

UNIVERSAL ACCESS AND AFFORDABLE MEDICINES

EPHA POSITION ON MEDICINES SHORTAGES IN EUROPE

POSITION PAPER
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About EPHA

EPHA is a change agent – Europe's leading NGO alliance advocating for better health. We are a dynamic member-led organisation, made up of public health civil society, patient groups, health professionals, and disease groups working together to improve health and strengthen the voice of public health in Europe.

About EPHA's Universal Access and Affordable Medicines advocacy

EPHA's Universal Access and Affordable Medicines advocacy promotes transparency, accountability and the public interest in the field of pharmaceuticals in line with the priorities of our members most active in this field. We aim to guarantee better and affordable medicines for Europe by questioning and calling for reforms to the current pharmaceutical business model to ensure better access to medicines for all.

See more at <https://epha.org/universal-access-and-affordable-medicines/>

THE FOLLOWING ORGANISATIONS HAVE CONTRIBUTED TO AND REVIEWED THIS PUBLICATION:

- European Academy of Paediatrics (EAP UEMS SP)
- European Association of Hospital Pharmacists (EAHP)
- Association of European Cancer Leagues (ECL)
- European CanCer Organisation (ECCO)
- European Hematology Association (EHA)
- France Assos Santé
- Romanian Health Observatory (RHO)

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EPHA POSITION ON MEDICINE SHORTAGES IN EUROPE

The increasing levels of medicine shortages across Europe pose severe threats to patient outcomes, patient safety and the patient care continuum. The European Public Health Alliance (EPHA) calls for an urgent resolution of the medicine shortage crisis through a coordinated response between EU Member States.

This paper outlines the nature, magnitude and impact of medicines shortages in Europe and makes tangible recommendations to remedy this pressing cross-border health threat.

The issue of medicine shortages has further deepened due to the current coronavirus crisis. Supply issues are now occurring for medicines used to treat patients with COVID-19, including in ICU, with devastating impact both for COVID patients and for patients with other conditions who also need these medicines (e.g. hydrochloroquine for rheumatological conditions such as systemic lupus).

EPHA makes 9 principal recommendations to address medicine shortages:

1. **Strengthen** the EU pharmaceutical legislative framework to improve notification of medicines shortages and reinforce obligations of the market Authorisation holders (MAHs) and wholesalers to supply the market.
2. **Require** all medicines marketed in more than one EU Member State to have accompanying European shortage management and prevention plans.
3. **Create** early warning systems on medicine shortage at both national and European level.
4. **Publish** new EU guidance elaborating on cases when free movement of medicines may be restricted in order to prevent and address medicine shortages.
5. **Publish** new EU guidance on prudent procurement practices to help prevent occurrence of shortages in generic medicines.
6. **Set up** a permanent system for monitoring of medicine shortages in the EU.
7. **Assess** the impact of shortages on patient health, treatment and care in the EU.
8. **Develop** a comprehensive EU strategy on medicine shortages with the active contribution of the European Parliament.
9. **Launch** an EU Joint Action focusing on the prevention of, and solutions to, medicine shortages.

1. HOW SERIOUS IS THE MEDICINE SHORTAGES CRISIS?

The incidences of medicines shortages reported in most EU countries have increased exponentially. For example, in France, there were 1,450 medicine shortages in 2019, compared to 868 in 2018 (compared to 44 in 2008).¹ In the Netherlands, the number of drug shortages almost doubled in 2019: 1,492 in 2019, compared to 769 in 2018.² In the Czech Republic, 2,208 products were affected by supply interruptions in 2019, compared to 1,630 in 2018 and 19 in 2008.³

The problem of medicine shortages affects all European countries, as evidenced in an annual survey report of the European Association of Hospital Pharmacists (EAHP). In 2018, 73% of European hospital pharmacists taking part reported experiencing medicine shortages on a daily or weekly basis.⁴ In 2019, shortages were considered a current problem in delivering the best care to patients and/or operating the hospital pharmacy by 95% of survey respondents, 10 percent more than in 2014. Medicine shortages are most frequently reported for anti-microbial agents, oncology medicines and anaesthetic agents.⁵

2. WHAT IMPACT DO MEDICINE SHORTAGES HAVE ON PATIENTS' AND PUBLIC HEALTH?

Shortages are defined in different ways in different countries and by different stakeholders. From EPHA's patient-centred perspective, a shortage occurs when a patient cannot receive their medicine in a timely manner.

The impact of medicine shortages on patients includes:

Disease progression and/or worsening of symptoms as a result of the delay of treatment: Treatment outcomes are negatively affected due to delay in treatment, interruption of medicine scheduling, and potential reduction of dose;

Avoidable transmission of infectious diseases: Vaccines are frequently reported as being in shortage, with Hepatitis B, Pneumococcal, Tuberculosis, Tetanus, HPV

1 <https://ansm.sante.fr/S-informer/Informations-de-securite-Ruptures-de-stock-des-medicaments>

2 KNMP Geneesmiddelen tekorten in 2019 verdubbeld <https://www.knmp.nl/actueel/nieuws/nieuws-2020/geneesmiddelen-tekorten-in-2019-verdubbeld>

3 Medicines shortages catalogue of the Czech National Agency for Medicines Control <http://www.sukl.cz/vypadky-leku>

4 2018 Medicines Shortages Survey of the European Association of Hospital Pharmacists (EAHP) - http://www.eahp.eu/sites/default/files/report_medicines_shortages2018.pdf

5 2019 Medicines Shortages Survey of the European Association of Hospital Pharmacists (EAHP) - https://www.eahp.eu/sites/default/files/eahp_2019_medicines_shortages_report.pdf

and Hepatitis A among those evidenced⁶; HIV and Syphilis treatments have also been missing over the past 10 years;

Increased exposure to falsified medicines: Medicine shortages can result in patients procuring treatment from unreliable sources (online, abroad, etc.) out of desperation;

Significant emotional distress for patients and their families: Delays in treatment of life-threatening diseases (including cancer) can be particularly traumatic. Indeed, a Medicines & Vaccines Shortages Survey⁷ carried out by France Assos Santé and BVA in December 2018 found that medicine shortages have generated anxiety in over 40 % of patients suffering from a chronic disease⁸.

Medicine shortages can also impair the health of patients who are switched to an alternative therapy, causing:

- Increased risk of medication or administrative errors;⁹
- Increased risk of adverse events, greater toxicity or development of drug resistance in some patients;
- Suboptimal treatment or therapeutic failures.

These concerns are particularly acute for populations that cannot use standard formulations. For example, children, the elderly and other vulnerable patient groups, such as those in critical care or with disability or those who cannot swallow medicines easily, need specific medications.

Additionally, medicine shortages also cause higher costs for the social security system (including hospitals) and more out-of-pocket expenses for patients.

3. WHAT IS CAUSING SHORTAGES OF MEDICINES?

The possible causes of medicine shortages are multifaceted. They include:

- Manufacturing issues: quality defects, raw material unavailability, non-compliance with the Good Manufacturing Practices regulations, closure of a manufacturing site, drug recall, unexpected disasters;
- Commercial decisions of the market authorization holder: withdrawal from a national market or complete stop of the production of a determined product;

6 https://www.eahp.eu/sites/default/files/eahp_opinion_on_vaccination.pdf

7 <https://www.france-assos-sante.org/wp-content/uploads/2019/02/Penuries-medicaments-Resultats-BVA-dec2018.pdf>

8 See note 6.

9 Medication errors are mentioned as one of the consequences of shortages by 25 % of hospital pharmacists (2018 Medicines Shortages Survey of EAHP).

- Production capacity: unexpected surges in demand or inaccurate estimation of needs;
- Supply issues: supply quotas and misuse of parallel trade, logistical inefficiencies.

However, there is a serious lack of information on the specific causes of single shortages. The causes declared by MAHs and/or published by medicine agencies are often very general (e.g. production issues; supply problems; commercial/marketing reasons; new batches not available; etc.) and differ from one country to another. This makes it difficult to plan effective management measures and to have a reliable picture of the European situation. Standards for public reporting of shortages across the EU are uneven, opaque and failing to deliver a strong and coherent picture in respect to causation.

4. HOW IS EUROPE ADDRESSING THIS CRISIS?

Most EU Member States have adopted national measures to help manage and fight shortages of medicines, with a clear acceleration during the past 3 years. Many of these initiatives are too recent to allow for an accurate evaluation of their effects, nevertheless, common issues can already be pinpointed:

- The adoption of new national regulations lacks European coordination and consequently reduces effectiveness of the measures, contributes to an inefficient allocation of stocks and causes shortages, both in Europe and globally;
- Member States restricting parallel trade to deal with current or anticipated supply disruptions of medicines face legal uncertainty (related to free flow of goods within the EU), as the current EU legal framework lacks clear guidance on eligibility of pausing export restrictions;
- In many countries, there is a gap between the legal provisions to address shortages and their enforcement, due to insufficient controls and the lack/limited application of sanctions.

In 2019, the joint Heads of Medicines Agencies-European Medicines Agency (HMA-EMA) Task Force on the availability of authorised medicines published a Guidance document on the detection and notification of shortages of medicinal products for MAHs and started a pilot programme on establishing a single point of contact (SPOC) network to improve information sharing between Member States, the EMA and the European Commission on shortages of critical medicines. While these initiatives are praiseworthy and need to be supported, their impact may be limited due to fact that:

- The Guidance's effectiveness will depend on the goodwill of MAHs,

- who have already requested to delay its implementation; and
- The SPOC network mainly focuses on crisis management and will not help prevent shortages.

5. WHAT MORE NEEDS TO BE DONE?

Medicine shortages are a European cross-border health threat. To have greater impact, national measures need to be coordinated, complemented and supported by EU initiatives.

EPHA makes 9 principal policy recommendations:

- 1. Strengthen the EU pharmaceutical legislative framework to improve notification of medicine shortages and reinforce obligations of MAHs and wholesalers to supply the market.**

Articles 81 and 23a of the Directive 2001/83/EC of the Community Code relating to medicinal products for human use have established general obligations of supply of medicines on MAHs and wholesalers, as well as an obligation of notification on MAHs in case of temporary or permanent supply interruption. However, these obligations have been unevenly implemented by Member States and the notification requirements also vary substantially country by country.

EPHA calls for a revision of the EU legislative framework on medicine shortages aimed at improving the notification of shortages, reinforcing obligations of MAHs and wholesalers to supply the market, and at making all obligations on medicine supply chain actors enforceable.

- 2. Require all medicines marketed in more than one EU Member State to have accompanying European shortage management and prevention plans.**

Shortage management and prevention plans are aimed at averting shortages and reducing their impact when they occur. They are based on an analysis of the manufacturing and distribution risks and should include clearly circumscribed measures in respect to stock maintenance, the diversification of raw materials supply sources (including the Active Pharmaceutical Ingredient), and the development of other

manufacturing sites for the purposes of production resilience.¹⁰

EPHA calls for a legal requirement that all medicines marketed in more than one EU Member State have accompanying European shortage management and prevention plans.

3. Create early warning systems on medicine shortage at both national and European level.

Some Member States have established early warning systems which facilitate the anticipation and the prevention of potential shortages, for instance monitoring the stocks of medicines. The adoption of similar systems in other EU countries or at EU level should be supported to allow health systems to take prevention/mitigation measures as early as possible.

EPHA calls for the establishment of an ad hoc coordinated pan-European system to ensure provision for the earliest possible warning about forthcoming medicine shortages.

4. Publish new EU guidance elaborating on cases when free movement of medicines may be restricted in order to prevent and address medicine shortages.

Parallel trade¹¹ of medicines between countries can be a cause of shortages when conducted without control of national authorities. Based on Article 36 of the Treaty on the Functioning of the EU, Member States may restrict the export of medicinal products by wholesale distributors to prevent or address shortages. These measures however need to be appropriate, necessary and proportionate so as not to expose the country to an infringement procedure. EU guidance to Member States on the scenarios when such restrictions can be imposed without threat of proceedings for breach of EU free movement rules would give countries more certainty and greater ability to respond quickly to emerging threats of medicine shortages.

EPHA calls for full and complete EU guidance on the measures that Member States can adopt to prevent and address medicine shortages, based on Article 36 of the Treaty on the Functioning of the EU.

5. Publish new EU guidance on prudent procurement practices to help prevent occurrence of shortages in generic medicines.

¹⁰ Article 4 of Décret n° 2016-993 du 20 juillet 2016 relatif à la lutte contre les ruptures d'approvisionnement de médicaments - <https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000032922434&categorieLien=id>

¹¹ Parallel trade is the cross-border sale of goods within the EU by traders outside of the manufacturer's distribution system without the manufacturer's consent

Shortages of generic medicines are often associated with a lack of suppliers in the market. Procurement practices focusing solely on price can result in suppliers pulling out of national markets, contributing to market consolidation and therefore increasing the risks of medicine shortages. Allowing more than one winner for tenders of pharmaceutical products lowers the risk of single supplier dependence.

EPHA calls for the publication of new EU guidance on medicine procurement to assist Member States with the adoption of prudent procurement practices and help prevent occurrence of shortages in generic medicines.

6. Set up a permanent system for monitoring medicine shortages in the EU.

At the present time, it is not possible to gain a comprehensive overview of shortage situations in the EU because there is no common platform through which information across Europe is publicly shared. Such a platform would increase the transparency on the scale and causes of shortages, would allow for a more efficient management of crisis situations, and create greater public accountability for the issue.

EPHA calls for setting up a permanent EU system for monitoring of medicine shortages that gathers and publishes all data reported at the national level.

7. Assess the impact of shortages on patient health, treatment and care in the EU.

EPHA welcomes the publication of a tender by DG SANTE for a study on the root causes of shortages in the EU. It is indeed important to collect evidence on the different causes and their relative weight by country and by class of therapy, and to analyse their consequences on shortage magnitude and duration.

The impact of shortages on patient care and health should also receive equal attention, as the threat of poor outcomes posed by drug shortages in the EU should be measured with robust data. All such studies should also be conducted transparently by reputable research organisations, free of potential commercial bias.

EPHA welcomes the announced study on the root causes of shortages in Europe and calls also for an investigation into the impact of shortages on patient health, treatment and care in the EU.

8. Develop a comprehensive EU strategy on medicine shortages and

ensure a meaningful contribution of the European Parliament.

The need for action to ensure an adequate supply of medicines in the EU was acknowledged within the Mission letter sent by EU Commission President Ursula von der Leyen to Stella Kyriakides on her nomination as European Commissioner for Health and Food Safety in December 2019¹². However, no global European strategy to resolve the medicine shortage crisis has yet been published.

In September 2019, EPHA and 40 civil society organisations sent a letter to the European Parliament’s Environment, Public Health and Food Safety (ENVI) Committee asking for an own initiative report on shortages of medicines. It is an opportunity for the Parliament to start working with stakeholders on possible solutions and contribute to the development of an EU strategy on this crucial issue.

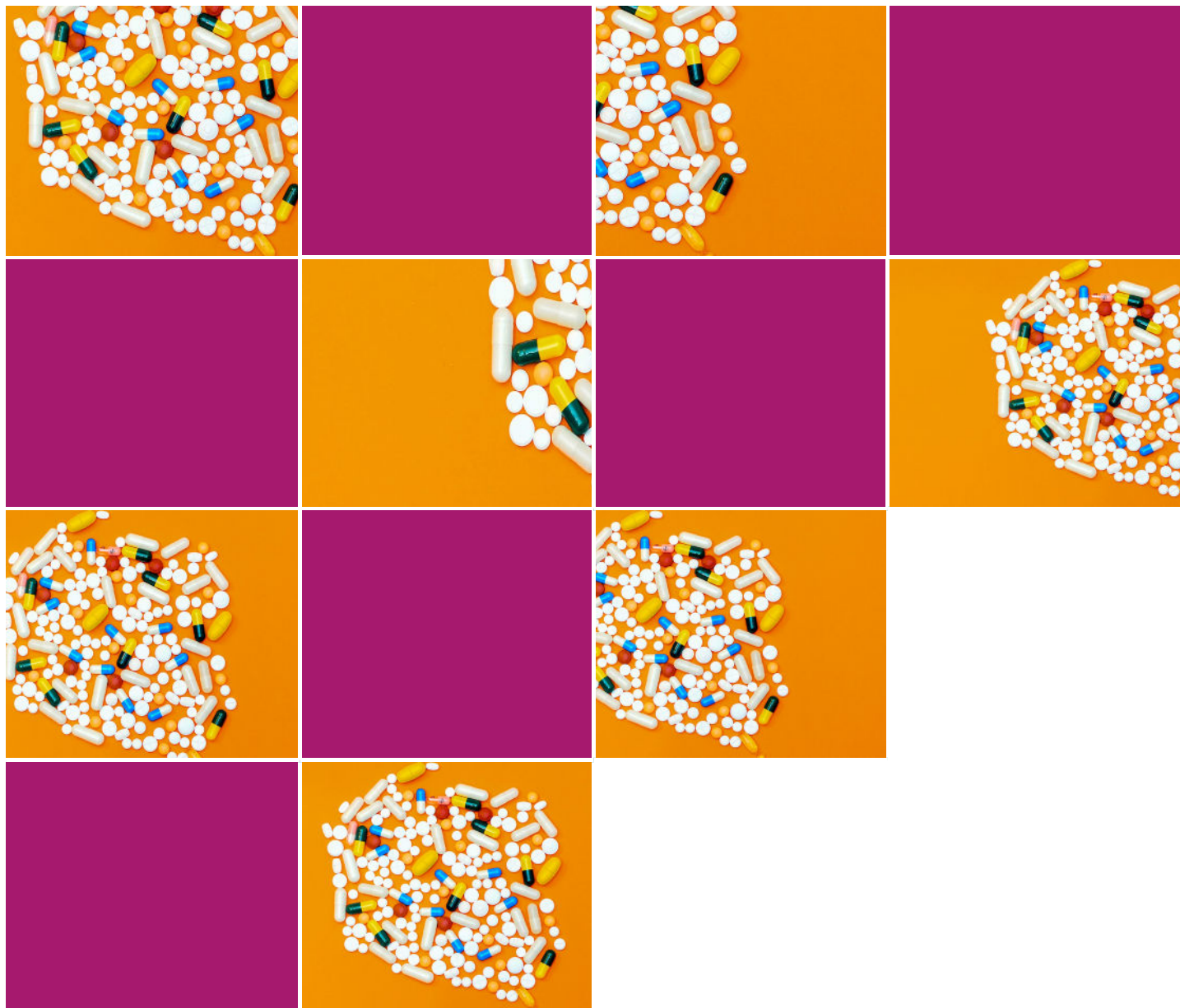
EPHA calls on the European Commission to develop a comprehensive EU strategy on medicine shortages, and on the European Parliament, as the elected representatives of European citizens, to actively contribute to this strategy through an Own Initiative Report or other available mechanisms.

9. Launch an EU Joint Action focusing on the prevention of and solutions to medicine shortages.

A framework for cooperation among EU countries on shortages has already been set up with the HMA-EMA Task Force on the Availability of Authorised Medicines created in December 2016. However, the Task Force focuses mainly on improving the management of shortages and the resources available for this European cooperation are scarce, delaying the implementation of the actions proposed. Another framework for collaboration between EU Member States could thus be envisaged to develop and share tools and methods to prevent medicine shortages, i.e., via a ‘Joint Action’ funded by the EU Health Programme.

EPHA calls for an EU Joint Action on the prevention of medicine shortages to further support the exchange of best practices among Member States and to help develop common prevention measures.

¹² https://ec.europa.eu/commission/commissioners/sites/comm-cwt2019/files/commissioner_mission_letters/mission-letter-stella-kyriakides_en.pdf



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