PGEU
European Community Pharmacists

Position paper on medicine shortages

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Executive summary

For over a decade PGEU has been publishing an annual medicine shortage report and over the years we saw the number of shortages growing progressively worse in all countries.

Despite continued pharmacists' efforts to find solutions, we witness a significant negative impact on patients' health and a concerning erosion of patients' trust in the healthcare system. The unavailability of a medicine causes inconvenience and distress to the patient, and it can lead to discontinuation of treatment, increased co-payments, medication errors and increased the risk of adverse events.

This situation generates frustration and stress also for pharmacists and imposes an additional administrative burden on pharmacies' daily work. In 2023 we estimated that every pharmacy across the EU spent on average close to 10 hours per week dealing with medicine shortages. This time has tripled over the last 10 years; precious time which could be devoted to other useful tasks such as providing advanced pharmacy services like vaccination.

To tackle this crucial challenge, PGEU calls for effective policy measures to **strengthen supply resilience** and to allow for **shortages mitigation**, including:

- The implementation of a **common definition of medicine shortages** across the EU and across the full supply chain to better identify and evaluate medicine shortages and to accelerate a coordinated response.

- **Timely reporting by marketing authorization holders** to allow community pharmacists to be informed about future and ongoing shortages and their expected duration and find solutions.

- **Allowing community pharmacists to make full use of their skills, knowledge and experience to find alternative treatments for their patients,** being it by dispensing the same medicine in a different formulation or pack size, performing generic substitution or therapeutic substitution, through an adequate shared decision-making process or compounding.

- **Enhancing transparency and authorities' oversight of the upstream supply chain** and ensuring that manufacturers have **robust shortages prevention and mitigation plans** in place.

- **Fostering EU solidarity and coordination among Member States** to facilitate the redistribution of medicines to those in need.

- **Optimizing European and national stockpile management** by progressively building rolling stocks, making them available to the Solidarity Mechanism, to mitigate the impact of shortages without generating unnecessary waste.

- **Better using procurement to secure long-term availability**, encouraging the use of MEAT criteria and splitting tender awards in procurement processes to achieve **supply chain**

diversity and **reduce downward price pressure** while **improving demand forecasting** from public sources and buyers.

- Clarifying and better **enforcing manufacturers' and wholesale distributors' supply obligations**.
- **Evaluating and addressing the impact of parallel trade and manufacturer-initiated supply quotas and allocations.**

Medicine shortages, a chronic issue

Medicine shortages are on the rise in Europe. In the last decade, European community pharmacists have consistently reported [1, 2] a worsening of the situation in all countries. The COVID-19 pandemic has shone light into medicine supply chain fragilities and acted as a catalyst to build momentum for action both at national and at European level.

Community pharmacists are at the very end of the pharmaceutical supply chain and are the face of the problem for patients. Repeated medicine shortages, impacting all medicine classes in all European countries[3], have caused distress and inconvenience to patients at best, but also discontinuation of treatment, increased co-payments, medication errors and increased the risk of adverse events. Patients' trust in their healthcare systems has been eroded by this chronic issue. Furthermore, the increasing number of medicine shortages raises stress for pharmacy staff and imposes a significant additional administrative burden on pharmacies' daily work.

In 2023 pharmacies across the EU spent on average almost 10 hours per week dealing with medicine shortages. This time has tripled over the last 10 years; precious time which could have been devoted to other useful tasks such as implementing pharmacy-led health services for patients in support of the health systems. The burden of managing medicine shortages is amplified due to the concurrent healthcare workforce shortage resulting in increased pressure and stress on pharmacy teams. In addition, pharmacists frequently suffer financial losses when finding alternative solutions for their patients, for example, by not receiving the full reimbursement for these medicines.

The root causes of medicine shortages in Europe are diverse and multi-factorial[4,5], and despite several attempts to characterize them and assess their relative importance, there is still a limited understanding of the main drivers of a shortage. Evidence suggests that medicine shortages can result from different economic, manufacturing, or regulatory causes, such as:

- The increasingly globalised nature of pharmaceutical manufacturing, including Active Pharmaceutical Ingredients (API), with production concentrated in only a few sites distributed around the world, the majority of them outside the EU.
- Shifts in demand, resulting from longer term factors such as demographic change, but also short-term factors such as tendering of medicines, which

[1] https://www.rtbf.be/article/les-pharmaciens-tirent-la-sonnette-d-alarme-une-grosse-penurie-de-medicaments-10062023;
https://nos.nl/artikel/2267384-weer-meer-medicijnen-niet-leverbaar;
https://www.euronews.com/health/2022/12/06/europe-medicine-shortages-where-why-low-drug-supplies-from-amoxicillin-to-paracetamol;
https://www.politico.eu/article/health-care-pharma-why-is-europe-running-out-of-medicines-and-whats-being-done-about-it/;
https://www.rte.ie/brainstorm/2023/0710/1393697-medicine-shortages-ireland-supply-chain-issues/;
https://www.lesoir.be/560292/article/2024-01-10/la-penurie-dozempic-medicament-contre-le-diabete-prolongee-au-moins-jusque-juin

[2] https://www.pgeu.eu/medicine-shortages/

[3] https://www.pgeu.eu/publications/pgeu-medicine-shortages-report-2023/

[4] OECD (2024), Securing Medical Supply Chains in a Post-Pandemic World, OECD Health Policy Studies, OECD Publishing, Paris, https://doi.org/10.1787/119c59d9-en

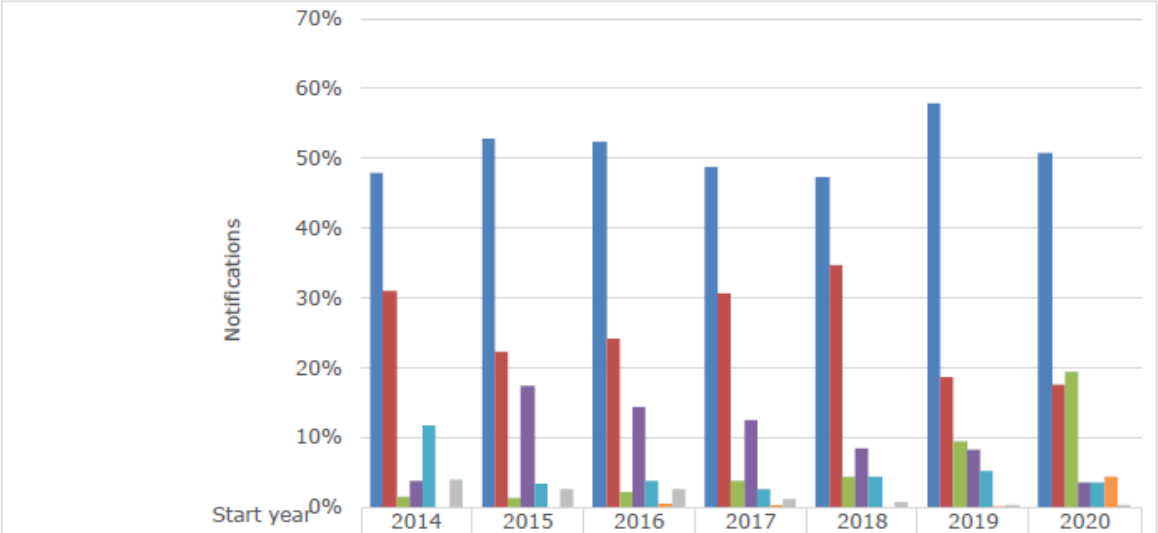
[5] European Commission, Directorate-General for Health and Food Safety, Jongh, T., Becker, D., Boulestreau, M. et al., *Future-proofing pharmaceutical legislation – Study on medicine shortages – Final report (revised)*, Publications Office of the European Union, 2021, https://data.europa.eu/doi/10.2875/211485

leads to difficulties in providing sufficient quantities of medicines for some markets.

- Pricing strategies, both low and high, and regulatory changes that in some cases may have an impact on supply.
- The imposition of fixed quotas or allocation of medicines by the pharmaceutical industry are often not sufficient in relation to patients' actual needs and require significant workload from all supply chain actors in their careful management.
- The shifting wholesaler models that are moving away from the traditional role of the full line wholesalers to short line wholesalers and Direct to Pharmacy (DTP) schemes in some markets.
- Inconsistencies and/or ineffectiveness of public service obligation and minimum national stock keeping requirements in some countries.
- The lack of priority given to smaller markets.
- The effects of the European internal market dynamics (e.g. exports).

According to a European Commission study published in 2021[5], most reported causes of medicine shortages appear to be related to quality and manufacturing issues, and this has been a steady trend since 2014.

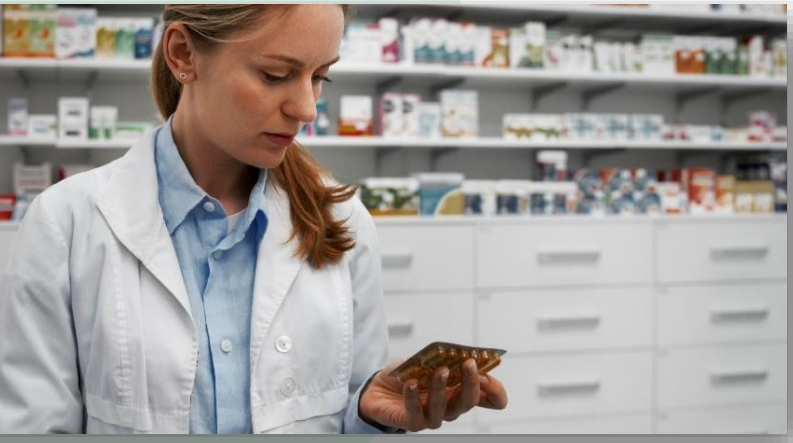
Figure 12 Time trends in reported root causes of shortages (2014-2020)



Start year	2014	2015	2016	2017	2018	2019	2020
Quality & Manufacturing issues	48%	53%	52%	49%	47%	58%	51%
Commercial reasons	31%	22%	24%	31%	35%	19%	18%
Unexpected increased demand	2%	1%	2%	4%	4%	10%	19%
Distribution issues	4%	17%	14%	13%	9%	8%	4%
Regulatory issues	12%	3%	4%	3%	4%	5%	4%
Unpredicted major events or natural disasters	0%	0%	1%	0%	0%	0%	4%
Other issues	4%	3%	3%	1%	1%	0%	0%

Source: Technopolis Group, based on notifications in national shortage registries. Share expressed as the number of shortages reporting a particular root cause relative to all shortages with a reported root cause that year. The period 2014-2020 was chosen as prior to this, information on root causes was too sporadic for proper trend analysis.

As the number of medicine shortages grows, so does the awareness about their frequency, consequences, and root causes. Awareness draws public and political attention and is propelling several initiatives in an attempt to find workable solutions. As part of a broader Pharmaceutical Strategy for Europe, the European Commission organized the Structured dialogue on security of medicines supply during 2021. While the work developed acted as the precursor to several measures currently being discussed, the outcomes[6] were lacking actionable solutions as it was clearly demonstrated by the shortages of antibiotics[7] during the winter 2022/2023. This issue compelled 22 Member States to co-sign a non-paper on Improving the security of medicines supply in Europe in 2023. In this non-paper[8] countries introduced the concept of an EU solidarity mechanism, reinforced the call for a European list of critical medicines and called on the European Commission to advance a Critical Medicines Act. This clear call to action is in parallel with the proposals advanced by the European Commission in its reform of the EU pharmaceutical legislation, the first version of the Union list of critical medicines published in late 2023, the European Commission Communication on medicine shortages[9], and the constitution of the Critical Medicines Alliance. The Alliance debuted its work in Spring 2024 and provides the background for the various actions at EU being developed to address the issue of medicine shortages in Europe.



[6] Staff Working Document on Vulnerabilities of the global supply chains of medicines – Structured Dialogue on the security of medicines supply
[7] European Medicines Agency, Shortages of amoxicillin and amoxicillin/clavulanic acid, EMA/27040/2023 Rev.1
[8] Non-paper – Improving the security of medicines supply in Europe – (BE, AT, NL, LU, HU, CZ, ES, FR, DE, EE, SI, RO, LV, LT, EL, MT, PL, IT, PT), 2 May 2023
[9] European Commission, Communication on addressing medicine shortages in the EU, October 2023, COM(2023) 672

Common understanding of medicine shortages

Across countries and institutions, medicine shortages are identified through a range of diverging definitions[10]. Furthermore, only 12 of the 26 countries that responded to the 2023 PGEU Shortages Survey mention that there is a commonly agreed definition of medicine shortages nationally, with only 5 referring that the definition is part of the national legislation3.

This variation in terms of definition, has compelled several actors to attempt to find a harmonised definition to allow a common understanding of the issue at European level. In 2019, the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) defined a medicine shortage, for the purpose of notification and detection as follows:

'A shortage of a medicinal product for human or veterinary use occurs when supply does not meet demand at a national level'.[11]

More recently, as part of the European Health Union legislative package, the Regulation (EU) 2022/123 on a reinforced role for the EMA enshrined an EU definition of a shortage in European Law:

'shortage' means a situation in which the supply of a medicinal product that is authorised and placed on the market in a Member State or of a CE-marked medical device does not meet demand for that medicinal product or medical device at a national level, whatever the cause'

Furthermore, demand is defined in relation to the request of healthcare professionals or patients in response to a clinical need, that is only satisfied if the medicine or medical device needed can be acquired in appropriate time and in sufficient quantity. Similarly, the supply is defined by the total quantity of a given medicine or medical device placed on the market by the marketing authorization holder or manufacturer.

In our annual shortages reports we defined a shortage as *every (temporarily) inability for a community pharmacist 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.* We also noted that this definition could be extended for medical devices. This definition is generally aligned with the Regulation (EU) 2022/123, except for national distribution issues that are not entirely captured in the regulation.

The broad range of definitions frequently fails to capture the full impact of the unavailability of medicines on patients, specifically impact on individual patients for whom even a short-term interruption of supply may signify treatment interruption, with the associated negative health consequences, distress and inconvenience.

[10] De Weerdt, Elfi et al. "Toward a European definition for a drug shortage: a qualitative study." Frontiers in pharmacology vol. 6 253. 30 Oct. 2015, available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4626567/

[11] EMA/HMA, Guidance on detection and notification of shortages of medicinal products for Marketing Authorisation Holders (MAHs) in the Union (EEA), July 2019, EMA/674304/2018

To empower the EMA work on medicine shortages, the Medicine Shortages Steering Group (MSSG) and the Solidarity Mechanism[12] among Member states, it will be necessary that a common definition of shortages is implemented, together with a clear understanding of what constitutes a *critical shortage*. Furthermore, to ensure the consistent monitoring of medicine shortages via the European Shortages Monitoring Platform (ESMP), it will be paramount to harmonise the shortage definition and reporting across Member States, especially considering the European Commission's proposal for a reform of the EU pharmaceutical legislation that includes provisions to expand the use of the ESMP.

Finally, to ensure agile information exchange between the EMA and Member States regarding medicinal products, the agency should fully implement the SPOR (Substance, product, organisation and referential) data following ISO IDMP standards to quickly identify medicines and find suitable alternative sources via the Solidarity Mechanism.

Recommendations

- Harmonise and adopt a common definition for medicines and medical device shortages, which considers the impact on patients. This definition should be implemented at European and national level, in an effort to better identify and evaluate impending and ongoing medicine shortages and to accelerate a coordinated response at European level.

- Empower the MSSG to monitor and respond to medicines shortages by fully leveraging the ESMP, SPOR and ISO IDMP to strengthen and simplify the EU Solidarity Mechanism.

- Define and establish a European standardised coding and identification system for all raw materials utilized in the medicines supply chain, including active pharmaceutical ingredients, their precursors, broad groups of medicinal products, and individual medicinal products in order to enable an objective quantification and reporting of supply issues, using appropriate metrics.

[12] EMA, MSSG Solidarity Mechanism, October 2023, EMA/323316/2023

Early warning and communication

While the first to experience the consequences of a shortage are frequently pharmacists, marketing authorization holders (MAH) are typically aware of supply constraints before they lead to a shortage. It is thus crucial to have effective communication channels for MAHs with competent authorities and policies to encourage early notification of expected or impending shortages.

As noted in a study of the European Commission, shortage reporting criteria are not harmonised in Europe nor are the reporting standards and systems for notification or the information requested by these systems. Regarding the information to be provided, the EMA and HMA have issued clear guidance, which include the expected date of the beginning of a shortage, its expected duration, its anticipated impact, and its root cause(s)[11]. The information to be provided by MAHs should be as detailed as possible and in a harmonised format to allow a complete leveraging of the ESMP when it becomes fully operational in 2025 to avoid duplication and asymmetries of reporting.

The information provided to national authorities should be assessed and then shared with impacted stakeholders, namely pharmacists. A common source of frustration among community pharmacists is the lack of communication about a shortage, its severity, potential alternatives and how long it will last. This information, if provided in a timely and efficient manner, would facilitate pharmacists to plan and manage supply appropriately, source necessary alternatives and by doing so, serve their patients better, minimising negative health outcomes. Specifically, it is crucial that pharmacists are provided with information about impending shortages, along with the available alternatives they can provide to their patients, the expected duration of the shortage and its causes. This information is not only helpful for pharmacists to be able to find solutions for their patients, but also to inform and empower patients about the shortage impacting them.

In this respect, the proposal for the reform of the EU pharmaceutical legislation[13] introduces important and useful tools to address medicine shortages, including the earlier notification of anticipated supply disruptions, marketing cessations and withdrawal notifications. Community pharmacists are supportive of strengthening Member States' coordination in monitoring and mitigating shortages, with stronger involvement of the European Medicines Agency (EMA) and a key role for the Executive Steering Group on Shortages and Safety of Medicinal Products, also known as Medicine Shortages Steering Group (MSSG) along with the expansion of the use of the ESMP to facilitate the collection of information on shortages, supply and demand for medicinal products, including information on marketing status and marketing cessations.

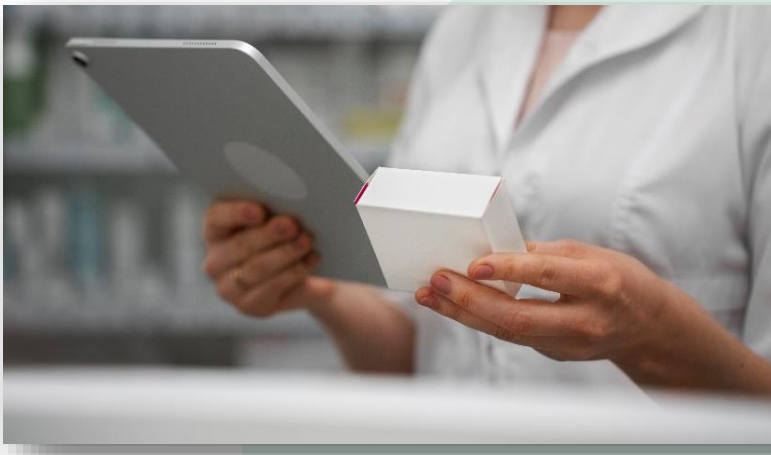
The European Medicines Agency and Heads of Medicines Agencies (EMA/HMA) task force on availability of authorised medicines for human and veterinary use (TF AAM), issued guidance

[13]https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en

on communication to the public on medicines' availability issues [14] outlining the information and timing of the communication of medicine shortages to healthcare professionals and the general public. In the European Commission proposal for the reform of the pharmaceutical legislation, there is a need for clearer provisions in this direction that offer more transparent and timely communication to the impacted stakeholders in a rational and phased manner. More recently, the same EMA/HMA task force issued good practice guidance for patient and healthcare professional organisations on the prevention of shortages of medicines for human use [15] outlining, among others the important role of healthcare professional organisations in detecting and reporting shortages.

It is important to ensure that information regarding ongoing shortages not only reaches pharmacists but also reaches prescribers to facilitate them to select alternative treatment for patients. This is already a practice in some European countries, where this information is included directly on prescription software, reducing the distress and inconvenience for patients [16] . Similarly, when patients are prescribed a medicine that is in short supply, access to electronic health records by their pharmacist is very helpful to find appropriate alternatives as part of a shared decision-making process with prescribers and patients, in accordance with national protocols.

In addition to reporting of shortages by manufacturers, reporting systems should be open to reports from all medicine supply chain stakeholders (including community pharmacists). The European Commission's proposal for reform of the EU pharmaceutical legislation includes provisions that foresee the possibility for supply chain actors to report medicine shortages to competent authorities, supporting that the information reported by these actors provides important insight into medicine shortages. These reports can then be interpreted as signals of potential medicine shortages and be periodically assessed by the national competent authorities (NCA) to monitor, detect or even prevent medicine shortages. Some countries, such as Denmark, Poland, Romania and Czech Republic have implemented systems for pharmacy stock reporting, either for a specified list of medicines or all prescription medicines available in pharmacies. While this approach has limited usefulness for medicine shortage prevention of monitoring, if implemented, it should be done in a simple fully digitalized manner and should not add to the workload of pharmacists.



[14] EMA/HMA TF AAM, Good practice guidance for communication to the public on medicines' availability issues, July 2019, EMA/632473/2018
[15] EMA/HMA TF AAM, Good practice guidance for patient and healthcare professional organisations on the prevention of shortages of medicines for human use, May 2022, EMA/397143/2020
[16] Pharmaceutical Committee 101st Meeting Summary Record, November 2023, PHARM 843

Recommendations

- Harmonise and standardise reporting systems, and information necessary for MAHs to notify ongoing and future shortages while encouraging detailed reporting and avoiding duplication.
- Ensure effective communication frameworks, allowing pharmacists to be informed of future and ongoing shortages and their expected duration.
- Leverage digital tools (e.g. prescribing software) and electronic health records to minimise impact of medicine shortages on patients and effectively find and allow communication of appropriate treatment alternatives between healthcare professionals.
- Implement robust reporting systems that allow pharmacists and other supply chain stakeholders to report medicine shortages.

Best practices

In the **Netherlands**, Farmanco[17], established by KNMP (the Royal Dutch Pharmacists Association) is a medicine shortage reporting system that is open to reports from manufacturers, wholesalers, pharmacists, other healthcare professionals and patients, and allows public access to the information. In addition, the KNMP has a *Supply Problems Monitor*[18] that contains data from the four largest full-line wholesalers in the Netherlands, listing medicines that cannot be immediately supplied by wholesalers.

In **France**, supply chain actors (manufacturers, wholesalers, community and hospital pharmacists) can notify shortages experienced at their respective level, both top-down and bottom-up through the electronic 'DP-Ruptures' system[19]. This automated system, developed by the French Chamber of Pharmacists, also connects the French Medicines Agency ANSM allowing for efficient exchange of information with supply chain stakeholders.

In **Slovakia**, the Chamber of Pharmacists (Slovenská Lekárenská Komora – SLK) runs a medicine shortages database and independently monitors and analyses the situation in pharmacies.[20]

[17] https://farmanco.knmp.nl/
[18] https://www.sfk.nl/rapportages/info-pagina/management/monitor-leveringsproblemen
[19] http://www.ordre.pharmacien.fr/Le-Dossier-Pharmaceutique/Ruptures-d-approvisionnement-et-DP-Ruptures
[20] Bochenek T, et al. Systemic Measures and Legislative and Organizational Frameworks Aimed at Preventing or Mitigating Drug Shortages in 28 European and Western Asian Countries. Front Pharmacol. 2018 Jan 18;8:942. doi: 10.3389/fphar.2017.00942.

In **Spain**, the Information Centre on Supply of Medicines (CISMED),**Erro! Marcador não definido.** established by the Spanish General Pharmaceutical Council (GPC) manages information about medicines not delivered to pharmacies by wholesalers which is sent automatically by pharmacies to the regional pharmaceutical councils and then processed by the GPC, who then reports the information to the National Competent Authority. The GPC also created FarmaHelp, an application that allows pharmacies to support patients with finding medicines in short supply that may still be available in nearby pharmacies. In 2023, pharmacists were able to offer patients a solution 7 out of 10 times with the use of FarmaHelp.[21]

In **Portugal**, the National Association of Pharmacies (ANF) set up a system that automatically registers information on medicines not delivered to pharmacies by wholesalers[13]. The information is used by CEFAR (centre for health research and evaluation) to produce a report quarterly and shared with the national agency (Infarmed). This system is voluntary and complementary to the shortages reporting system set up and managed by Infarmed.

In **Belgium,** the PharmaStatus[22] platform is developed, supported and maintained by the competent authority (AFMPS/FAGG). The platform not only reports shortages but is also implemented in several legislations as the official source of shortage information to enhance and optimise their management, e.g. by allowing pharmacists to substitute medicines in short supply or to compound a magistral formula to ensure treatment continuity.

In 2019-2020, a **Digital Health Europe Twinning project**[23] led by GPC and funded by the European Commission, brought together national organisations from Italy, France, Portugal and Spain to exchange information on supply issues detected during this period. This project was recognised as one of the Best Innovative Practices in the European Union and took CISMED as a reference. In 2022, GPC started a second phase of the project aiming at harmonising pharmacy-based shortage reporting for early detection, involving organisations from Germany, Ireland, the Netherlands, Portugal and Spain.

[21] https://www.farmaceuticos.com/internacional/news/farmahelp-app-provides-more-than-10000-pharmacies-to-help-patients-locate-missing-medicines/
[22] https://pharmastatus.be
[23] https://digitalhealtheurope.eu/twinnings/dhe-twinning-results/cismed/

Empowering pharmacists to find solutions for patients

The type of solutions community pharmacists can offer to patients in case of a shortage differs between European countries as a result of national legislation and regulations. They include:

- *Dosage/strength/formulation substitution*

This means substituting a medicine for another with the same active substance, but with different dosage, strength and/or pharmaceutical form, making the necessary and appropriate adjustments to posology to achieve the same therapeutic effects. For example, in Spain, during the shortage of paediatric antibiotic formulations in the winter of 2022/2023 community pharmacists were allowed to preform dosage and formulation substitution to mitigate the ongoing shortage[24].

- *Generic substitution*

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

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

In the very few countries where pharmacists cannot perform generic substitution the consequences of medicine shortages are felt more acutely by patients.

- *Therapeutic substitution*

Therapeutic substation is the practice of exchanging, at pharmacy level, one medicine for another with a different active substance while retaining the therapeutic intent, in consultation with the prescriber and patient or in accordance with national/local protocols.

Currently, in the few EU countries where therapeutic substitution is permitted in case of medicine shortages, it is facilitated in consultation with the prescriber and patient. In early 2019, in the UK, changes to the legislation allowed the Government to use Serious Shortage Protocols (SSPs) in the event of a serious shortage of medicine. These protocols allow UK pharmacists to perform therapeutic substitution, without consultation with prescriber, amongst other options, as a solution to manage the medicine shortage [25] . Pharmacists in France will be allowed to perform therapeutic substitution without

[24] https://www.aemps.gob.es/informa/la-aemps-emite-recomendaciones-para-paliar-los-problemas-de-suministro-con-las-suspensiones-pediatricas-de-amoxicilina-250mg-5ml/

[25] https://psnc.org.uk/contract-it/brexit-and-community-pharmacy/serious-shortage-protocols-ssps/

prescribers' approval. This measure is part of the national shortages strategy[26], and it will be possible based on specific recommendations and protocols from the medicines agency (ANSM) and health authority (HAS), establishing matching lists for prescribers and table of equivalences for pharmacists. Similarly, in Ireland there is an ongoing legislative process to facilitate a medicine shortage protocol that will provide for therapeutic substitution by a pharmacist in limited circumstances when a medicine is in short supply.

In most European countries, therapeutic substitution by community pharmacists is still not legally allowed. In these countries pharmacists cannot facilitate patients in need, with an alternative medicine in case the medicine prescribed do not have a generic substitute, although they have the most appropriate professional skills and medicines knowledge. This requires pharmacists to contact the prescriber and sometimes patients have to return to their prescribing doctor in order to obtain a new prescription for the available alternatives, causing a significant burden and delay in treatment for patients already in a fragile position. It also adds a considerable administrative burden on pharmacists and results in frustration for patients and pharmacy staff in case the alternative cannot be found immediately.

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

- Compounding

In certain circumstances it may be possible for pharmacists to compound medicines in short supply. To ensure this mitigation option remains available it is important to stimulate and encourage pharmaceutical compounding in community pharmacies and to have the necessary raw materials available. Specifically, it will be relevant to ensure the ability of Member States to organise pharmaceutical compounding as it best suites their health systems in the revision of the pharmaceutical legislation. In addition, when the need arises, it will be important to implement regulatory flexibilities to allow for magistral preparations to be prepared in advance during a shortage period. These flexibilities are crucial to ensure that patients can access to their compounded alternative in a timely manner. Furthermore, in the case of reimbursed medicines, patients should not be imposed higher out-of-pocket

[26] https://www.ordre.pharmacien.fr/les-communications/focus-sur/les-actualites/penuries-la-feuille-de-route-ministerielle-2024-2027

payments for these medicines than they would for the medicine in short supply.

For example, in France there are "special" hospital and pharmacy formulae part of the strategy to address medicine shortages. The 2024 Health and Budget Law [27] allows authorized pharmacies to compound "special officinal preparations" during shortages or serious health threats, ensuring patients continue to have access to medicines in the event of shortages or discontinuation of the industrial preparations. This measure is granted on an exceptional and temporary basis by the medicines agency (ANSM) or the Minister of Health.

- Searching the medicines from an alternative source

In some countries, pharmacists can source medicines in short supply from alternative sources, namely by importing medicines from other Member States. This solution is not applicable to most cases and requires significant administrative work to ensure patients can still receive their treatment, however, the patient often is confronted with higher co-payments and in some cases has to pay the full price of the medicine. In some other cases, it falls in part on the pharmacy to cover this price differential.

Over the last decade, the time pharmacists spent finding solutions for patients whose medicines were unavailable has consistently increased. While the time devoted to mitigating medicine shortages is important to ensure patients receive treatment, the true impact of this increasing workload has not been appropriately acknowledged. First, this forces a diversion of time from other important tasks such as the development of pharmacy services with health benefits for patients. Second, the employment of resources and time is not financially neutral for pharmacies, that frequently absorb part of the cost of the shortage.

Recommendations

- Allow pharmacists to perform therapeutic, strength, formulation or dosage substitution, when applicable according to national legislation, in a shared decision-making process with prescribers and patients, when necessary and in case of medicine shortages, for example through dispensing protocols.

- Ensure pharmacists can perform generic substitution. Allow pharmacists to substitute also interchangeable biologic medicines in case of medicine shortages.

[27] https://www.ordre.pharmacien.fr/les-communications/focus-sur/les-actualites/plfss-2024-ce-qu-il-faut-en-retenir

- Resort to pharmaceutical compounding to mitigate medicine shortages by implementing regulatory flexibilities allowing pharmacists to compound in advance in such cases.

- Ensure that alternative treatments found by pharmacists as a response to a medicine shortage do not result in patient inconvenience or additional co-payments.

Fostering EU solidarity

Recently, the European Commission and the Health Emergency Preparedness and Response (HERA) have launched the Critical Medicines Alliance, *a consultative mechanism which brings together all relevant stakeholders, to identify priorities for action and propose solutions to strengthen the supply of critical medicines in the EU, to better prevent and combat their shortages*. PGEU aims to be an active partner in this initiative and provide the Alliance with community pharmacists perspective and best practices for tackling medicine shortages. We are hopeful that this initiative will be able to ensure balanced representation and participation of the various stakeholders to ensure actionable outcomes.

In December 2023, the European Medicines Agency published the first Union list of critical medicines, this list will be crucial for the work of the Critical Medicines Alliance and to ensure security of supply and shortage prevention for critical medicines in Europe. Community pharmacists highlighted that the list requires constant monitoring and maintenance to ensure its appropriateness and that measures to prevent shortages are urgently applied to these medicines. Notwithstanding, medicines not included in these lists should also receive attention and benefit from wider-scoped measures, in order to avoid deterioration of their supply resilience.

Regarding the MSSG Solidarity Mechanism[12], it will be important to clarify how the European Commission and Member States intend to operationalise the mechanism, in particular in what concerns the interplay between the MSSG Solidarity Mechanism and the national reserves being implemented across Member States. Furthermore, it would be useful to ensure pharmacists are informed of potential stock redistributions to ensure their awareness and readiness to dispense the redistributed stock.

PGEU welcomes a close collaboration between Member States and the EMA via the Medicine Shortages Steering Group (MSSG). This work has already allowed Member States to find a joint response to shortages impacting the whole continent. It will be crucial to continue this effort and to strengthen communication about medicine shortages. A comprehensive EU communication strategy on shortages could ensure that information to healthcare professionals and the public on medicine shortages is universally accessible across Europe. Similarly, this close cooperation and other ongoing joint actions[16] allow Member States to share best practices and prevent potential negative impact of national measures adopted on neighbouring countries. It will be crucial to coordinate of all ongoing and planned actions to ensure a cohesive response to the issue of medicine shortages. To this end, the EMA can act as a facilitator and best practice repository for the competent authorities from the Member States.

Recommendations

- Guarantee a balanced stakeholder involvement in the Critical Medicines Alliance.
- Make use of the Union list of critical medicines as a prioritisation tool, but not at the exclusion of measures to prevent shortages of medicines outside the list.
- Clarify the functioning of the MSSG Solidarity Mechanism and potential expectations of supply chain actors.
- Strengthen cooperation, information and best practice sharing via the MSSG and Joint Actions with the involvement of community pharmacists as appropriate.

Strengthening supply chain resilience

According to the European Commission study on medicine shortages, the majority (half) of medicine shortages seem to be related to quality and manufacturing issues5, as reported by manufacturers. This root cause is then followed by commercial reasons (quarter) and then by unexpected demand and distribution issues (each with less than a tenth). In line with these observations, several measures have been proposed by both stakeholders, governments and European institutions.

A key measure under discussion is related to a strategic approach to manufacturing, with stated intentions of several Member States[28,29] to reshore or nearshore production of critical medicines. While a closer supply chain can help react faster to changes in the European environment, it must be acknowledged that this solution is not applicable to all medicines and will be met with conflicting interest from healthcare systems: maintaining the relatively low price of most critical medicines and the higher cost of manufacturing in Europe due, for example, to higher environmental standards and labour costs[30]. In the various available mechanisms advanced by the European Commission, it will be critical to ensure that investments made in production in Europe are competitive and sustainable in the long term to ensure that they are not wasted. Similarly, the European Commission and Member States should be clear on the expectations towards manufacturers that decide to bring manufacturing to Europe with the appropriate provision of public support mechanisms.

To be able to assess the robustness of supply chain, it is important to upskill European and national competent authorities with the expertise and resources to assess the upstream supply chain resilience. This would not only ensure greater transparency regarding potential supply chain fragilities, for example due to overlapping active pharmaceutical ingredient suppliers of different marketing authorisation holders, but also allow for these overlaps to be taken into account in procurement and provisioning decisions. In addition, ways to encourage and facilitate diversification of the upstream supply chain should be assessed and implemented whenever possible.

Community pharmacists are supportive of the measures being introduced in the reform of the pharmaceutical legislation that require manufacturers to have better oversight of their supply chain by requiring them to have in place shortages prevention and mitigation plans. It is essential that these plans are transparent and accessible to the medicines regulators and that they are efficiently implemented once a shortage is anticipated or

[28]https://www.lemonde.fr/en/france/article/2023/06/13/france-to-re-shore-production-of-50-key-medicines_6031218_7.html
[29] https://www.politico.eu/article/belgium-leads-charge-eu-commission-medicine-pharma-reshoring-plans/

[30] https://think.ing.com/articles/why-there-is-no-end-in-sight-for-the-eu-drug-shortage-crab-carolina-lal-pharma/#:~:text=Naturally%2C%20supply%20chain%20disruptions%20caused,the%20shortage%20of%20medicines%20further

confirmed.

An additional measure being implemented by several Member States is stockpiling. Here there should be common strategic approach that guarantees national stockpiles will not jeopardize the general supply of medicines, nor they should generate unnecessary waste. This can be addressed by ensuring progressive requirements for rolling buffer stocks, allowing for these to be built over time rather than all at once and through proper stock management. In addition, there should be clarity and transparency regarding how these stocks are managed, held, utilised and paid for, with several models being suggested depending on the primary objectives [31] . This will allow mechanisms such as the MSSG solidarity mechanism to fully function without being hindered by specific national requirements for stock levels. Furthermore, strategic stocks at European level should be considered while avoiding overlap with the existing national stocks.

It is also relevant to improve current forecasting capabilities. In this regard, ensuring that forecast information is improved from public information sources to facilitate industry's own forecast exercises, without removing the responsibility of marketing authorisation holders from developing robust methodologies to secure a stable supply. Furthermore, industry's forecasting models could be made available to competent authorities in case of an impending shortage, to assess the impact on the supply of available alternatives. Lastly, to the extent possible, demand from public buyers should be better communicated to avoid unnecessary spikes in demand that can cause constraints to the supply of the whole market.

According to a recent report from OECD, price pressure, particularly in generics, seems to be an issue impacting supply reliability, in some cases leading to withdrawals and market concentration. In this regard, procurement practices can create incentives for manufacturers to strengthen supply and even create buffer stock. OECD also suggests that cross-country pooled procurement can be helpful to enhance supply security and demand prediction, while mentioning that public procurement should consider the utilisation of "most-economically advantageous tender" (MEAT) criteria as recommended by the European Commission and implement diversification of supply as a rationale for splitting tender awards[4].

While the previous measures help to address manufacturing and unexpected demand issues, a clarification of manufacturers and wholesale distributors obligations could help address distribution issues by defining their respective responsibilities. A 2018 survey[32,33] of Member States, highlighted a heterogeneous transposition by EU Member States of Article 23a and Article 81 of EU Directive 2001/83/EC[34]**.** The proposed reform of the pharmaceutical legislation addresses these issues, and it will be important to maintain a clear definition in the final text to ensure the appropriate and continued supply. Furthermore, the national transposition of the relevant articles should also strengthen their enforcement to guarantee their effective application resulting

[31] IQVIA, Agile Stockpiles, An Insurance for Drug Supply, November 2020
[32] https://ec.europa.eu/health/sites/health/files/files/committee/ev_20180525_summary_en.pdf
[33] https://ec.europa.eu/health/sites/health/files/files/committee/ev_20180525_rd03_en.pdf
[34] https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf

in a smoother supply chain for the benefit of patients.

In addressing the shortcomings from the EU internal market, it will also be relevant to ensure supply continuity. To this end, and as previously recommended by the European Parliament[35], Member States should achieve better understanding of the impact of parallel trade and supply quotas and allocations, their dynamic both on the national market and European internal market, thus facilitating appropriate action to address supply interruptions impacted by these market dynamics.

Recommendations

- Establish a cohesive strategy to ensure that effective European instruments are employed to support local manufacturing which will increase supply chain resilience and contribute to the security of supply in the long-term.
- Increase the transparency of the upstream supply chain by granting national and European competent authorities the necessary resources to assess and detect supply fragilities earlier to facilitate better mitigation and less patient impact.
- Strengthen supply chain oversight, ensuring manufacturers are required to have shortages prevention and mitigation plans and for these to be made available to competent authorities.
- Improve procurement processes by introducing MEAT criteria and splitting tender awards to achieve supply chain diversity and reduce downward price pressure leading to withdrawals and concentration.
- Ensure that national stockpiles or stockpiling obligations do not negatively impact medicine supply nor generate unnecessary waste, by progressively building rolling stocks and making them available to the MSSG solidarity mechanism.
- Build European rolling stockpiles for critical medicines which can be readily made available to use in case of shortages.
- Improve demand forecasting, particularly from public sources and public buyers.
- Clarify manufacturers and wholesale distributors obligations and provide cohesive strengthening of their enforcement at national level.
- Evaluate and address the impact of parallel trade and manufacturer-initiated supply quotas and allocations.

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

About Us

The Pharmaceutical Group of the European Union (PGEU) is the association representing community pharmacists in 33 European countries. In Europe over 400.000 community pharmacists provide services throughout a network of more than 160.000 pharmacies, to an estimated 46 million European citizens daily.

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