

## POLICY PROPOSALS TO MINIMISE MEDICINE SUPPLY SHORTAGES IN EUROPE

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

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

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

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

EFPIA calls for:

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

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

The causes of unavailability of medicines in EU Member State markets are broadly threefold: i) products not being authorized; ii) products being authorized but not marketed; iii) products being authorized and marketed but unavailable due to shortages. This policy paper focuses on the last of these. Unequal availability and patient access to centrally approved medicines within the EU requires a separate in-depth discussion<sup>1</sup>.

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

## **1. Better understanding of the root causes of drug shortages**

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

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

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

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

Any work aimed at better understanding the causes of shortage in the supply chain and aspiring to propose meaningful solutions should start from the premises of the most correct measurement of the phenomena. Supply chains nowadays (including pharmaceuticals) rely on increasingly global and digitalised networks.<sup>4</sup> This evolution has driven increased attention in the last forty years, both by the industry and by academic research, on defining and developing the right performance measures and metrics<sup>5</sup> and equips us with a multitude of empirically tested supply chain measures and systems (Mishra et al., 2018), under the overarching principle that without correct measurements in place there cannot be any improvement in overall performance.<sup>6</sup> EFPIA, therefore, highlights the need to enrich the current count of individual shortage events with a more comprehensive set of supply chain performance measures.

### *Causes and main drivers of shortages*

The following table<sup>7</sup> provides a visual representation of the majority of root causes of shortages. While the table aims to provide an easy-to-use overview, it has to be understood that shortages sometimes have multiple root causes which are intertwined and compound and exacerbate their cumulative effect. An in-depth analysis can only be carried out on a product (SKU) basis.

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

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

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

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

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

In recent years, the industry has engaged with all relevant industry<sup>8</sup> and supply-chain stakeholders<sup>9,10</sup>, to address medicinal product shortages and seek solutions in partnership.

Despite multiple country reports, there is a lack of sound evidence and knowledge about the key drivers and extent of drug shortages. Most country information systems are based on different/diverging definitions of shortage, without any agreed view of what would be a meaningful disruption in the supply of medicines<sup>11</sup>. Furthermore, most country information systems and most do not make any distinction between ‘suspected medicine shortage’ and ‘actual medicine shortage’. If the problem is to be effectively tackled, there needs to be a commonly agreed definition of what constitutes a genuine material disruption in the supply of medicines.

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

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

The use of the repositories systems for the monitoring of shortages would benefit from further discussion between National Competent Authorities and relevant supply chain stakeholders with the goal of using every tool available to protect patient safety and public health<sup>12</sup>.

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

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

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

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

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

## 2. Better Reporting of Shortages

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

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

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

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

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

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

<sup>14</sup> Directive 2001/83/EC on the Community Code relating to medicinal products for human use provides that a public service obligation must be warranted on grounds of public health protection, and proportionate in relation to the objective of such protection, [2001] O.J. L.311/67, Article 81, Recital 38.

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

In this context, the industry welcomes the July 2019 Guidance on detection and notification of shortages of medicinal products for MAHs in the Union endorsed by EMA and Heads of Medicines Agencies<sup>15</sup>, which aims at providing a harmonized approach to the definition, detection and notification of shortages of medicinal products in the EEA. The definition of shortage (and demand) included in the Guidance will need to be interpreted in line with Article 81 of Directive 2001/83/EU focussing on patients' needs.<sup>16</sup> Although the Guidance proposes a general reporting of any early detection of potential shortages, it should be understood that not all products have the same criticality and impact in terms of patient needs and supply. Priority must be given to critical products with a high impact rather than products with a moderate or low patient need where, for instance, there are alternative medications readily available. While aiming for a harmonised approach, the Guidance seems to exempt current/existing national reporting practices and tools which counters harmonisation efforts, adds further complexity and prevents a full standardization of the information to be reported in terms of content and format.

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

### **3. Effective Enforcement of Existing Regulatory Obligations**

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

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

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

<sup>15</sup> [https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-detection-notification-shortages-medicinal-products-marketing-authorisation-holders-mahs\\_en.pdf](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-detection-notification-shortages-medicinal-products-marketing-authorisation-holders-mahs_en.pdf)

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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



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

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

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

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

### Call for Action

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

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

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

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

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

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

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

Legislation should contain a clear definition of “shortage” as a trigger event.<sup>26</sup> By way of illustration, Romanian<sup>27</sup> measures define a shortage as a decrease of stocks below the national monthly average for 7 consecutive days.

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

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

### **2. Systems to identify actual and potential shortages**

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

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

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

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

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

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

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

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

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

Responsibility should remain with the competent authorities to ensure the effectiveness of the emergency measures. Requirements on distributors to obtain pre-export written authorisations from manufacturers/MAHs (and prohibition of exports by distributors who do not possess such written authorisation) should be avoided including because they expose the stakeholders to competition compliance issues<sup>29</sup>.

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

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

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

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

#### **4. Review mechanism**

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

#### **5. Appeal process**

Shortages legislation should provide for an effective and timely appeal process which allows affected stakeholders to challenge decisions imposed by the authorities to address shortages. For example, the adopted legislation in Poland<sup>31</sup> in 2015 allows distributors to appeal against an export refusal decision within 7 days of receipt of the decision.

#### **6. Penalties**

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

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

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