösen.

Die Kommission ist der Auffassung, dass ein strukturierter Dialog unter Einbeziehung aller relevanten Parteien rasch stattfinden sollte. Die Kommission wird die Mitgliedstaaten weiterhin in ihren Bemühungen unterstützen, sicherzustellen, dass die Bürger einen zeitnahen Zugang zu einer hochwertigen und bezahlbaren Gesundheitsvorsorge und Heilbehandlung haben. Zu diesem Zweck wird sie mehr Informationen von den Mitgliedstaaten und anderen Interessenträgern einholen, um die Umsetzung der gemeinwirtschaftlichen Verpflichtungen und Ausfuhrbeschränkungen in der Arbeitsgruppe „Arzneimittel“ (Ausschuss für Humanarzneimittel) der Kommission zu erörtern.

Hintergrund:

Der Parallelhandel ermöglicht es Großhändlern, Arzneimittel in einem Mitgliedstaat zu kaufen (in der Regel dort, wo die Preise für Arzneimittel niedriger sind) und sie in anderen Mitgliedstaaten zu verkaufen (wo die Preise höher sind). Parallelein- und -ausführen von Arzneimitteln sind mit dem freien Warenverkehr (Artikel 34 [AEUV](#)) vereinbar.

Es können jedoch ausnahmsweise Beschränkungen eingeführt werden, wenn dies durch zwingende Erfordernisse des Allgemeininteresses wie den Schutz der menschlichen Gesundheit und des Lebens gerechtfertigt ist und für die Erreichung dieses Ziels keine anderen, weniger restriktiven Mittel zur Verfügung stehen (Artikel 36 [AEUV](#)).

Die Frage der Engpässe bei Humanarzneimitteln in der EU wurde auf der informellen Tagung der Gesundheitsminister am 3. und 4. Oktober 2016 in Bratislava erörtert.

Die Kommission stellt fest, dass das Europäische Parlament am 2. März 2017 eine [EntschlieBung](#) zu den Optionen der EU, den Zugang zu Arzneimitteln zu verbessern, angenommen hat. In dieser EntschlieBung forderte das Parlament die Kommission und den Rat der EU auf, die Ursachen für Engpässe bei Arzneimitteln zu analysieren, um die Einhaltung der EU-Vorschriften über die

Verpflichtung zur Gewährleistung kontinuierlicher Lieferungen von Arzneimitteln zu überwachen (Artikel 81 der [Richtlinie 2001/83/EG](#)). Dies ist untrennbar mit der Erschwinglichkeit von Humanarzneimitteln für Patienten und der damit verbundenen Preispolitik in verschiedenen Mitgliedstaaten verbunden, einem Bereich, der in die ausschließliche Zuständigkeit der Mitgliedstaaten fällt.

Am 8. Dezember 2017 führte der Rat einen Meinungsaustausch über die Arzneimittelpolitik in der EU. Dort bekräftigte die Kommission ihre Zusage, die Mitgliedstaaten dabei zu unterstützen, das Recht der Bürger auf einen zeitnahen Zugang zu einer bezahlbaren präventiven und kurativen Gesundheitsversorgung von guter Qualität zu gewährleisten.

Weitere Informationen:

- Zu den wichtigsten Beschlüssen zu Vertragsverletzungsverfahren im Mai 2018 siehe [MEMO/18/3446](#)
- Zu Vertragsverletzungsverfahren allgemein siehe [MEMO/12/12](#)
- Zum [EU-Vertragsverletzungsverfahren](#)

IP/18/3459

Kontakt für die Medien:

[Lucia CAUDET](#) (+32 2 295 61 82)

[Maud NOYON](#) (+32 2 298 03 79)

[Victoria VON HAMMERSTEIN-GESMOLD](#) (+32 2 295 50 40)

Kontakt für die Öffentlichkeit: [Europe Direct](#) – telefonisch unter [00 800 67 89 10 11](#) oder per [E-Mail](#)

PHARMAZIE

LEHREN AUS DER SARTAN-KRISE

Warum es im Arzneimittelmarkt dringend mehr Transparenz braucht

STUTTGART - 11.09.2020, 11:45 UHR



Valsartan, Candesartan, Irbesartan, Olmesartan – es gibt zahlreiche Wirkstoffe zur Blutdrucksenkung und noch mehr entsprechende Fertigarzneimittel. Aber wie unterscheiden sich eigentlich die Wirkstoffe in den jeweiligen Präparaten? Woher beziehen die Zulassungsinhaber ihren Wirkstoff? (c / Foto: Schelbert)

Menschen interessieren sich zunehmend für Lieferketten. Sei es beim Kauf von Kleidung oder – wie zuletzt in der Coronakrise – in der Fleischindustrie. Es geht dabei um Menschenrechte und Umweltschutz, aber auch darum, selbst möglichst wenige Schadstoffe wie Antibiotika und Pestizide aufzunehmen. Doch wie ist es eigentlich um die Transparenz der Lieferketten unserer Arzneimittel bestellt? Am Beispiel der Sartan- und schließlich Nitrosamin-Krise des Sommers 2018 lässt sich praktisch nachvollziehen, warum wir im Arzneimittelmarkt dringend mehr Transparenz brauchen.

Transparente Lieferketten werden – nicht nur den Verbrauchern – vor allem in der Mode- und Lebensmittelindustrie immer wichtiger. Bei Arzneimitteln bevorzugen zwar auch viele Patienten den Originalhersteller – woher aber der Wirkstoff in einem Arzneimittel stammt, das wissen nicht nur die Kunden, sondern auch die Apotheker (meist) nicht. Daher dürften Apotheker den Vorstoß der Arzneimittelexpertin der Linksfraction im Bundestag, Sylvia Gabelmann, vom vergangenen Mittwoch begrüßen: Sie fordert ein strenges Lieferkettengesetz für Arzneimittel. Aus ihrer Sicht unternimmt die Bundesregierung zu wenig, um schwarzen Schafen in der Medikamentenproduktion Einhalt zu gebieten. Sie bezieht sich dabei auf Verstöße gegen die GMP-Vorschriften, aber auch auf den Umweltschutz und die Einhaltung von Menschenrechten.

Die Mehrheit der Apotheker wird basierend auf ihrer persönlichen Erfahrung vermutlich ein Lied davon singen können, wie intransparent es teilweise im Arzneimittelmarkt zugeht. Die zahlreichen und undurchsichtigen Lieferengpässe führen es den Apothekern immer wieder vor Augen. Wer sich außerdem an die Nitrosamin-Krise des Sommers 2018 erinnert, dem wird die Wichtigkeit von Transparenz in der Lieferkette von Arzneimitteln vor allem auf einer Ebene deutlich: Neben Umwelt und Menschenrechten tritt das eigene unmittelbare Risiko durch die Aufnahme möglicher Verunreinigungen in den Mittelpunkt. Denn woher wissen wir, wie sicher und gut unsere Arzneimittelhersteller arbeiten, wenn wir die eigentlichen Wirkstoffhersteller überhaupt nicht kennen?

Laufendes Klageverfahren gegen öffentliche Informationen über Wirkstoffhersteller

Mit dem Gesetz für mehr Sicherheit in der Arzneimittelversorgung (GSAV) ist im vergangenen Sommer eigentlich bereits eine neue Transparenzvorschrift in Kraft getreten: Der oder die Wirkstoffhersteller von Arzneimitteln sollen künftig in einer öffentlichen Datenbank zu finden sein. Was aus dieser öffentlichen Datenbank geworden ist, wollte DAZ.online schon im Januar 2020 wissen. Da war es fünf Monate her, dass das GSAV in weiten Teilen in Kraft getreten war. Das Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) erklärte damals: „Das BfArM arbeitet zusammen mit dem DIMDI intensiv an einer schnellstmöglichen technischen Umsetzung. Es ist geplant, diese zusätzlichen Informationen in den bereits vorhandenen öffentlichen Datenbanken bereitzustellen. Das heißt beim DIMDI im öffentlichen Teil der AMIS-Datenbanken und unter PharmNet.Bund.“ Nachfragen nach einem möglichen Zeithorizont blieben allerdings unbeantwortet. Auf erneute Nachfrage teilt das BfArM gegenüber DAZ.online nun mit, dass „es – bedauerlicherweise – noch keinen neuen Stand“ gibt. Die Bundesoberbehörde verweist auf ein laufendes Klageverfahren.

Mehr zum Thema



UMSETZUNG DES GSAV

Wo bleiben die öffentlichen Informationen über Wirkstoffhersteller?



PRÜFPFLICHT BIS 1. JULI 2021

Auch biologische Arzneimittel könnten Nitrosamine enthalten

Tatsächlich versuchten zwei Phyto-Hersteller beim Verwaltungsgericht Köln eine einstweilige Verfügung gegen das BfArM zu erwirken. Sie wollten der Behörde vorläufig untersagen lassen, die Namen und Adressen der Wirkstoffhersteller in verschiedenen arzneimittelrechtlichen Informationssystemen zu veröffentlichen. Sie argumentierten, dass sie durch die Veröffentlichung der Informationen in ihrer wirtschaftlichen Existenz gefährdet seien. Die fraglichen Arzneimittel seien Phytopharmaka, die nur aus spezifischen Ausgangsmaterialien und in einem spezifischen Herstellungsverfahren durch einen bestimmten Wirkstoffhersteller hergestellt werden könnten. Generika-Hersteller könnten sie bei Kenntnis des Wirkstoffherstellers leichter nachahmen. Das Gericht wies die Anträge als unbegründet ab. Das heißt allerdings nicht, dass das Verfahren beendet ist – insbesondere eine Hauptsacheklage ist noch möglich.

„Vor dem Hintergrund, dass das BfArM auf den zeitlichen Verlauf solcher gerichtlicher Verfahren keinen Einfluss hat und auch der mögliche Instanzenweg nicht vorhersehbar ist“, teilt das BfArM gegenüber DAZ.online nun mit, dass man weiterhin keine Aussage zum Zeithorizont machen könne, wann öffentliche Informationen über Wirkstoffhersteller verfügbar werden.

DAZ.online hat nun die Forderung der Linken-Abgeordneten Gabelmann nach einem Lieferkettengesetz für Arzneimittel zum Anlass genommen, nochmals einen Blick in den Abschlussbericht (23. Juni 2020) der Europäischen Arzneimittelbehörde (EMA) zur Sartan-Krise zu werfen: „Lessons learnt from presence of N-nitrosamine impurities in sartan medicines“. Was ist damals eigentlich genau passiert? Der Bericht verdeutlicht, warum mehr Transparenz im Arzneimittelmarkt so wichtig ist.

Die Sartan-Krise: Wenn keiner weiß, was der andere tut

Aus dem EMA-Dokument geht hervor, dass die Behörden international in einer ersten Reaktion auf das Bekanntwerden einer Nitrosaminverunreinigung zwischen Juni und Juli 2018 schnell reagierten – nachdem ein potenzieller Kunde des chinesischen Wirkstoffherstellers Zhejiang Huahai den Wirkstoffhersteller über eine unerwartete Verunreinigung im Wirkstoff Valsartan

informiert hatte. Ab August 2018 entwickelte sich die Situation dann allerdings schnell weiter. Es bestätigten sich nämlich der Verdacht, dass die Nitrosaminverunreinigungen sich nicht nur auf den Wirkstoff Valsartan von Zhejiang Huahai beschränken. Die EMA und die national zuständigen Behörden standen damit der Herausforderung gegenüber, schnell herauszufinden, welche Fertigarzneimittel tatsächlich betroffen sind.

Mehr zum Thema



KOMMENTIERENDE ANALYSE

Valsartan, Ranitidin, Metformin – und jetzt?

In dem Dokument heißt es, dass dabei eine Reihe von Systemmängeln angesichts „eines Vorfalles solchen Ausmaßes“ deutlich wurden:

- Erstens verfügten die **Regulierungsbehörden** nicht über geeignete Datenbanken, um die Wirkstoffhersteller mit den Endprodukten zu verknüpfen, unter Berücksichtigung von **ASMFs (Wirkstoff-Stammdokumentation)** und **CEPs (Certificate of Suitability of Monographs of the European Pharmacopoeia)**.
- Zweitens hatten auch die **Zulassungsinhaber** offenbar keine leicht zugänglichen Informationen darüber, welche Fertigarzneimittel mit den betreffenden Wirkstoffchargen hergestellt worden waren und wohin sie weiter verkauft worden waren.
- Drittens hatten wiederum die **Wirkstoffhersteller** wohl nur wenige Informationen darüber, welche Fertigarzneimittel ihre Wirkstoffe enthalten.
- Viertens wurde die Rückverfolgung der betroffenen Produkte durch das Vorhandensein von **Parallelimporten** beeinträchtigt. In manchen Fällen seien diese mit den Originalnamen gekennzeichnet worden, obwohl es sich um generische Versionen gehandelt habe. Dadurch wurde zusätzlich erschwert, schnell zu ermitteln, welche parallel importierten Produkte Valsartan von Zhejiang Huahai und anderen betroffenen Wirkstoffherstellern enthielten.
- Und als wäre all dies nicht genug, wird in dem Dokument als fünfter Mangel aufgeführt, dass auch die Nutzung von ASMFs und CEPs zusätzliche Komplexität in die Verfolgung betroffener Produkte gebracht habe. Denn häufig habe es hinsichtlich wichtiger Details wie Namen und Adressen von Firmen **Diskrepanzen zwischen den Dossiers, CEPs und ASMFs** gegeben.

Schließlich sei die Rückverfolgung der Herkunft von Wirkstoffen zwar nicht die einzige Herausforderung gewesen, die sich den Zulassungsbehörden mit zunehmendem Ausmaß des Falls präsentierte. Auch der Mangel an validierten analytischen Methoden bedeutete, dass einige Zulassungsinhaber und Hersteller nicht wussten, wie man auf Nitrosamine testet. Letztlich sei aber schon allein herausfordernd gewesen, den sich schnell entwickelnden Fall überhaupt im Blick zu behalten, da es keine zentrale Datenbank gab, um die Entwicklungen zu erfassen. Zusätzlich habe die Gefahr bestanden, dass nicht alle nationalen Behörden immer über die aktuellsten Informationen verfügten, weil das E-Mail-System die Nutzung einzelner Mail-Adressen erforderte – sodass manche vergessen werden konnten.

So komplex sich also die Nitrosamin-Krise entwickelt haben mag. Es lässt sich kaum bestreiten, dass – neben mangelndem pharmazeutischen, analytischen und chemischen Wissen – vieles hätte besser laufen können, wären die Lieferketten im Arzneimittelmarkt transparenter.

Mit mehr Transparenz könnte man in einer weiteren Krise nicht nur schneller reagieren. Wahrscheinlich wäre auch, dass mit den Lieferwegen vonseiten der Pharmaunternehmen bereits präventiv verantwortungsvoller umgegangen wird. Mit dem Gewinn an Wissen über die beteiligten Firmen ließe sich schließlich nicht nur ein mögliches Verunreinigungsrisiko besser nachverfolgen, sondern auch Umweltaspekte und Menschenrechte könnten in der Arzneimittelindustrie zunehmend berücksichtigt werden.

Mehr zum Thema

**BEIRAT ZUR BEWERTUNG DER VERSORGUNGS-LAGE**

BMG will Wirkstoff-Liste: Was soll wieder in der EU produziert werden?

**AOK BADEN-WÜRTTEMBERG**

Bauernfeind: Mechanik der Rabattverträge wirkt Engpässen entgegen

Nicht zuletzt geht das Dokument auch auf einen weiteren bereits viel diskutierten Punkt ein, der durch mehr Transparenz offengelegt werden würde: Die starke Abhängigkeit von einem einzelnen Wirkstoffhersteller (und den zugehörigen Arzneimittelherstellern und Zulassungsinhabern) – zur Sicherstellung der Qualität und Sicherheit des Wirkstoffs. Sie zeige ein Problem auf, das erkannt und angegangen werden sollte, heißt es.

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Diana Moll, Apothekerin, DAZ.online
redaktion@daz.online

[deutsche-apotheker-zeitung.de](https://www.deutsche-apotheker-zeitung.de)

Lieferengpässe: Niederländer legen „eiserne Arzneimittel-Reserve“ an

Dr. Helga Blasius (hb)

4 Minuten

Ab dem nächsten Jahr müssen Großhändler und Pharmahersteller in den Niederlanden eine „eiserne Reserve“ an Arzneimitteln aufbauen, um das Land besser gegen Lieferengpässe zu wappnen. Die Zusatzvorräte sollen den Bedarf für fünf Monate decken.

Die Briten betreiben Brexit-bedingt eine Vorratshaltung an Arzneimitteln. [Auch die Niederländer greifen jetzt zu einer solchen Maßnahme](#). Sie wollen damit unabhängiger von Versorgungsengpässen werden. Die neue „eiserne Reserve“ soll jeweils für fünf Monate reichen. Die zusätzlichen Lagerbestände sollen nicht nur für bestimmte, sondern für alle Arzneimittel angelegt werden. Die Vorratsbildung soll im nächsten Jahr beginnen und stufenweise umgesetzt werden. Das soll durchschnittlich zwei Jahre dauern. Die Maßnahme kostet nach Angaben des Gesundheitsministeriums rund 25 Millionen Euro. Sie soll 85 Prozent der vorübergehenden Verknappungen abfangen können, so die Hoffnung.

Angebot und Nachfrage besser abstimmen

Die zusätzlichen Lagerbestände werden bei Firmen und Großhändlern aufgebaut. Der niederländische Minister für die

medizinische Versorgung Bruno Bruins will dazu mit verschiedenen Parteien Vereinbarungen treffen. Sie sollen gemeinsam festlegen, mit welchen Arzneimitteln am besten begonnen werden kann. Außerdem sollen sie Vorkehrungen treffen, mit denen eine unnötige Vernichtung von Arzneimitteln verhindert werden soll. Daneben führt der Minister Gespräche mit Unternehmen, Großhändlern, Apothekern und Krankenversicherern über die Finanzierung der Lagerbestände. Neben einer intensivierten Zusammenarbeit sollen die Parteien sich auch darum bemühen, die Nachfrage nach Arzneimitteln besser vorherzusagen, um Angebot und Nachfrage optimal aufeinander abzustimmen.

Das kostet etwas, spart aber auch

Die Bevorratung koste zwar Geld, bringe aber auch Gewinn, weil Apotheker und Großhändler im Falle eines Mangels weniger Zeit für die Suche nach alternativen Arzneimitteln aufwenden müssten, gibt das Ministerium als Begründung für die Initiative an. Außerdem müsse nicht auf teurere Ersatzmedikamente ausgewichen werden. „Ich denke, dass in einem Land wie den Niederlanden, in dem die Gesundheitsversorgung einen hohen Standard aufweist, Medikamente immer verfügbar sein müssen“, stellt Minister Bruins fest. „Die Konstruktion dieser eisernen Reserve verhindert, dass Patienten mit leeren Händen an der Apothekentheke stehen. Sie reduzieren einen Großteil der Defizite. Darüber hinaus kann sich der Apotheker mehr auf die Patientenversorgung konzentrieren als auf die tägliche Suche nach anderen Arzneimitteln.“

Europäischer Ansatz muss ebenso verfolgt

werden

Neben dieser nationalen Initiative hält Bruins den europäischen Ansatz jedoch für ebenso wichtig, um die Defizite strukturell anzugehen. Europa sei zunehmend abhängig von der Tatsache, dass die Herstellung von Rohstoffen und Arzneimitteln in immer weniger Ländern außerhalb Europas stattfindet, so seine Auffassung. Er tausche sich daher mit anderen europäischen Mitgliedstaaten aus, um die Produktion nach Europa zurückzubringen.