

Addressing shortages of medicines

SUMMARY

Medicines shortages have been a growing problem in the European Union (EU) in recent years. As the coronavirus outbreak unfolds, the risk of bottlenecks in the supply of medicines to patients has become particularly high. More broadly, problems with the availability of, and access to, new medicines – most frequently associated with high-priced medicines – have also been a central topic in political debates for some time now.

The causes underlying medicines shortages are complex and multi-dimensional. The European Commission links them to manufacturing problems, industry quotas, legal parallel trade, but also to economic aspects, such as pricing (which is a competence of the Member States). The coronavirus crisis has brought to the fore the geopolitical dimension of these shortages, that is, the EU's dependency on countries beyond its boundaries, especially China and India, for the production of many active pharmaceutical ingredients and medicines.

Solutions to the problem are believed to entail collaboration and joint action, as well as the involvement of multiple stakeholders, including regulators, industry, patients, healthcare professionals, and international players. The Organisation for Economic Co-operation and Development and the World Health Organization, in particular, are conducting work to improve access to medicines. Medicines supply-chain stakeholders have all weighed in on the debate, offering explanations and recommendations for addressing the problem.

Key EU institutions, several Council presidencies and the Member States have addressed the challenge of shortages and more broadly, that of safeguarding access to medicines, through various initiatives. The European Parliament has specifically addressed the issue in a March 2017 resolution. Ensuring the availability of medicines and overcoming supply-chain problems revealed by the coronavirus crisis are also expected to be important topics in the Commission's forthcoming pharmaceutical strategy.



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Issues of medicines availability

Medicines shortages, affecting both essential life-saving and common-use medicines, have been a growing problem in the European Union (EU) in recent years. The risk of bottlenecks in the supply of medicines to patients has become particularly real amid the unfolding coronavirus pandemic. In early April 2020, for instance, the European University Hospital Alliance ([EUHA](#)) raised the alarm that, with rising demand for medicines needed in intensive care units – such as sedatives, muscle relaxants, opioids, anaesthetics and antibiotics – stocks could soon run out. At the end of March, the World Health Organization (WHO) also [cautioned](#) against using 'therapeutics that have not been demonstrated to be effective in the treatment of Covid-19', expressing concern that this could create 'shortages of those medicines to treat diseases for which they have proven effective'. One example is the politicised debate about the use of the antimalarial medicine [hydroxychloroquine](#) to treat Covid-19. This has given rise to concerns about possible shortages of this medicine, which is [vital](#) for the treatment of autoimmune diseases, such as lupus.¹

More broadly, problems with the availability of, and access to, new medicines – most frequently associated with high-priced medicines – have also been a central topic in political debates. One such example is a [novel gene therapy product](#) to treat babies and young children with spinal muscular atrophy, considered one of the most expensive medicines in the world. Its price – €1.9 million – has [drawn criticism](#) both from patients and politicians, [as has](#) the [international 'lottery'](#) launched in early 2020 by the product manufacturer to make it available for free to a lucky few. While the organisation and delivery of health services and medical care, and the pricing and reimbursement decisions that influence access to medicines, are a Member State competence, the EU can complement national action by providing support and coordination.

Causes and drivers

The causes underlying medicines shortages are complex and multi-faceted. According to the European Medicines Agency (EMA), they include manufacturing difficulties or [problems affecting the quality of medicines](#), while according to the European Commission, [they](#) include manufacturing problems, industry quotas, legal parallel trade,² and economic aspects, such as the pricing of medicines, which is a competence of the Member States.

According to a March 2020 Commission [note](#) to the Pharmaceutical Committee (more on this in the section on 'Action at European level' below), shortages of medicines are part of the wider problem of access, affordability and availability of medicines in the EU. The note explains that a shortage occurs 'when supply of an already marketed medicine does not meet demand at a national level from healthcare professionals or patients in response to clinical needs'. Shortages are understood to pose risks to patients' health due to under-treatment, medication errors, increased length of hospital stay and adverse reactions from attempts to substitute unavailable medicines. The note states that shortages are more and more frequent for widely used essential products that have been on the market for many years.

EU global trade in pharmaceuticals

The EU is the world's biggest trader in pharmaceutical and medicinal products. EU-27 exports and imports in pharmaceuticals and medicines reached €203 billion and €93 billion respectively in 2019. The United States and Switzerland were the EU's main trading partners for these goods in 2019. Imports to the EU are dominated by Switzerland (32%) and the United States (31%).

Source: Eurostat, [The EU – world's leading exporter of pharmaceutical products](#) and [International trade in medicinal and pharmaceutical products](#).

Action at EU and Member State levels

Solutions to the problem of medicines shortages are believed to require [collaboration and joint action](#), as well as the [involvement](#) of multiple stakeholders, including regulators, industry, patients, healthcare professionals and international players. Tackling shortages and, more broadly,

safeguarding access to medicines is understood to require measures both at EU and national levels. The European Commission, European Parliament, Council under several Council presidencies, as well as the Member States have addressed this challenge through various initiatives. EU medicines legislation (Articles 23a and 81 of [Directive 2001/83/EC](#) on the Community code relating to medicinal products for human use) requires companies to ensure a continuous supply of marketed medicines and to notify the competent authorities two months before any temporary or permanent interruption of supply occurs. As the Commission has noted, EU legislation does not oblige companies to maintain medicines on the market, should they decide to withdraw. Member States are responsible for enforcing the relevant legislation.

The geopolitical dimension of medicines shortages

[Amid the coronavirus crisis](#), in particular, the [geopolitical dimension](#) of the medicines shortages has become apparent, highlighting the EU's dependency on countries outside its borders for the production of active pharmaceutical ingredients (APIs) and medicines. According to [generics industry](#) information, China is a major producer of pharmaceutical inputs, and in particular, of key starting materials, intermediate materials and APIs. The country is also thought to be by far the leading supplier of APIs or key intermediates for certain essential medicines, such as analgesics (painkillers) or anti-infectives. The 2008 [impact assessment](#) of the [Falsified Medicines Directive](#) stated that 90 % of APIs for generic medicines are sourced from India and China.¹ According to recent [news reports](#), 80 % of the APIs in medicines and 40 % of finished medicines sold in Europe come from China (two-thirds) and India (one-third). These two countries reportedly produce 60 % of the world's paracetamol, 90 % of its penicillin and 50 % of its ibuprofen. Another [news article](#) specifies that India controls almost 26 % of the European formulations in the generic space, while the Indian pharmaceutical industry in turn relies on China for almost 70 % of the APIs for its medicines. In the context of the coronavirus crisis, India has decided to limit the export of dozens of medicines, such as paracetamol, to favour its domestic market. In the meantime, it [has reportedly pledged](#) to lift its ban on the export of paracetamol, but to maintain its export ban on the active ingredients of paracetamol and on hydroxychloroquine (with a few exceptions). According to a [recent article](#), 'Europe is seen facing imminent risk of critical medicines shortages'. Bringing the manufacture of APIs back to Europe has been mentioned as forming part of a strategy for tackling rising medicines shortages.

European Commission

The Commission has addressed issues of access to medicines through various studies and evaluations, such as a [report](#) on external reference pricing,³ a [report](#) on biosimilar competition⁴ and an [opinion](#) on innovative payment models that was produced by the Expert Panel on effective ways of investing in health (EXPH). Policy discussions on issues of medicines availability with the Member States take place in several fora, and in particular, the [Pharmaceutical Committee](#) – an advisory body set up to examine questions relating to medicinal products for human use, including matters concerning the launch of new legislative initiatives. It is composed of public health experts from the Member States' administrations and is chaired by a Commission representative.

In May 2018, in response to calls from the co-legislators to monitor the obligation of continuous medicines supply laid down in EU legislation, the Commission held an [ad-hoc technical meeting](#) with national experts from the Pharmaceutical Committee to discuss medicines shortages. Following the meeting, the Commission published a [paper](#) agreed with the Member States, and a [summary](#) of the Member States' measures to ensure continuous supply, including national measures to address shortages. In its [note](#) to the November 2019 Pharmaceutical Committee meeting, the Commission recognised that the availability of high-quality APIs for the production of medicines for the EU market is a growing concern. It stated that manufacturing issues, often related to the quality of APIs, 'are one of the major reasons of shortages of medicinal products in the EU'. The note indicates that, as regards the EU's dependency on APIs manufactured in China, the Commission services have initiated a dialogue to explore the possibility of facilitating API production in Europe, and organised meetings with API producers and pharmaceutical industry representatives 'to explore the current market situation and possibilities of alliance between API and finished medicinal products producers'.

Commission guidelines to avoid shortages of medicines during the pandemic and establish a coordinated approach across Europe

In April 2020, the European Commission published its [Guidelines on the optimal and rational supply of medicines to avoid shortages during the Covid-19 outbreak](#). As the document [notes](#), the pandemic has highlighted significant challenges in ensuring the supply of the critical medicines needed. According to the Commission, the risk of shortages is due primarily to the increase in demand for medicines to treat Covid-19 patients in hospitals – such as anaesthetics, antibiotics, muscle relaxants, resuscitation medicines and anti-diuretics for patients who need intubation, as well as respiratory and cardiac medicines, analgesics and anti-clotting medicines, among others, for intensive and supportive care of such patients. Other factors that play a role on the demand side include stockpiling (of non-prescription painkillers, for instance) by citizens, and an increased demand for experimental medicines to treat the coronavirus disease.

On the supply side, the introduction of protectionist measures within and outside the EU (such as export bans and national stockpiling) play a role. Decreased production capacity, closure of raw material/API suppliers' businesses, logistics issues in affected countries, and transportation barriers between countries also have a direct impact both on the availability of medicines and the development of new treatments against Covid-19. Lastly, worldwide confinement measures have led to disruptions and increased air freight and shipping prices. The Commission says that the proposed actions should allow for a more coordinated approach across the EU (see Table 1).

Table 1 – Guidelines to optimise supply and avoid medicines shortages during the coronavirus pandemic

Showing solidarity	Ensuring supply	Optimal use of medicines in hospitals	Optimisation of sales in community pharmacies to avoid hoarding
<ul style="list-style-type: none"> • Lifting export bans and restrictions • Avoiding national stockpiling • Avoiding that misinformation leads to improper use and unnecessary stockpiling 	<ul style="list-style-type: none"> • Increasing and reorganising production • Ensuring manufacturing continues at full capacity • Implementing regulatory flexibility • Monitoring available stocks at national level • Ensuring necessary support to the wholesale sector • Fully enforcing the 'green lanes'* • Facilitating air freight and other forms of transport • Ensuring fair distribution of supply 	<ul style="list-style-type: none"> • Equitable distribution of available medicines • Exchanging hospital protocols to treat patients • Considering alternative medicines on the basis of hospital protocols and national guidelines • Extending the expiry dates of medicines • Considering the use of magistral preparations or veterinary medicines • Encouraging clinical trials for medicines used off label* 	<ul style="list-style-type: none"> • Introducing measures to reassure persons reliant on medication • Introducing restrictions on sales in community pharmacies • Limiting online sales of products at risk

* In the EU's coronavirus response, '[green lanes](#)' in cross-border transport are border crossings open to all freight vehicles, where procedures should be minimised and streamlined to what is strictly necessary.

* '[Off-label use](#)' is the use of a medicine for an unapproved indication or in an unapproved age group, dosage, or route of administration.

Source: European Commission, [Guidelines to optimise supply and avoid medicines shortages](#), April 2020.

A Commission [note](#) to the March 2020 Pharmaceutical Committee meeting concerns the EU's dependency on APIs and chemical raw materials imported from third countries and the possible links between this dependency and medicines shortages experienced in Europe. The note states:

We are concerned that our dependency on imports of APIs and chemical raw materials will put increasingly at risk the supply of certain essential medicines and threaten the EU's strategic autonomy. The recent outbreak of Covid-19 shows that a disruption of supply from India and China in the pharmaceutical value chain could present a major health security issue.

According to another Commission [note](#) to the Pharmaceutical Committee's March 2020 meeting, which refers to a planned study on medicines shortages, the Commission's Directorate General for Health and Food Safety (DG SANTE) is reflecting on additional measures to address shortages 'beyond the current legal obligation for the pharmaceutical industry to ensure supply of marketed medicines'. The note states that a study will be launched to provide data on the causes of shortages, assess the current legal obligations to ensure continued supply, and identify and benchmark possible actions to address further risks of shortages.

The EU also funds initiatives through the EU health programme (for instance, the [Euripid](#) project on [medicinal product pricing](#)) and the EU's research and innovation programme, Horizon 2020. One such recent initiative, [PEARRL](#), consists of a multi-sectorial team of European regulatory authorities, academic leaders and pharmaceutical companies. The project will train researchers to act as communication bridges between research and regulatory science, the rationale being that, to maintain global leadership, the European pharmaceutical industry has to respond to challenges from low-cost producers, such as China, by bringing new drug molecules to the market in a streamlined, cost-effective manner.

European Medicines Agency and Heads of Medicines Agencies network

According to the European Medicines Agency (EMA), [improving the availability](#) of medicines authorised in the EU is a key priority of the [European medicines regulatory network](#), the closely coordinated regulatory network of [national competent authorities](#) (medicines agencies) in the Member States of the European Economic Area (EEA)⁵ working together with the EMA and the European Commission. As the EMA notes, shortages or other problems with the availability of medicines create challenges for the medicines supply chain, which can have serious consequences for human health. Because of the EU's subsidiary competence in matters related to health, most medicines shortages are dealt with by the national competent authorities. The EMA can be involved, for example, when a shortage is linked to a safety concern or affects several Member States. The EMA states that 'regulatory authorities within and outside Europe are increasingly working together to prevent shortages and to limit their impact whenever they occur'. The EMA produces a [public shortages catalogue](#) that provides information and, if relevant, recommendations, to patients, healthcare professionals and other stakeholders.

Moreover, in 2016, the EMA and the [Heads of Medicines Agencies](#) (HMA) network created an [HMA/EMA task force](#) on the availability of authorised medicines. The task force was established to better address potential problems with medicines supply and to develop and coordinate actions to facilitate the prevention, identification, management of, and communication about, shortages. Since April 2019, the task force has been running a pilot programme on establishing a single point of contact (SPOC) network to improve information-sharing between Member States, the EMA and the Commission on important medicines shortages. This includes information-sharing on alternative medicines that are available in other Member States. In a [document](#) addressed at marketing authorisation holders, the HMA/EMA task force offers them guidance on reporting of shortages in the EU. This document provides a common definition of a medicines shortage agreed by all stakeholders: 'A shortage of a medicinal product ... occurs when supply does not meet demand at a national level'. It gives recommendations aimed at facilitating the detection and reporting by marketing authorisation holders to the competent authorities of impending shortages. Furthermore, the guidance notes that early notification to the competent authorities is a key aspect

in the prevention or mitigation of a shortage by allowing sufficient time to make contingency arrangements, where necessary. Another [document](#) published by the HMA/EMA task force complements the one mentioned above, and focuses on guidance regarding good practices for communication to the public on medicines' availability issues.

Acknowledging the important role stakeholders play in preventing and managing medicines availability issues, the HMA/EMA organised a [multi-stakeholder workshop](#) in November 2018, to brainstorm ways to better address potential medicines supply issues and avoid shortages. According to the [report](#) from the meeting, the workshop illustrated the complexity of availability problems and their multifactorial causes. Among other things, there was consensus that an EU-wide harmonised definition of a shortage is essential for good shortage management. The HMA website provides an [overview](#) of the Member States' situation as regards medicines availability problems (also compiled in a single document, [Availability of pharmaceuticals for human use](#), October 2019). This includes a mapping of solutions or best practices within each Member State.

Industry single-point-of-contact system

To support availability of medicines during the coronavirus pandemic, the EMA, together with the pharmaceutical industry, is currently setting up the [i-SPOC](#) (industry single-point-of-contact) system. Through the system, pharmaceutical companies can report directly to the EMA any issues related to the availability of crucial medicines being used in the context of the coronavirus pandemic, while continuing to report to the Member States concerned.

Guidance to stakeholders on more regulatory flexibility for medicines

Moreover, the Commission, the EMA and the European medicines regulatory network have developed a [Q&A document](#) to provide guidance to stakeholders on more regulatory flexibility for medicines to address challenges arising from the pandemic, with a particular focus on crucial medicines for use in treating Covid-19 patients. The measures cover different areas of medicines regulation, such as marketing authorisations, manufacturing and import of APIs and finished products, quality variations, and labelling and packaging requirements, with flexibility to facilitate the movement of medicinal products within the EU.

European Parliament

The European Parliament has specifically addressed the issue of medicines shortages in its March 2017 resolution on EU options for improving access to medicines ([2016/2057\(INI\)](#)). Parliament notes with concern that the EU lags behind the US as regards a standardised and transparent reporting mechanism on the causes of medicines shortages, and invites the Commission and the Member States to put such an instrument in place. It calls on the Commission and the Council to formulate a better definition of medicines shortages and analyse their causes, and, in this regard, to assess the impact of parallel trade and supply quotas, establish and update a list of essential medicines that are in short supply, monitor compliance with Article 81 (on shortages of supply) of Directive 2001/83/EC, explore mechanisms to address the withdrawal of effective medicines from the market for purely commercial reasons, and take action to remedy these shortages. Parliament also calls on the Commission and Council to establish a mechanism whereby medicine shortages across the EU can be reported on an annual basis.

There have been several parliamentary questions on medicines shortages in the current as well as in previous parliamentary terms.⁶ MEPs wanted to know, among other things, whether the Commission was aware of the existence of medicines shortages and had looked into their causes, what possible solutions the Commission had in mind, and whether it had devised a European strategy to address this problem (see text box on the right). In January 2020, the Parliament's Environment, Public Health and Food Safety (ENVI) committee [coordinators](#) decided to adopt an oral question with a motion for a resolution on the issue of medicines shortages.

Council and presidencies

The issue of access to medicines has been addressed by rotating Council presidencies on several occasions. The June 2016 [Council conclusions](#) on strengthening the balance in the pharmaceutical systems of the EU and its Member States, for instance, invite the Member States to consider, among other things, further developing voluntary cooperation between their relevant authorities and payers, who 'share common interests in relation to pricing and reimbursement of medicinal products and to explore possible areas in which such voluntary cooperation can contribute to higher affordability and better access to medicinal products' (more on this under the 'Member States' sub-section below).

During the Employment, Social Policy, Health and Consumer Affairs Council of 9-10 December 2019, the ministers discussed possible solutions to the problem of access to medicines in the EU. The exchange of views was steered by a [discussion note](#) prepared by the Finnish Presidency. The note argues that ensuring access requires efficient measures at all phases of a medicinal product's lifecycle: 'Mechanisms supporting research and development, controlled introduction, achieving equal access to new medicines, price competition, continuous supply and maintaining old medicines on the market should be sustainable, while taking into account the needs of the national healthcare systems'. According to the [Council](#), many delegations have supported the idea of developing an EU work agenda on pharmaceutical policy to avoid medicines shortages. Possible measures highlighted in the debate include:

- encouraging the relocation of medicines production back to the EU;
- transferring medicines from one Member State to another, with some exemptions concerning the requirements for the information accompanying the products concerned;
- exchanging information on stocks;
- using early warning mechanisms; intensifying market surveillance;
- strengthening cooperation at EU level.

Member States

In recent years, new forms of voluntary cooperation among Member States have emerged. One example has been the Commission-facilitated network of competent authorities on pricing and reimbursement (CAPR), created in 2008 for the exchange of best practices among the Member States. Other examples of bilateral and multilateral [voluntary cooperation](#) between Member States include, among others, the Valletta,⁷ [Beneluxa](#),⁸ FINOSE⁹ and Nordic Pharmaceuticals Forum (NLF)¹⁰ initiatives. Launched in October 2019, the International Horizon Scanning Initiative ([IHSI](#)) – a Beneluxa [spinoff](#) – consists of a central database that will assist nine European countries¹¹ in [preparing for the arrival](#) of new, potentially expensive medicines on the market.

A pharmaceutical strategy for Europe

In its answers to parliamentary questions, the Commission has repeatedly stated that it is aware of the growing concerns regarding shortages of medicines. Among the causes of such shortages it has listed manufacturing problems, industry quotas, legal parallel trade, and economic aspects, such as medicines pricing, which is a competence of the Member States. The Commission has stated its commitment to improving the supply of affordable medicines to meet Europe's needs, while at the same time assisting the European pharmaceutical industry in maintaining its status of world leader in innovation. To this end, it has announced in its 2020 work programme that it would launch a pharmaceutical strategy for Europe in the last quarter of this year. According to the Commission, the strategy will aim to deliver a future-proof pharmaceutical policy to address all levels of the value chain, from research and development, to authorisation of, and patients' access to, medicines. The strategy will also address the issue of the pharmaceutical industry's dependency on the manufacturing capacities of, and the supply of starting materials and APIs from, third countries. It will be about ensuring the quality and safety of medicines and consolidating the pharmaceutical sector's global competitiveness, as well as making sure that all patients can benefit from innovation while resisting the pressure of increasing costs of medicines.

Source: [2020 Commission work programme](#) and [EP Legislative Train Schedule on the pharmaceutical strategy](#).

International organisations' work

Organisation for Economic Co-operation and Development

Access to medicines is one of the areas of work of the Organisation for Economic Co-Operation and Development (OECD). The OECD report, [Pharmaceutical Innovation and access to medicines](#), addresses current challenges in pharmaceutical markets, such as the increasing prices of new medicines. It also looks at pharmaceutical industries' activities and performance, and proposes policy options to address the challenges they face. Building on this, the OECD has undertaken several studies co-funded by the EU health programme:

- [Using routinely collected data to inform pharmaceutical policies](#), which explores countries' routine collection of data on prescribed and dispensed medicines to identify best practices and to assess the potential impact on health and pharmaceutical policy;
- [Improving forecasting of pharmaceutical spending](#), which explores countries' approaches to tracking pharmaceutical utilisation and expenditure and anticipating changes in pharmaceutical markets;
- on [building capacities for improved pricing and reimbursement negotiations](#), which mainly consisted of experience-sharing and a review of the experience with [performance-based managed entry agreements](#) (that is, arrangements between companies and healthcare payers that allow for coverage of new medicines while managing uncertainty around their financial impact or performance);
- on addressing the specific challenge posed by the pricing of oncology treatments (final report forthcoming).

United Nations and World Health Organization

The United Nations (UN) [High Level Panel on Access to Medicines](#) is composed of experts from diverse stakeholder groups. In its September 2016 [report](#), it formulates recommendations 'to help improve research and development of health technologies and people's access to vital therapies that are currently priced out-of-reach of patients and governments alike'. The recommendations cover intellectual property laws and access to health technologies; new incentives for research and development of health technologies; and governance, accountability and transparency.

At the global level, the World Health Organization (WHO) addresses access issues from different angles in documents such as a [roadmap 2019-2023](#) on comprehensive support for access to medicines, vaccines and pharmaceuticals; a 2018 [report](#) on the pricing of cancer medicines and its impacts; and a 2016 [report](#) on shortages of essential medicines and health products. It is also producing lists of essential medicines, the latest being the [21st WHO Essential Medicines List \(EML\) and the 7th WHO Essential Medicines List for Children \(EMLc\)](#), updated in 2019.

The WHO Regional Office for Europe (WHO Europe) focuses on access to new medicines in Europe in a 2015 [review](#) of policy initiatives and opportunities for collaboration and research. Its 2016 [report](#) on challenges and opportunities in improving access to medicines through efficient public procurement notes that the introduction of new medicines and other medical technologies, together with rising expectations from patients and demographic changes, threaten the fiscal sustainability of healthcare systems. According to the report, it is important to ensure affordable prices and supply security, and procurement strategies have to consider both. In 2018, WHO Europe's [European Observatory on Health Systems and Policies](#), an intergovernmental partnership that supports evidence-based health policy-making, published a [policy brief](#) on 'Ensuring access to medicines: How to redesign pricing, reimbursement and procurement?'. It addresses the affordability of very expensive new medicines that have entered into the European market. The paper mentions cancer, autoimmune and diabetes treatments as being the key drivers of growth in public pharmaceutical expenditure, with emerging cell and gene therapies likely to drive such expenditure even further up.

Stakeholders' views

Players involved in the debate have offered explanations for the causes involved in medicines shortages and have proposed recommendations for tackling them. Examples of such explanations and recommendations are presented below.

Pharmaceutical and generics industries

In its [policy proposals](#) to minimise medicines supply shortages, the European Federation of Pharmaceutical Industries and Associations (EFPIA) calls for: better understanding of the root causes and drivers of shortages, which requires identifying the bottlenecks in the supply chain (the European Medicines Verification System, set up in the context of the Falsified Medicines Directive, could be used for this purpose); better reporting of shortages through enhanced cooperation between supply chain stakeholders and the EMA/HMA task force; effective enforcement of existing regulatory requirements on all players in the supply chain at national level, coupled with measures to enhance transparency within the supply chain and support further stakeholder dialogue; emergency intervention as the last resort, with greater solidarity among Member States to reduce supply chain disruptions by abolishing the distortive effects of national schemes incentivising imports from lower-income to higher-income Member States or imposing national stockpiling obligations limiting supply for other EU markets; and, where needed, temporary emergency measures enacted at national level to prevent shortages due to exports. According to a separate EFPIA [statement](#), industry is working with the EMA and the HMA to ensure that their guidance on detection and notification of shortages is being effectively implemented, so as to enable all EU competent authorities to receive harmonised information about any potential disruption or interruption of supply at a very early stage. In a March 2020 [statement](#), the EFPIA said that there is limited immediate risk that the pandemic would affect manufacturing and supply of branded medicines in Europe.

In its [position paper](#) and wider [reading list](#), generic medicines industry association Medicines for Europe looks at the causes of medicines shortages ('pressure of costly regulatory/quality procedures and cost-containment measures on generic medicines industry') and makes recommendations, both to prevent shortages and to mitigate them once they occur. These include: ensuring market predictability; improving regulatory efficiency to reduce the administrative and cost burden of keeping medicines on the market; managing the available market stock information with a non-coercive system; and introducing specific regulatory measures to mitigate imminent medicines shortages.

In a 2019 [open letter](#), Medicines for Europe said that, although the provision of generic medicines has increased access to medicines in Europe, 'cost containment, industrial factors and new regulatory requirements threaten that'. The letter calls on the European Commission to prioritise shortage prevention in pharmaceutical policy by implementing four recommendations: establishing a cooperation mechanism to coordinate EU and national policies for the purpose of reducing the risk of shortages and avoiding spill-over effects through which one country's policy would create supply issues in another; engaging ministries of health and industry to identify policies that would stimulate investment in manufacturing; introducing measures to reduce the complexity and cost of EU regulation in the off-patent sector and facilitate shortage mitigation; and engaging with ministries of health on cost-containment measures that have reduced competition in the generic medicines sector.

According to a 2019 [common position paper](#) by several supply-chain stakeholders, medicines shortages can have multiple root causes linked to issues of regulation, manufacturing and quality, but also to economy-related and supply-chain issues. These stakeholders believe that the root causes of shortages can be addressed by: harmonising and monitoring medicines shortages at EU level; creating regulatory incentives for essential low-priced medicines; allowing regulatory flexibility and improving regulatory efficiency to mitigate shortages; and ensuring market stability and sustainability.

The European Healthcare Distribution Association's 2018 [position paper](#) argues that the causes of medicines shortages seem to differ from country to country and from product to product, although some common underlying causes for supply disruption can be identified. These include: the complexity and globalisation of production, where APIs are sourced in one country, while end products are manufactured in another and then packaged in a third country; the unavailability of APIs complying with EU standards,¹² which leads to production and supply disruptions; and the lack of market attractiveness for certain (older) medicines, which results in manufacturers stopping production of some low-income generating products. Compounding the problem are ongoing healthcare budget challenges and procurement policy failures. Further causes of shortages put forward by the paper are the stringent supply quotas imposed by pharmaceutical manufacturers on pharmaceutical healthcare distributors; and parallel trading by distributors, often cited as a contributing factor. However, the association 'would caution against forming conclusions without evidence to support this'. Of note, the paper also mentions that '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'.

Parallel traders

According to the European parallel traders' association Affordable Medicines Europe, the [main causes](#) of medicines shortages are fuelled by: product withdrawal; production and quality problems; and quota systems imposed by manufacturers in many countries to limit the potential for competition. Affordable Medicines Europe notes that short-term, parallel imports are 'the most efficient' tool in the fight against shortages. 'Our industry has the ability to mitigate shortages by bringing medicinal products that are suffering from problems of supply in one country[,] from another market in which there is a surplus. Parallel traders' capacity to repackage and relabel products, in addition with their knowledge of the different markets and distribution network, gives them the chance to swiftly introduce a medicine in the market with supply problems with full safety assurance for the patient.' The association points out that parallel imports are not from low-income countries, and that parallel trade does not drive shortages.

Pharmacists and healthcare professionals

In its 2019 [survey](#) (conducted between November 2019 and mid-January 2020), the European Association of Hospital Pharmacists (EAHP) collected information on medicines shortages from hospital pharmacists, patients and healthcare professionals such as physicians and nurses. According to the EAHP's subsequent [report](#), the survey shows that more and more patients are seeing their health status deteriorate, as they cannot receive their prescribed medicines promptly, and that – with the coronavirus pandemic unfolding in Europe – the situation will probably worsen. The survey finds that the type of medicines most frequently in shortage are antimicrobial agents (63 %), oncology medicines (47 %) and anaesthetics (38 %). The impact medicines shortages had on patients included delays in care or therapy (42 %), suboptimal treatment (28 %), cancellation of care (27 %), and increased length of hospital stay (18 %). The EAHP also gathered information on possible reasons for shortages. For hospital pharmacists, the global shortage of an API and supply chain problems ranked the highest. Physicians named the prices of medicines, supply chain problems and issues related to parallel export as the main reasons for shortages. Nurses noted that shortages were caused by medicines pricing, as well as by problems related to manufacturing and the supply chain.

An academic view on the causes of shortages

A recent article on medicines shortages in Europe explains that these can be due to supply-related factors (such as manufacturing issues, regulatory issues, logistics, distribution) and demand-related ones (for instance, fluctuating demand, parallel trade, tendering, price and reimbursement policies). Moreover, extraordinary geopolitical events (such as Brexit) may also affect medicines' availability. The article notes that one of the reasons for the failure to define problem-solving strategies is the fragmentation of the European regulatory framework, starting with the lack of a univocal definition of 'medicine shortage'.

Source: Musazzi U.M. et al., [New regulatory strategies to manage medicines shortages in Europe](#), *International journal of pharmaceutics*, vol. 79, pp. 119171, 15 April 2020.

The report stresses that 'a strong EU commitment is very much needed to adequately address certain causes of medicines shortages', and asks that the measures at European level be supported by national action.

In its 2019 [survey](#) on medicines shortages from the community pharmacists' perspective, the Pharmaceutical Group of the European Union (PGEU), defines 'medicine shortage' 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'. The survey's key findings include: the high incidence and ongoing rise of the number of medicines shortages in most European countries; the daily and burdensome impact of medicines shortages on patients and pharmacy practice across Europe; and the gap in information, tools and legal solutions available to community pharmacists in many European countries for providing solutions to patients in case of a shortage. According to the survey, all classes of medicines are affected by shortages. Respiratory medicines have been in short supply in the highest number of countries (87 %), while biological medicines¹³ have least often been indicated as in short supply (42 % of countries). In the majority of responding countries (67 %), over 200 medicines were listed as being in short supply, with five countries indicating that more than 400 medicines were in short supply. In its [position paper](#), the PGEU calls for a number of coordinated actions – such as ensuring availability, widening professional competence, improving communication, compensating the financial impact, and developing effective governance systems – that should be taken at different policy levels to reduce the impact of medicines shortages on patients.

Patient and health groups and statutory payers

In a 2019 [open letter](#), more than 30 patient and health groups call for the Commission to investigate the factors leading to medicines shortages, so as 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. Picking up on this call, the European Public Health Alliance (EPHA), in a 2019 [article](#) on 'Medicines shortages – the new cancer of Europe', notes that shortages have become a 'massive access issue in Europe and their consequences on people's health classify them among the worst public health emergencies, especially when they affect essential medicines and last for long time periods'. The article underlines that true cooperation at EU level, based on thorough and transparent information on the root causes of shortages in EU countries, is urgently needed. It considers the recommendations of the [EMA/HMA task force on availability of medicines](#) to be 'a step in the right direction', albeit with a limited expected impact due to their exclusive reliance on the goodwill of stakeholders and Member States. 'Without a bold initiative of the new European Commission promoting a common policy on shortages, more and more Europeans may not have access to the essential medicines they need in the coming years.'

Amid its [call](#) for 'fair medicines prices', the International Association of Mutual Benefit Societies (AIM) has put forward a [proposal](#) for setting the price of new medicines in such a way as to make them accessible. The AIM calls for a 'fair European maximum price calculation model'. It further states that medicines should be considered a public good; prices should be more in line with the costs of research and development; access to affordable medicines should be promoted globally; prices of medicines need to be predictable; a European model for the calculation of fair medicines prices should reward what (really) matters; prices must take the added therapeutic value into account; a fair price model should be subject to some flexibility; corrective measures against parallel trade and medicines shortages should be introduced.

Looking ahead

Scheduled for publication in the course of 2020, the European Commission's aforementioned study on medicines shortages is expected to provide a summary of the shortages in the EU and their causes,

an assessment of the current legal provisions and an outline of the pros and cons of possible future action. Medicines availability and supply-chain problems revealed by the coronavirus crisis are also [expected](#) to be an important theme in the Commission's forthcoming pharmaceutical strategy.

MAIN REFERENCES

- Ferguson, C., [European Union response to coronavirus threat](#), European Parliament, EPRS, 2020.
- Scholz N., [Boosting cooperation on health technology assessment](#), European Parliament, EPRS; 2019.
- Scholz N., [Les médicaments dans l'UE: prix et accès](#), European Parliament, EPRS, 2015.
- Scholz N., [Medicinal products in the European Union: The legal framework for medicines for human use](#), European Parliament, EPRS, 2015.

ENDNOTES

- ¹ On 25 March 2020, India – [one of the world's largest](#) hydroxychloroquine manufacturers – put export restrictions on the medicine.
- ² 'Parallel trade' in medicines is based on the EU principle of free movement of goods in the internal market. Products are bought from one Member State and sold into another outside the formal channels established by manufacturers or licensed distributors. As the Commission [points out](#), parallel imports tend to occur when price levels for similar products between two Member States are significantly different. This creates an incentive for traders ('parallel traders') to buy products in the country where they are priced lower and sell them in the country where they are priced higher, at a price that allows the trader to make a profit.
- ³ [Defined](#) as the practice of using the price(s) of a medicine in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country.
- ⁴ According to the report, 'biosimilar medicines' are highly similar in all essential aspects to already approved biological medicines, which are increasingly used to treat chronic conditions, such as cancer, diabetes or inflammatory diseases. A key argument for the introduction of biosimilars is to increase patient access by lowering prices.
- ⁵ The EEA [consists of](#) the EU Member States and Iceland, Liechtenstein and Norway.
- ⁶ In this parliamentary term, for instance: [P-001269/2020](#), [E-000633/2020](#), [E-000380/2020](#), [E-000328/2020](#), [E-004370/2019](#) (see also the Commission [answer](#)), [E-003268/2019](#) ([answer](#)), [E-002981/2019](#) ([answer](#)), [E-002503/2019](#) ([answer](#)), [E-002284/2019](#) ([answer](#)), [E-002161/2019](#) ([answer](#)).
- ⁷ It [comprises](#) Croatia, Cyprus, Greece, Ireland, Italy, Malta Portugal, Romania, Slovenia and Spain.
- ⁸ Comprising Austria, Belgium, Ireland, Luxembourg and the Netherlands.
- ⁹ Finland, Norway and Sweden.
- ¹⁰ Denmark, Iceland, Norway and Sweden.
- ¹¹ Belgium, Denmark, Ireland, Luxembourg, the Netherlands, Norway, Portugal, Sweden and Switzerland.
- ¹² The Falsified Medicines Directive mandates that APIs imported into the EU must comply with European good manufacturing practice ([GMP](#)) guidelines.
- ¹³ [Defined](#) as medicines made by or derived from a biological source, such as a bacterium or yeast. They can consist of relatively small molecules, such as human insulin, or complex molecules, such as monoclonal antibodies.

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