# Medicine Shortages

*EPSA Position Paper*

*Endorsed by:*

**European Association of Hospital Pharmacists (EAHP)**

**European Federation of Psychology Students' Association (EFPSA)**

**European Early Career Nurses and Nursing Students' Association (ENSA)**

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**JANUARY 2024**

## Executive Summary

Access to medicines is a human right. However, this right is put under pressure now the European healthcare system faces significant challenges due to medicine shortages. This results in adverse effects, cancelled or delayed treatments, higher costs for patients and healthcare systems and increased aggression against community pharmacies. This position paper presents solutions and consequences related to the issue of medicine shortages, focusing on several European countries. Pharmacy students across Europe present their opinions and call for action to develop a better future for European healthcare, thus, healthcare studies in universities and students' overall satisfaction in pursuing a career in healthcare.

## Definition of Medicine Shortages

A Medicine shortage is a supply issue that affects how the pharmacy and/or hospital pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent.

## About the Associations contributing to this position paper

AISFA, Italy 🇮🇹

ANEPF, France 🇫🇷

APEF, Portugal 🇵🇹

GPSF, Greece 🇬🇷

PPSA, Poland 🇵🇱

FASFR, Romania 🇷🇴

DŠFS, Slovenia 🇸🇮

CzPSA, Czechia 🇨🇿

K.N.P.S.V., The Netherlands 🇳🇱

## Introduction

Access to medicines constitutes a fundamental human right, as they are crucial in healthcare. The World Health Organization (WHO) defines essential medicines as those that meet the primary healthcare needs of the population. Unfortunately, the existing issue of drug shortages poses significant challenges to the healthcare system and puts this right under pressure. The WHO recognises the shortage of medicines as a growing health concern affecting the nations that comprise the European Economic Area. This shortage leads to adverse reactions occurring due to patients not receiving the exact treatment, cancelled or delayed treatments, and increased costs for individuals and healthcare systems.

The reasons behind the disruption in the regular availability of medicines are diverse and worldwide, involving various stakeholders in the complex supply chain. The efficiency of this supply chain relies on the collaboration and effectiveness of these different actors.

According to the European Association of Hospital Pharmacists (EAHP) 2023 Shortages Report, 95% of hospital pharmacists reported that medicine shortages are a current problem. Antimicrobial agents continue to remain the area that most frequently experiences shortages. The revision of the EU's General Pharmaceutical Legislation should be used to tackle shortages through a mix of reactive and proactive measures. Additionally, according to the survey conducted on the issue in 2022 by PGEU, 100% of the respondents stated they experienced shortages of medicines in community pharmacies. 75.86% of them stated the situation had worsened in the previous 12 months, and no one thought it got better. The responses showed how this situation affected patients, such as distress and inconvenience (93.10%), interruption of treatments (89.66%), increased co-payments (72.41%), sub-optimal treatment (58.62%), medication errors (34.48%), adverse events (21.14%) and even leading to death (13.79%). Lastly, according to EAHP's 2018 Survey on Medicines Shortages, a pharmacist in the team spends about 8 hours per week solving drug shortage problems to improve patient outcomes, which is not ideal and causes the pharmacist distress, lowering their job satisfaction.

According to the opening remarks by Commissioner Kyriakides at the press conference on addressing medicine shortages in the EU, a new approach to better tackle medicine shortages is needed. It is acknowledged that shortages cannot disappear overnight because their causes are long-standing and multi-factorial. Today, collective actions at the EU level are being put forward to improve the situation for the citizens, but also the medium- and long-term, such as setting up a new Voluntary Solidarity Mechanism, working with the Member States to anticipate in a coordinated way elements from the pharmaceutical reform, keeping the Union list of critical medicines updated and promoting it, structured and coordinated industrial approach to tackle shortages, add an industrial policy pillar to our European Health Union, set up a Critical Medicines Alliance starting in early 2024, and last but not least international cooperation is essential, especially in achieving more diversity in our supply chains. The objective is to have safe, effective and affordable medicines guaranteed for every citizen in the EU. Still, a significant step in working ahead of the reform of the pharmaceutical legislation to put some measures into place is being taken, which will tackle shortages in the short- and medium-term.

This position paper aims to compile the steps taken to tackle medicine shortages in Europe and their effects. This document also bears the views of European Pharmacy Students on the issue and a call for action directed at all stakeholders so that, together, we can build a better future for the medicines of Europe. Students from France, Greece, Italy, Poland, Portugal, Romania, Slovenia, Czechia and The Netherlands collaborated on this project.

## Definition and overview of medicine shortage and its consequences

Medicine shortages pose a severe challenge to the healthcare sector, affecting patients and healthcare professionals. Drug shortages, defined as the short-term or long-term unavailability of essential pharmaceuticals, can occur in various circumstances, impacting specific geographic areas and undermining the ability of the healthcare system to deliver optimal treatment.

Shortages of medicines can be short-term or long-term, and they are frequently caused by a variety of circumstances, including interruptions in the production process, regulatory problems, supply chain concerns, and market distortions. It is critical to differentiate between

acute and chronic shortages depending on their severity and duration. Acute shortages refer to brief disruptions, while chronic shortages persist over an extended period, creating more severe implications for healthcare and patients. To maintain the continuity of treatment and the well-being of the patients, it is crucial to address both sorts of shortages.

From the perspective of healthcare, medicine shortages present numerous difficulties. When patients' prescription drugs are not accessible, healthcare professionals are responsible for identifying alternatives or starting additional treatments for patients. This frequently results in medication errors and time constraints, endangering patient safety and the standard quality of care provided for the patient. Healthcare professionals must collaborate and develop efficient strategies to lessen the effects of shortages. Communicating with patients clearly and more effectively about other options, possible side effects, and expected delays is essential. Additionally, medicine shortages impose a financial and moral burden on healthcare systems, and interdisciplinary coordination and teamwork are necessary to overcome these issues. As a result, healthcare personnel could feel burned out and have lower job satisfaction.

Patients are directly affected by medicine shortages, often with negative consequences. They may notice more side effects or find the new medications do not work as planned. Another problem coming from the unavailability of prescription drugs is higher costs since more expensive alternative treatments may be required. Moreover, there is a risk of delays in receiving necessary care due to the need for increased monitoring, often leading to severe complications and sometimes even death. In some instances, the lack of essential drugs can cause symptoms to worsen and illnesses to advance. The psychological impact should also be considered, as medicine changes induce stress and fear. Particularly vulnerable groups are more at risk. And in all patients who encounter medicine shortage issues, their trust in healthcare often decreases, leading to drug discontinuation or severe side effects.

In times of drug shortages, community pharmacies, vital to providing medications, face unique difficulties. The PGEU Medicine Shortages Survey 2022 results show that pharmacy management of the effects of shortages on patients requires navigating supply chain complexity and confirming the impossibility of satisfying prescriptions. These difficulties

result from both distribution network dysfunction and issues with production. Market imbalances and regional differences also contribute to the unavailability of certain medicines.

In times of medicine shortages, wholesale distributors also encounter numerous difficulties. A supply order placed by a Wholesale Distributor that has yet to be satisfied by a Marketing Authorisation Holder constitutes an availability issue. This reveals distribution system flaws that lead to market inefficiencies and regional inequities. As opposed to shortages brought on by production issues, such unavailability emphasises the need for improved distribution dynamics and cooperation among stakeholders.

Medicine shortages have far-reaching consequences, impacting healthcare providers, patients, pharmacies, and wholesale distributors. Unavailability, unlike shortages, generally does not occur uniformly throughout the country and is due to market distortions often linked to the dynamics of the distribution circuit. Therefore, in these cases, the medicinal product, although present in the deposits of the Marketing Authorisation holder, is not available in some regional deposits and/or pharmacies.

Addressing this complex issue requires a collaborative approach involving healthcare professionals, regulatory bodies, manufacturers, and distributors.

Commenting on the problem that medicine and device shortages cause for patients, Nenad Miljković, EAHP's President-Elect and Board member responsible for the topic, stressed that "Shortages went beyond healthcare and affect society as a whole. Hospital pharmacists have worked tirelessly to alleviate shortages and call for a well-coordinated, transparent, and multi-stakeholder engagement at the European level to target the essence of shortages in all its multifaceted nature, covering aspects of production, procurement and supply".

## Leading causes at the European level

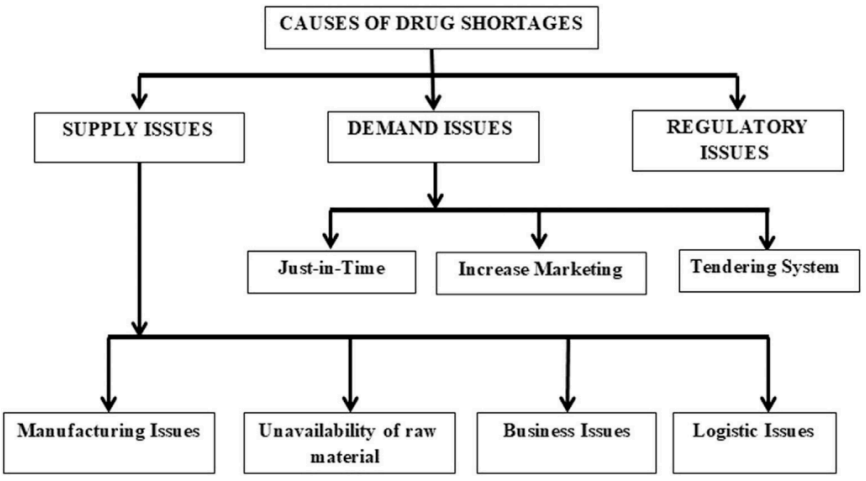



**FIGURE 2 |** Causes of drug shortages.

Firstly, the production and supply of active pharmaceutical ingredients (APIs) are the two important causes. It is noted that 60-80% of the products used in medicines are produced in China and India. In the COVID-19 pandemic, shortages of active pharmaceutical ingredients (APIs), excipients, and drugs occurred worldwide. As a result, the countries (India, China, and the United States), the producers of APIs stopped supplying some APIs to other countries, which led to a global shortage of many drugs. Moreover, many other challenges, including shortage of packing material, disrupted transport, delayed shipping, delayed customer clearance, and restricted import-export of APIs and drugs worldwide. Another reason is the war in Ukraine delaying distributions, the main reason for drug shortages. Unfortunately, Europe has chosen to depend significantly on China and India for pharmaceutical raw materials.

According to high-ranking officials in the sector, the objective of the European Commission is to "move" production from Asian countries to Europe to facilitate the supply of medicines within the continent. Of course, in this particular time, with inflation soaring and the energy crisis exponentially increasing the cost of drug production, insecurity is being cultivated as to whether Europe will be able to respond to a new wave of shortages of even more essential drugs.

Secondly, pricing is one of the most important causes. There are a lot of factors that lead to the unprecedented EU-wide shortage of medicines and related issues. Those factors can be located at almost every level of the supply chain of medicines, ranging from the supply of crucial materials and energy to logistic operations. It can be safely presumed that the main driving forces behind those turbulences are the aftereffects of the COVID-19 pandemic, the military conflict on European soil, and inflation.

The turbulence mentioned above has led to the dramatic increase in prices of materials, machinery and energy, which threaten the existence and, nonetheless, expansion of operations of (mostly generic medicines) manufacturers given that the regulated prices for medicines have mainly remained unchanged or increased at a rate lower than that of other goods and services available at the European market, favouring exports to more competitive countries. Complimentary to the above sits Europe's dependency on third parties, such as the United States, the People's Republic of China, and India, for its supply of materials and medicinal products. This dependency has rendered the European countries vulnerable to external policies and conflicts involving those parties, such as "trade wars".

The European Commission has highlighted that "legal parallel trade" is also to blame for the shortcomings in the availability of medicines. The "direct to pharmacy" is like the parallel trade, another phenomenon threatening the supply chain and its monitoring. It consists of directly acquiring the medicine from the manufacturer to the pharmacy, bypassing the wholesaler. This possibility has always existed but worsened during the pandemic; the pharmacy derived an economic benefit only in 20% of cases (according to Prof. Erika Mallarini). On the other hand, it remits the distribution system, which can equally spread the availability among the served pharmacies regarding their turnover on ethics and their actual needs.

It is therefore concluded that the sheer variety and complexity of the forces mentioned above and the involvement of many stakeholders and interests have led to today's severe mismatch of supply and demand of medicines potentially essential for the life of many European citizens.

## Actions Done by Various European Countries to Tackle Medicine ShortagesMedicine Shortages in Various European Countries

In recent discussions in the European Parliament's Public Health Committee (SANT), experts addressed medicine shortages as EU lawmakers prepared to discuss the pharmaceutical package.

Flemming Sonne, the chief executive officer of Amgros, a pharmaceutical procurement firm in Denmark, has highlighted the complexity of drug shortages. He explained that drug shortages depend on the product's life cycle, with innovative drugs protected by patents being less prone to experiencing shortages. At the same time, older medications that have few manufacturers and are less profitable are more susceptible. This highlights the need for effective drug management strategies to ensure that the availability and accessibility of essential medications are maintained.

One solution to these challenges is to provide pharmaceutical manufacturers with a stable market through fixed-price purchasing commitments. Regional cooperation, like Denmark's cross-border tendering with Norway and Iceland, has also proven effective. Achieving an EU-wide solution is challenging, but regional groups can be a first step.

Ilaria Passarani, Secretary General of the Pharmaceutical Group of the European Union (PGEU), highlighted the seriousness of the issue, citing their 2022 survey showing over 600 medicines in short supply in many countries, with cardiovascular and antibiotics being the most affected. She mentioned successful models in Spain, Italy, France, and Portugal, where councils or digital reporting systems help monitor and respond to shortages. This shows the value of collaboration and information sharing.

**Some examples of addressing medicine shortages and the actions taken by various European countries include**

**Italy** 🇮🇹

With the recent worsening of the shortages situation, the Ministry of Health, in collaboration with AIFA (National Medicines Agency) and all the different stakeholders involved, has launched a new discussion table on the subject to share and intensify the supervisory activities on the concrete application of the regulations in force regarding the distribution of medicines through controls on the territory.

According to Federfarma (National Association of Pharmacy Owners), among the top 50 shortages in 2023, we find antiepileptics, drugs for gastroesophageal disorders, chronic obstructive pulmonary disease, asthma, anti-inflammatories, antihypertensives and antibiotics. On an AIFA dataset of 3192 medicines currently in short supply (data for the three years 2020-2022), in 57,8% of cases (1200 references), the reason can be traced back to a cessation of marketing of the product, followed by production problems, temporary end of marketing, high demand of product and combination of these last two factors. Unfortunately, the latter scenario has affected several major medicines and is being addressed with extensive resources.

An example of this is the Amoxicillin case, which, from the last months of 2022 until today, registered an increased amount of communications about the shortages by marketing authorisation holders of different medicines for treating flu symptoms based on this API. Amoxicillin has also been used mainly for streptococcus, an infection treatment in the pediatric population, and in addition to its previous supply difficulties, an intervention was required. Consequently, thanks to the national market disponibility of bio-equivalent medicines, access to patient care has been possible in most cases. In parallel to this, "Compounding of Amoxicillin Oral Suspension" has been released, a guideline by SIFO (Italian Society of Hospital Pharmacy and Pharmaceutical Services of Healthcare Companies) and SIFAP (Italian Society of Preparatory Pharmacists) for community and hospital pharmacists, useful to contrast the unavailability of the industrial product.

Italy has implemented several initiatives and suggestions to solve the shortages of medicines. These include initiatives for compounding, supply chain monitoring, a computerised alert system, law enforcement measures, and advice for medical practitioners. To guarantee a sufficient and consistent supply of medicines in Italy, regulatory bodies, healthcare providers, and industry stakeholders must continue to work together.

Supply Chain Monitoring:

AIFA records the data through direct communications from the marketing authorisation holders and through the IT flow from the Regions, which collects the data from the pharmacies through the trade associations. The list of deficient drugs is periodically published on the AIFA portal.

The computerised alert system called "Drughost" proposed and powered by the Hospital Pharmaceutical services and put online by SIFO (Italian Society of Hospital Pharmacy) and AIFA (Italian Medicines Agency) has so far allowed hospitals to intercept in advance the "unavailability" even before they turn into "deficiencies" protecting until today the hospital setting from the problem.

Law enforcement measures recently used (directly or indirectly) for resolution purposes:

application of the provisions of Legislative Decree 19 February 2014 n17 in a parallel trade manner: "Wholesalers must permanently guarantee an assortment of medicines sufficient to meet the needs of a given geographical area and to arrange for the delivery of the requested supplies in a very short time throughout the site in question; to this end, all medicines burdened by specific provisions aimed at limiting states of shortage or unavailability, in the absence of valid therapeutic alternatives, cannot be withdrawn from distribution and sale";

according to the D.M. 11 May 2001, AIFA, to ensure the availability of essential and irreplaceable medicines, can authorise temporary imports from other countries where such medicines are still available for marketing. The import procedure is managed by hospital pharmacies or local health authorities (ASL). In detail, in the presence of a drug for which the "determination for importation has been issued to the MA holder, the missing medicinal product, imported by the MA holder, is dispensed in the period of absence from the hospital pharmacy or ASL upon presentation of the doctor's prescription and, in some cases, of a

declaration of irreplaceability of the medicine". Neither of these two cases falls within the scope of conventional pharmacies.

Compounding:

In light of the growing shortages of medicines of industrial origin, SIFAP has prepared a questionnaire to collect information on the type of pharmaceutical forms set up in pharmacies throughout the country. The data collected was made public and shared with organisations and associations to help citizens search for the type of preparation needed and the closest pharmacy in the area;

the annual draft law on competition (still pending): in particular in article 8, an amendment to the Industrial Property Code is established, Legislative Decree 30/2005 (art. 68, paragraph 1, letter c), eliminating the expressions "provided that substances produced on an industrial scale are not used". Removing this constraint would allow the pharmacist to purchase the patent-protected active substance for galenic preparation. The elimination of the galenic exception in the Competition Bill could change the various aspects of the work of pharmacists and patients; despite this, only a tiny quota of galenic preparations would benefit from this new provision.

Indications for pharmacists and general practitioners:

In the event of a "missing" medicine, consult the Vademecum on the AIFA online portal: it contains the information necessary to understand the situation and suggestions for patient management. Suppose the indication is to proceed with an alternative treatment. In that case, the advice is to "contact the specialist or general practitioner (GP), who can evaluate equivalent or therapeutic alternatives on the market. In the case of specific and justified situations in which the specialist doctor or GP deems it necessary to import the missing medicine, it is possible to activate the procedure".

Indications on veterinary prescriptions:

The pharmacist can replace the veterinary medicinal product with an equivalent due to the urgency of starting the therapy if it is not immediately available and for reasons of economic convenience.

**Portugal** 🇵🇹

Portugal is facing significant challenges related to medicine shortages, leading to increased respiratory infections and a decline in pharmaceutical wholesaling. The National Association of Pharmacies (ANF) and the Portuguese Pharmaceutical Industry Association (APIFARMA), among other stakeholders, are actively working to address these issues.

In Portugal, 2019 was the year with the highest number of effective ruptures in drug presentations recorded, decreasing this number in 2020 and 2021.

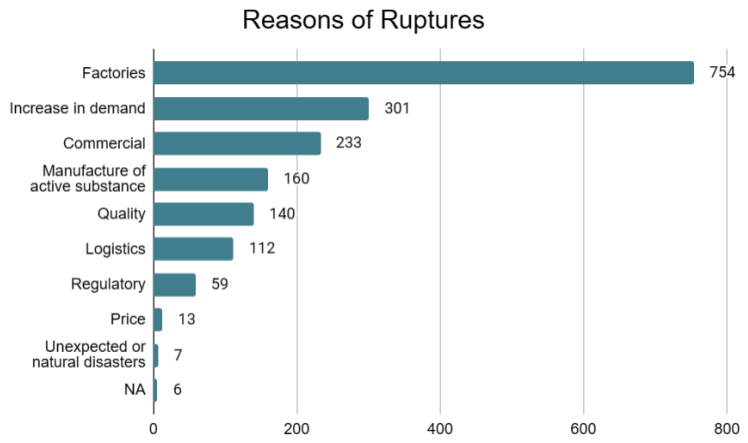
Despite the pandemic, the availability of medicines in Portugal improved during 2021, compared to the total number of effective ruptures between 2019 and 2021. In 2021, Portugal had the lowest number of rupture presentations of the last quadrennium, totalling 1,785 ruptures, corresponding to 474 substances of different assets. There was a 34% decrease in the number of effective ruptures per presentation compared to 2020. Advance notice by market authorisation holders also improved, demonstrating the pharmaceutical companies' commitment to improving the management of unavailability situations.

Additionally, it was found that the following market authorisation holders were responsible for the highest number of ruptures with medium and high impact during the year 2021:

| Holders | Number of ruptures |
|---|---|
| Generis Pharmaceuticals SA (Generis Farmacêutica S.A.) | 31 |
| Aspen Pharma Trading Ltd. | 13 |
| Accord Healthcare, S.L.U. | 11 |
| Fresenius Kabi Pharma Portugal, Lda. | 10 |
| Labesfal, Almiro Laboratories S.A. (Labesfal, Laboratórios Almiro S. A.) | 10 |
| Octapharma - Produtos Farmacêuticos Lda | 10 |
| Kern Pharma (Pharmakern Portugal - Produtos Farmacêuticos, Sociedade Unipessoal, Lda.) | 9 |
| Sanofi Ltd. | 8 |

| | |
|---|---|
| Pfizer Laboratories, Ltd. | 7 |
| Teva Pharmaceutical Industries Ltd. | 7 |

Reason for medicine shortage in 2021:




(From top to bottom: Problems in production, high demand, commercial issues, API production, quality, logistics, regulation, pricing, Natural disasters or unpredictable factors, not known)

However, the National Association of Pharmacies (ANF) has noted a worsening shortage of medicines in Portugal since the last quarter of 2022 but assured that there have been alternatives on the market for the missing drugs. The reasons that are pointed out are the same as those exposed before (global context, the role of China as a supplier, inflation, etc.) as well as the rising in respiratory infections in Portugal, leading to scarcity of medicines like ibuprofen, acetaminophen, and some antibiotics. However, the central nervous and cardiovascular systems were the most affected pharmacotherapeutic groups. ANF states that this scarcity is not a constant rupture that is felt because it ends up being replenished over time and highlights that pharmacies have ensured that a "person never goes without treatment and that they always have an alternative in terms of therapy".

Another factor that has been linked to medicine shortages in Portugal is the descending number of companies that maintain the pharmaceutical wholesale market. Between 1993 and 2000, there were 200 wholesalers in Portugal, whereas today, there are only around 15, most of them being big multinationals. This growing monopoly is reflected in the re-exportation of medicines made by some companies to entities that belong to them or are directly linked.

On the other hand, the Portuguese Pharmaceutical Industry Association (APIFARMA) indicates another reason for the lack of medicines in the country, which is low pricing since Portugal has one of the lowest medicinal prices in the European Union. Additionally, there are

inefficiencies in managing the Strategic Reserve for medicines in Portugal, where companies should guarantee stocks. This is similar to what happens in the USA, where the government defines a reserve and hires producers to ensure this reserve, managing it with the sales made. In Portugal, medicines from the Strategic Reserve are stored; meanwhile, as the expiration date passes, they go to waste, and the state needs to buy more.

Portugal has implemented various measures and proposals to address medicine shortages, including suspending exportation, participating in task forces, establishing notification systems, authorising the marketing of medicines without valid authorisation, and providing clinical guidelines. Encouraging pharmaceutical reindustrialisation and enhancing health literacy are additional strategies to ensure a stable supply of medicines and improve patient care. Continued collaboration among regulatory authorities, healthcare professionals, and industry stakeholders is essential to effectively address medicine shortages in Portugal.

Temporarily Suspended Exportation

This suspension aims to ensure the normalisation of the supply of critical medicines that were out of stock and those being supplied under the authorisation of exceptional use.

Participation in HMA/EMA Task Force on Availability of authorised medicines for human and veterinary use (TF AAM), EU SPOC network.

Notification of:

- Unavailable medicines (>12h) - pharmacies and wholesale distributors of medicines for human use through web service or health professionals, citizens, and associations representing citizens with illness can communicate these absences by email.
- Medicine shortages - Communication of situations of temporary, potential or actual unavailability of a given product presentation on the national market is carried out by marketing authorisation holders (AIM) in the Information System for the Assessment of Health Technologies (SiATS).

Whenever an AIM holder becomes aware of some restriction of market supply, potential or actual disruption, is obliged to notify the Infarmed at least two months in advance. Infarmed is the entity responsible for, together with MA holders, wholesale distributors and pharmacies,

taking the necessary measures so that patients are not deprived of their treatment or access to the medicine they need.

- Cessation of commercialisation - The communication of the permanent unavailability of a given product presentation on the national market is made by marketing authorisation holders via SiATS.

Authorisation to market medicines without a valid authorisation or registration in Portugal (SAR) - INFARMED may authorise for well-founded public health reasons, the marketing of medicinal products that do not benefit from a valid authorisation or registration in Portugal or that have not been the subject of a proper application for authorisation or registration. Authorisation to market medicines without a valid authorisation or registration in Portugal is only granted to medicinal products subject to a marketing authorisation valid in the Member State of origin.

Parallel Import Authorisation (AIP)
Parallel import consists of marketing a medicine from another Member State, similar to a medicine authorised in Portugal, by an entity other than the MA holder of the national medicine.

Parallel distribution (DP)
It consists of distributing a medicinal product, authorised by a centralised Community procedure, from one Member State to another by a distributor independent of the marketing authorisation holder.

The insulin case:
An extended period of unavailability of different insulins by Sanofi is estimated, which should start during May and extend until the end of this year. The National Commission on Pharmacy and Therapeutics of Infarmed (national medicine authority) published a set of guidelines to support the clinical decision of prescribing physicians and other health professionals in

substituting another insulin, which differs, however, in the form of presentation, concentration, pharmacokinetic profile and requires their administration device.

Doctors:

When thought from the doctors' side, new treatments with these drugs should not be started.

Timely insulin replacement should be promoted for patients being treated with these drugs.

Upon replacement, patients should be monitored more frequently in the first weeks of using the new treatment.

Patients and/or caregivers must be instructed in correctly handling the new administration device.

Pharmaceutical intervention:

Patients should contact the doctor for timely replacement.

Doctors should support patients in using the new administration device.

Doctors should clarify doubts about dosages, posology and possible adjustments to concomitant medication.

It is important to consistently monitor blood glucose levels during the early stages of replacement therapy with reinforcement and rigour.

Lastly, pharmaceutical reindustrialisation should be encouraged, and Europe's capacity to produce raw materials and improve literacy in Health should be increased.

**Poland** 🇵🇱

POLISH PHARMACEUTICAL STUDENTS' ASSOCIATION

Medicine shortages in Poland are influenced by a combination of factors, including dependence on Asian production, the impact of the flu epidemic, the ongoing COVID-19 pandemic, the war in Ukraine, and the energy crisis. These challenges have disrupted supply chains and violated the principle of international solidarity. In collaboration with the Ministry of Health, the pharmaceutical industry needs to address these issues through strategic planning, diversification of suppliers, and contingency measures. Ensuring a stable supply of medicines is essential to safeguarding patient access to vital medications.

Dependence on Asian production - According to 2014 and 2017 data, more than 70% of active ingredients come from China, with a few more per cent from India. It is now estimated that this could be as high as 80-90%.

The reason for the shortage of some APIs is also the observed winter and spring 2023 flu epidemic - which caused drug sales to increase after the first 15 days of December 2022 compared to the same period in 2021. In the case of prescribed drugs, by 12.8%, and OTC drugs by as much as 24.5%. And compared to data from the first 15 days of November 2022. - an increase of 20.9% for prescribed and 33% for OTC drugs, respectively. Another cause of drug shortages continues to be the COVID-19 pandemic.

The Polish Association of Employers in the Pharmaceutical Industry - National Drug Manufacturers, which represents 18 of the country's leading drug manufacturers. - As a result of production disruptions in local factories and global transportation, as well as increased demand for pharmaceuticals worldwide, the principle of international solidarity has been violated, which has translated into shortages of drugs and active substances, as the national drug manufacturers point out.

The drug market has also been affected by the war in Ukraine and the resulting energy crisis in Poland. The refugee crisis, in turn, has resulted in increased demand for medicines. In addition, the war caused a break in some supply chains - some medicines flowed into the EU via Odessa. The war in Ukraine resulted in an economic and energy crisis - there is practically

no industry in Poland that was not directly affected by this crisis; however, drug manufacturers cannot pass on increased production costs to customers due to prices agreed with the Ministry of Health.

Sometimes, the cause of drug shortages can be increased demand due to new product applications, as shown in Ozempic.

Poland has implemented several measures to address medicine shortages, including monitoring availability, publishing an anti-exposure list, establishing dedicated teams, and improving access to drug availability information. These initiatives demonstrate the government's commitment to ensuring a stable supply of medicines and enhancing the efficiency and effectiveness of the healthcare system. Continued efforts in monitoring, collaboration, and technology integration will be crucial in effectively addressing medicine shortages in Poland.

Action taken by government:

Monitoring the availability of medicines through cooperation with subordinate offices - Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL), National Health Fund (NFZ) and the e-Health Center - Integrated System Monitoring the Trade in Medicinal Products (ZSMOPL) and MERL.

The publication of the so-called anti-exposure list - a list of drugs, foodstuffs for particular nutritional purposes and medical devices most at risk of unavailability in the territory

also created the Team for counteracting shortages in the availability of medicinal products as a subsidiary body of the Minister of Health.

The Minister of Health has established a Team to assess interoperability in ICT systems and medical registries used in drug policy as a subsidiary body of the minister in charge of health.

To strengthen supervision of the drug market by integrating multiple information systems and exchanging data between them.

Work is underway to implement in the gabinet.gov.pl (Page where professionals wrote e-prescriptions) application access to information on the availability of drugs by persons authorised to issue prescriptions.

France

ANEPF ASSOCIATION NATIONALE DES ETUDIANTS EN PHARMACIE DE FRANCE

According to the French National Agency for the Safety of Medicines, more than 3,000 molecules were unavailable in France this winter.

Until now, shortages in France have concerned only cutting-edge treatments that are little known to the general public. The French National Agency for the Safety of Medicines (ANSM) has been recording shortages in France for around fifteen years. Between 2008 and 2018, drug shortages increased 20-fold, with some highly sought-after molecules in short supply.

The majority of shortages concern so-called mature drugs. These are drugs whose Marketing Authorisation is more than ten years old. This is because their exclusive patent rights are ending, making them cheaper and, therefore, less profitable and less attractive to the pharmaceutical industry. They very rarely concern innovative medicines since these are fairly profitable for companies.

Treatments for cancers, infections and nervous system disorders account for more than half of these shortages and are known as essential medicines.

The causes are multifactorial:

- Insufficient French production capacity.
- Increase in sales volume.
- The particularly low prices of drugs in France.
- Lack of raw material supply, and European dependence on Indian and Chinese production chains. Today, these countries are requisitioning their stock to meet their national needs.
- Lack of supply of packaging materials (with the war in Ukraine)
- Unforeseen fluctuations in the market, with doctors' prescriptions varying and not respecting standard dosages. These standard dosages can vary from one country to another, making it difficult for companies to produce boxes with an appropriate number that comply with the recommendations.
- Transport problems.
- Regulatory constraints with very high-quality standards (the increase in the level of technology required and the regulatory constraints applicable to the drugs produced

means that sites are specialised by the type of process and molecule manufactured. This explains why only one site is chosen for production, as it is the only one with the technological equipment and trained personnel. In this context, in the event of a problem on the production line that cannot be 100% avoided, the risk of disruption is very high from the outset.

What are the consequences for patients?

One French person in three has already had to deal with a shortage of medicines.

45% of people facing shortages have been forced to postpone, modify, abandon or stop their treatment. For example, bladder ablations have already been carried out because there are no drugs available to treat bladder cancer.

Delayed access to treatment has been observed in 59% of cases and even treatment cancellation in 39% of cases. This exposes patients to considerable risks and weakens healthcare systems. Not to mention the worsening of antibiotic resistance, the short- and long-term consequences for patients with chronic diseases, the loss of life expectancy in cases of cancer, and the time spent by healthcare professionals in finding alternatives.

Some patients exchange boxes of medicines for treatment or have even reached the stage where they stock up in anticipation and keep the boxes they no longer use to give to other patients.

In conclusion, France is heavily affected by shortages, and the government and all healthcare professionals and manufacturers must take action to reduce these shortages and their impact.

The French Medicines Agency (Agence du Médicament) and the French Directorate-General for Health have drawn up a "winter epidemic preparedness plan" (with, for example, the following recommendations: better control of the credibility of manufacturers' forecasts ahead of the winter season, for the most essential products and, in the event of a shortage, more reliable information for healthcare professionals and the public on the state of stocks at each stage of the supply chain) to ensure that there is no shortage of medicines, and therefore to monitor the stocks available in all specialities. In the "most critical" cases, "a white medicine plan will be developed". The aim is to anticipate the coming winter seasons better.

The government has drawn up a list of essential medicines assessed according to the risk of stress. It includes 450 medicines. Based on this list, specific work will be undertaken to guarantee better availability.

Within these 450 is a core list for which the production chain must be relocated. This shortlist includes 50 drugs, 25 of which will see their production relocated or significantly increased in France within five years—prevention strategy with vaccination and better prescription of medicines.

As for the next steps, in France, the social security financing bill is voted on every year, and this year, some of the measures concerned actions to reduce shortages in France. They have not been voted on yet, and they are being debated:

- Unit dispensing: The government wants to make it compulsory to dispense certain antibiotics individually in case of a shortage.
- Packaged dispensing: antibiotics if a diagnostic test is carried out.
- Creation of the status of "special officinal preparations." A helpful alternative in the event of shortages, the intention is to extend the authorisation for the production of certain medicines to dispensing pharmacists under the supervision of the ANSM.
- Ban antibiotic prescriptions via teleconsultation in the event of a shortage.
- Require the pharmaceutical industry to continue manufacturing mature drugs. However, if they can no longer do so, they must sell their marketing authorisation to another company. If there is no buyer, manufacturing will go to an industry designated by the State. This measure has been introduced to prevent manufacturing stoppages.

**Greece** 🇬🇷

Greece faces a chronic shortage of certain drugs as it exports them to other countries since it has the lowest prices for medicines in the EU, ensuring large profits for drug distributors. Therefore, certain medicines can give up to 15 times more profit to the pharmaceutical warehouse if they are available abroad through parallel exports than in a pharmacy in the Greek market.

According to the Panhellenic Pharmaceutical Association, there is a lack of medicines for chronic and severe diseases such as heart disease, respiratory diseases, osteoporosis, diabetes, epilepsy, neurological disorders, psychiatric illnesses and glaucoma. Shortages are found in medicines mainly concerning children, such as antibiotics and inhaled medicines. The outbreak of seasonal viruses, a lack of raw materials for the packaging of medicines, and low stock in the pharmaceutical warehouses have aggravated the problem. However, the current shortage in medicine, such as antibiotics and analgesics, is due to the global lack of raw materials, reduced production due to the pandemic, the energy crisis and supply chain issues.

Finally, the solution of generic drugs that many patients refuse due to unawareness could reduce healthcare costs. There is a widespread belief that if consumers are made aware of what generics are and of the controls that must be submitted to be released on the market in periods of shortages, we will not face such a severe issue of treatments. On a positive note, Greece has a wide production of pharmaceuticals and can supply patients with generics in most cases.

Greece has taken several measures to address medicine shortages, including calling for European Commission intervention, adjusting the prices of low-cost drugs, implementing an app to register shortages, and prioritising the supply of medicines without generic alternatives. These efforts demonstrate the Greek government's commitment to ensuring the availability of essential medicines and addressing shortages at both national and European levels. Continued collaboration with relevant stakeholders and implementation of comprehensive policies will be crucial in effectively tackling medicine shortages in Greece.

Greek Health Minister Thanos Plevris has called on the European Commission to intervene in medicine shortages.

According to the Greek Health Ministry, in January 2023, Plevris sent a letter to the commissioner for health, Stella Kyriakides, asking for "a central policy at the level of the European Union for the problem of shortages of medicines faced by all member-states of the European Union".

He drew attention to the fact that member-states are trying to deal with this problem through internal procedures. Still, there must be centralised policies at the EU level to deal with the situation.

The Greek Health Ministry has also announced a series of measures to address the shortages. These include an increase in the prices of very low-cost drugs so that they are promoted in the Greek market and not in the international market, where their prices are much higher.

The Greek National Organization for Medicines (EOF) has established an app for registering medicine shortages per drug and follows up by performing investigations on the producing industries and storage units. For drugs that suffer from shortages, storage units are to send a board with their brand name and quantity to the EOF to communicate their numbers to community pharmacies. Parallel exports of these drugs are also banned for as long as it is needed; continuing checks on wholesalers are made to ensure the exports are not going ahead with medications needed in Greece and that they have enough stock for the Greek market, particularly for fever-reducing drugs and for children's medication. The EOF is also committed to prioritising the supply of medicines for which no generic alternatives exist. The Institute of Pharmaceutical Research and Technology, part of the EOF, conducts urgent imports of this type of medicine. It also covers individual cases through Insurance Funds and penalties when there is an implicit need to supply patients with these medicines.

**Romania** 🇷🇴

Romania has proposed several measures to address medicine shortages, including eliminating non-existent reference prices, equalising and reducing the claw-back tax, actualising prices for low-cost molecules, maintaining communication with patient organisations, and regularly updating the list of reimbursed drugs. These measures aim to improve pricing accuracy, support pharmaceutical companies, enhance patient access to medicines, and ensure a more sustainable and efficient pharmaceutical market in Romania. Continued collaboration among stakeholders and effective implementation of these proposals will be crucial in addressing medicine shortages in the country.

Measures proposed:

- Eliminating the products that established the price of reference and that weren't on the market in Romania. That was a situation that led to the disappearance of all the drugs from the same category because, as a reference, they had a minimal price for a non-existent product.
- Equality and reduction of the claw-back tax because it was differentiated; some paid 15% and others 20% (referring to the generic production). The alienation of the claw-back tax meant a uniformisation of 15%, which benefited all drug producers and reduced the claw-back tax by 5%.
- Actualisation of the prices for the very cheap molecules. The products with a value of up to 50 lei, meaning thousands of products from the market, will support a price rise between 7% and 14% to support production companies with high production costs.
- Maintaining communication with the patient organisations to improve patient access to drugs.
- Proposal of actualisation of the reimbursed drugs 3 or 4 times a year, including all of the drugs that have the approval of the National Agency of Drugs and Medical Devices (ANMDM).

## Conclusion and solutions proposed

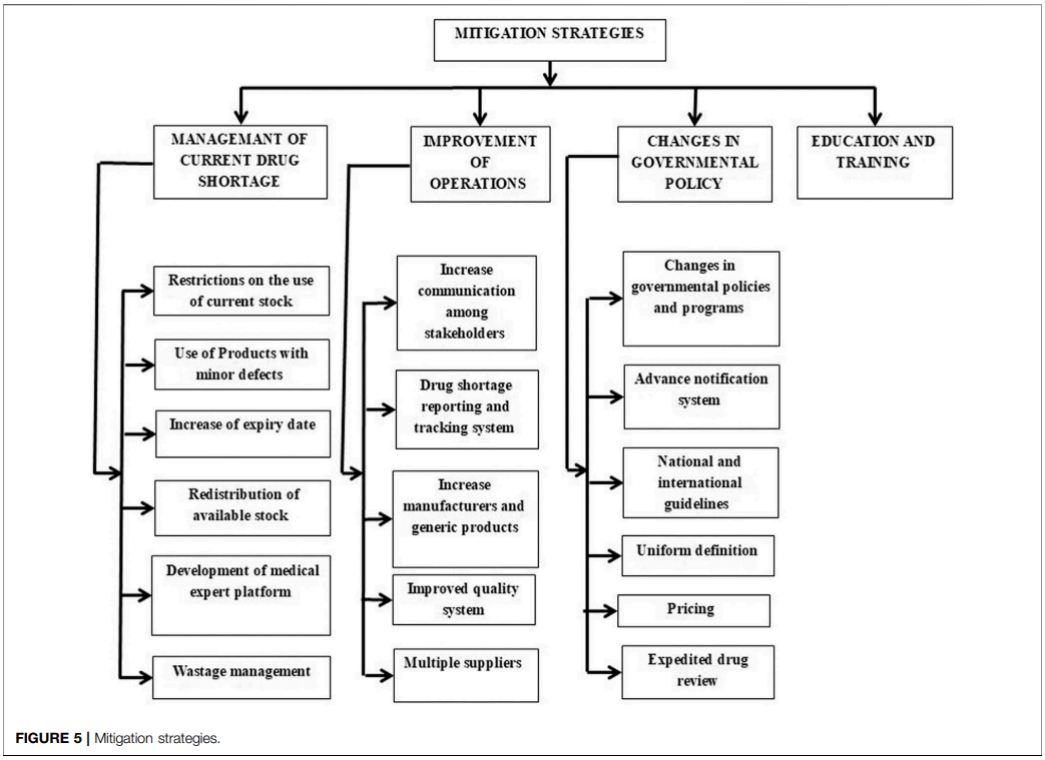



**FIGURE 5 |** Mitigation strategies.

The World Health Organization (WHO) has taken significant steps to combat drug shortages globally by establishing comprehensive mitigation strategies. These strategies operate at four distinct levels, encompassing various approaches and actions to overcome drug shortages.

Firstly, the WHO has focused on immediate solutions to tackle the current shortage of essential drugs. This involves implementing workarounds and alternative measures to ensure critical medications are available to those in need. These emergency interventions may include sourcing medicines from alternative suppliers, promoting therapeutically equivalent substitutes, or redistributing existing stocks to areas experiencing shortages.

Secondly, the WHO recognises the importance of operational improvements to mitigate the risk of future drug shortages. This entails implementing measures to enhance the efficiency and resilience of the global drug supply chain. By improving manufacturing processes, optimising inventory management systems, and enhancing distribution networks, the aim is to minimise the likelihood and impact of drug shortages in the future.

Thirdly, the WHO acknowledges the role of governmental policies in addressing drug shortages. The organisation advocates for changes in policies and regulations at the national

and international levels to ensure better management and prevention of drug shortages. This may include streamlining regulatory processes, facilitating the importation of essential medications, and fostering collaboration among governments to address supply chain disruptions.

Lastly, the WHO emphasises the importance of education and training for all health professionals regarding effectively managing drug shortages. By equipping healthcare providers with knowledge and skills to handle and navigate drug shortages, the WHO aims to improve preparedness and response capabilities at the frontline. This includes training on alternative treatment options, rationing strategies, and effective communication with patients and other healthcare stakeholders.

By implementing these multi-level strategies, the WHO aims to tackle drug shortages comprehensively and address the complex challenges associated with global medication supply. The organisation's efforts encompass immediate actions, long-term improvements, policy changes, and education to ensure the availability and accessibility of essential drugs for all populations worldwide.

## Call for Action

It is essential to recognise that access to treatment is a fundamental human right, and, consequently, medicines must be accessible to the entire population. The current issue of medicine shortage demands attention from all concerned parties, and appropriate measures must be taken to guarantee that everyone has equal access to medicines.

The European Union (EU) has recently published a list of critical medicines, and it is now time to take appropriate actions based on this list. A new approach is needed to tackle medicine shortages in the EU better. During the 2023 European Health Emergency Preparedness and Response Authority (HERA) Conference, Commission President Ursula von der Leyen stated, "Together, we will identify the best measures to prevent and address shortages, such as diversification, de-risking, and increasing manufacturing in Europe" .

It is encouraging to witness the efforts by authorities and organisations to address the ongoing challenges arising from the current situation. EPSA is committed to giving its support to these initiatives, as well as to continue advocating for the pressing matter of medicine

shortages. EPSA stands ready to collaborate with stakeholders in the pursuit of effective solutions and to contribute its expertise and resources.

With the current situation in consideration, EPSA believes the following points should be adopted/addressed:

**EPSA calls upon the European stakeholders to:**

- Have a robust emergency response and plan for future emergencies to enhance reactivity and adaptability.
- Identify the countries most endangered by the shortages and create adequate measures to help them.
- Consult the relevant Healthcare associations when developing a list of critical medicines.
- Initiate joint procurement, if necessary, to help tackle inequalities between countries regarding access to medicines.
- Involve pharmacists in dealing with medicine shortages and harmonising their role to make them the central actors of the collaborations.
- Support pharmacists and smoothening the complex procedures for dealing with medicine shortages, reducing administrative burden and difficulties reaching out to supplies.
- Smoothen the declaration of shortages for pharmacists and healthcare professionals.
- Increase the production of API and vulnerable substances in Europe.

**EPSA calls upon the EU Member States, Ministries of Health, Ministries of Education and Faculties of Pharmacy in Europe to:**

- Increase the workforce capacity in hospitals, community pharmacies, and industries to communicate and collaborate to anticipate shortages.
- Develop efficient tools such as improving national reporting systems and also stimulating the performing of risk assessment to enable pharmacists to report any shortages they may encounter promptly.
- Enhance collaborations with stakeholders and better communication with the patients.

- Implement practical sessions for the healthcare students to be aware of and able to explain shortages to the patients.
- To facilitate access to correct information regarding medicine shortages to patients.
- To encourage healthcare workers to inform patients about generic drugs when prescribing medications.
- Work on implementing policies that reinforce the need for a more competitive market in the production of medicines and encourage collaboration between the State and stakeholders to optimise the production of medicines.

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## About EPSA

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