AESGP, EAHP, EAEPC, EFPIA, EIPG, GIRP, Medicines for Europe, PGEU

Joint Supply Chain Actors Statement on Information and Medicinal Products Shortages

Introduction

Shortages of medicinal products are a growing issue of concern across the European Union[i,ii,iii] and indeed globally (2012, 2014)[iv]. There is increasing evidence that shortages occur across the EU and that a wide range of medicines are affected[v,vi,vii,viii,ix,x]. Several factors can give rise to the cause of medicines shortages [xi , xii , xiii , xiv] . The causes of shortages are understood to be multifactorial, including problems in production, global consolidation of manufacturing, unintended impacts of pricing and tendering policies, as well as problems within the supply chain. This paper does not expand further on issues of causation and, by extension, solution. Rather, it addresses the need for better information collection, communication and transparency in order to: ameliorate patient care impacts via improved management of shortages; and, to enhance understanding of the extent and nature of medicines shortages.

Despite steps already taken to address some of the causes of medicine shortages, the problem persists. It is clear that without reliable information regulators, industry, parallel distributors, pharmaceutical wholesalers, health professionals and, of course, patients, cannot take steps to limit the negative effects that interruptions in medicines supply have upon patient care and health system performance.

European associations representing manufacturers of medicinal products, parallel distributors, pharmaceutical wholesalers and pharmacists have come together to work jointly on proposed principles for improving collection, communication and transparency of information on shortages of medicines[xv]. Everyone is in agreement that reliable information systems are an essential step in communicating the problems of shortages. Whilst it is recognised that such systems need to be implemented at national level, and therefore to be responsive to specific national concerns and regulation, a number of principles underpin efficient, effective and reliable information systems.

Our primary concern, and the main motivation for forming this joint statement, is the health and wellbeing of patients. It is our ethical and public duty as actors within the pharmaceutical supply chain (manufacturers, parallel distributors, pharmaceutical wholesalers and health professionals) to minimise the impact of shortages, where we are capable of doing so. This statement is part of this process and focuses solely on one issue of potential redress: improved information collection and publication about shortages.

Better information about medicines shortages is required in order to:

- Put in place contingency solutions to minimise negative impacts to patient care (e.g. initiate urgent communication to prescribers / pharmacies / wholesalers and preparation of bespoke out-of-license or magisterial products)

- Enable best management and distribution of existing stocks

- Provide verified and meaningful information to patients about why a disruption, delay or change in their therapy is necessary, and when resumption of supply is anticipated

- Implement a rapid alert and solution finding process between the Supply Chain Actors in urgent cases with severe health related implications

- Improve understanding of the nature of the problems, the balance of causes and main policy dynamics to be addressed to prevent shortages occurring in the first place

- Mitigate the impact on patients by providing clear and properly evaluated information for communication with healthcare professionals (e.g. the INN) to facilitate:
    - Generic substitution[1] or, where this is not an option,
    - Therapeutic alternatives[2]

The purpose of this statement is to outline guiding principles about medicines shortages information and to make recommendations on the specific features of the ideal information systems. We hope that these recommendations will help to enhance systems at the national level, and potentially form the basis of future European level action.

Examples of best practice, illustrating the principles of the paper, are provided in the Annex.

Principles

*1 Detection and Assessment of a Shortage**

There is no universally accepted definition of a medicine shortage in Europe. For the purpose of setting up an effective information system of medicine shortages we suggest a conceptual approach (Figure 1: Potential system of detection and assessment of a medicine shortage) that would lead to early detection of shortages upon appropriate assessment of reports of suspected shortages, and ultimately will help to understand and prevent medicine shortages related problems.

For this kind of system to work it is important to define a 'suspected medicine shortage' and establish a simple mechanism to assess a 'signal' and decide on whether it is an actual medicine shortage. We adopt a patient centred view in defining a 'suspected medicine shortage' and, as such, we define a suspected medicine shortage, for the purposes of an information and reporting system, as "the inability for a community or hospital pharmacy, as a result of factors beyond their control, to supply a medicinal product to a patient within a defined period, for example 72 hours"[3]. While creating such a definition, it should be noted that it is the impact on patients arising from the unavailability of the medicine they require that is paramount. Therefore, we

[1] Where permitted by national rules

[2] In consultation with, or with referral to the prescriber

[3] Agreed definition by the Supply Chain Supply Chain Actors Working Group on 8th July 2015, adapted definition from the French Public Health Code and later adopted in the Decree on Medicine Shortages https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000032922434&categorieLien=id

believe that it is important that all suspected shortages of medicines are recorded whether they are single or multi-source products.

The report of suspected medicine shortage does not necessarily mean that a medicine is in short supply. The evaluation of signal(s) of a potential shortage is required to establish whether or not there is a potential negative public health impact arising from shortage of medicine.

Another important factor to consider when assessing a suspected shortage is whether the product is multi-source or single-source. In general, if the product is of multi-source origin (and can therefore be substituted by another product where permitted) then this may be decided not to be recorded as an actual shortage.

Additionally, the nuances of national reimbursement and substitution rules need to be taken into consideration. Whilst respecting Member States' competencies in the domain of substitution and reimbursement, we believe that, in the case of shortages of specific reimbursable medicinal products, national reimbursement rules should not impede the provision of alternative medicines to patients.

All supply chain actors involved in supply of the concerned product should take part in the assessment of a suspected medicine shortage (a supply chain stakeholder panel) and ensure that the most up-to-date information on a medicine is made available.

In cases where a medicine shortage is confirmed, a supply chain stakeholder panel may decide to make this information public and provide further information to authorities and patients.

**Section 1 should not be taken in isolation. We note that the European Medicines Agency (EMA) is leading work on the European level to develop definition(s) for medicine shortages in collaboration with supply chain stakeholders and we strongly support this effort to ensure harmonised definitions, which in turn should enable comparing data within and between countries in order to understand the root causes of shortages better[xvi]. Under the auspices of the work led by EMA, industry trade associations have also proposed a definition of "meaningful [supply] disruption" for European use, which refers to disruptions due to manufacturing or quality issues, which may or may not result in shortages[xvii].*

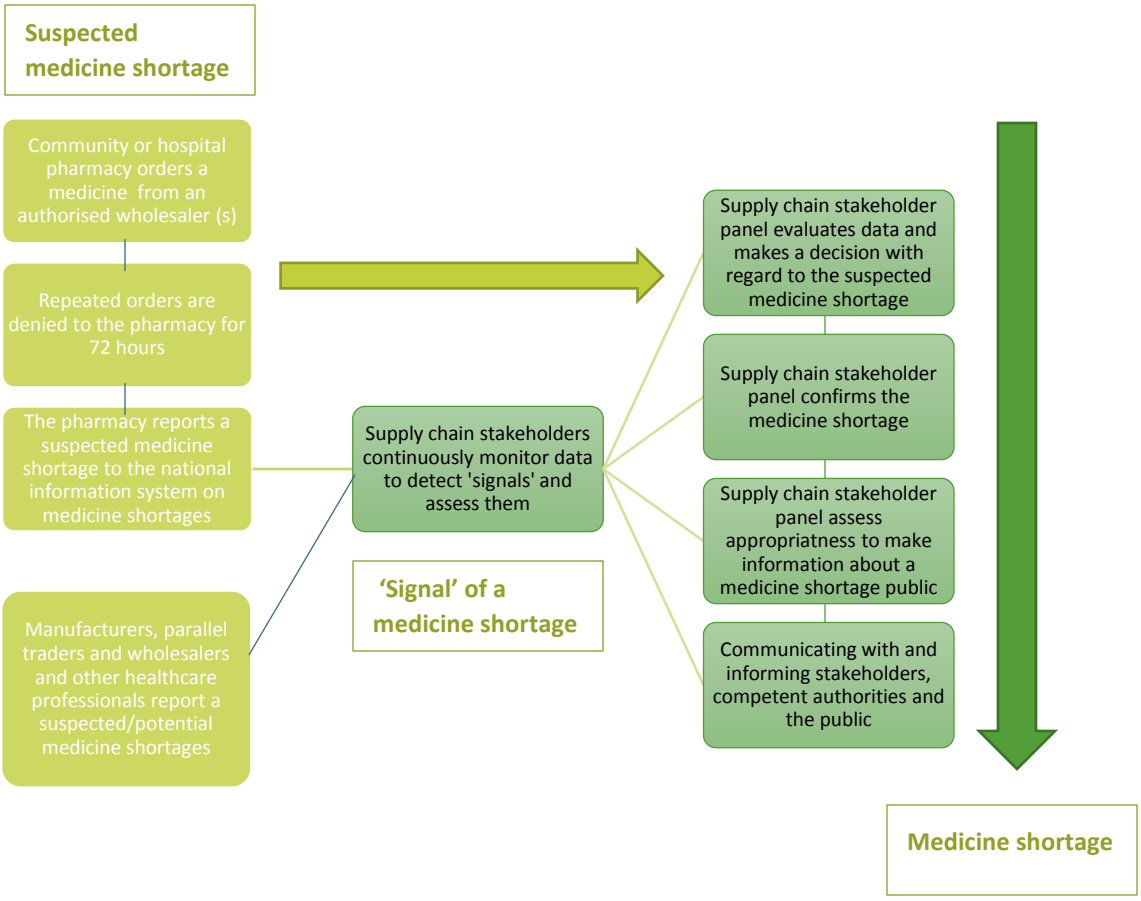

FIGURE 1: POTENTIAL SYSTEM OF DETECTION AND ASSESSMENT OF A MEDICINE SHORTAGE

2 *SOURCES OF INFORMATION*

Visibility of supply information and awareness of shortages across the supply chain must be improved to allow a more responsive reaction to interruptions in supply. For example, manufacturers will be aware of a potential supply disruption of their products due to manufacturing/quality issues which are obliged to be reported to Competent Authorities following EU legislation (cf. Annex II). Sometimes pharmacists experience or foresee supply difficulties before the industry or wholesalers are aware that there is, or will be, a problem.

We believe that information systems should therefore be open to reports from manufacturers, wholesalers, parallel traders, pharmacists and other healthcare professionals, with reference to the origin of reports of suspected shortages. We are also aware that in an age of widespread use of social media and mobile technology, patients/the public are increasingly taking a more active role in their care. As such, it is desirable that information systems give thought to a mechanism for patient engagement where appropriate (e.g. the potential to signal a suspected shortage, as is the case for the Farmanco system in the Netherlands[xviii]).

It is important to reference the origins of reports of suspected shortages, e.g. whether they are from Supply Chain Actors, public authorities or elsewhere in order to help to evaluate the accuracy of the reports. We recognise, that some reports may be inaccurate – for example, they may be out of date. Reports therefore should, where possible, be verified with relevant Supply Chain Actors (e.g. via a Supply Chain Stakeholder Panel). The process of verification does not grant Supply Chain Actors a veto over the suspected shortage reports. Disputes about the veracity or accuracy of a report could be settled by agreement among Supply Chain Actors in accordance with a national Supply Chain Actors' Code (see below point 8).

In order to aid clear and consistent reporting of suspected shortages, a standardised reporting template is suggested and the reporting template of the Parenteral Drug Association (PDA) in their "Technical Report No. 68 (TR 68), Risk-Based Approach for Prevention and Management of Drug Shortages" provides a good case study.[xix]

3 Level of Access

Patients and the public, the ultimate payers of medicine, need timely access to medicines. They also require access to information from their healthcare professional and other sources to support the use of their medicines. In the case of a medicine shortage, patient organisations may be involved in mitigating potential risks and help to support patients with information and advice.

Principles of disclosure and transparency are being adopted in a number of areas in the pharmaceutical sector as a whole. In this spirit, we believe that access to information on confirmed shortages should be generally made available where appropriate. Information should be collated and appropriately assessed, verified, non-alarmist, non-prescriptive and made available to all who provided it.

There is a potential that wider general access to certain information may in itself lead to supply distortions, possibly exacerbating or even causing shortages[xx]. Therefore only verified information should be made available. The potential for such distortions needs to be addressed within an appropriate ethical context during assessment process, and should not be considered a blanket objection to open access.

Beyond this, we believe that open access to verified information about medicines shortages should be the default position of information systems, such as that of the FDA, ASHP and EMA at international levels[xxi, xxii], with restricted access imposed only on reasonable and justifiable grounds, on an *ad hoc* basis, and in accordance with a national Supply Chain Actors Code. Assurances should be established about the information flow and where the publication of specific information should be restricted to Supply Chain Actors as fear of inappropriate publication of certain sensitive information may act as a disincentive to its disclosure.

To avoid the potential for misattribution of blame by lay readers of the database, information about known, or indeed unknown, supply disruption causes should be provided e.g. "temporary

disruption to manufacturing process by required upgrade", "no disruption at manufacturing level, "unknown supply chain problem."

4 Content

We believe that information systems should be as reliable, up-to-date and as comprehensive as possible. It should allow identification of the medicinal product in short supply (in accordance with the principles above, this should be by brand where appropriate), and where possible the cause and likely duration of the shortage.

Information systems should ideally contain forms of archiving to enable an overview of trends in shortages to be provided. This can further enhance public understanding of the nature of the problem and help to better direct policy interventions. An example of this is provided by University of Utah monitoring and analysis of drug shortages over time in the USA, providing new insights into the nature of the problem and where the best focus of long term policy resolution may lie.

We also believe that if a medicine suspected to be in shortage has an alternative, i.e. via generic substitution[4] or, in the case of a proprietary non-prescription medicine, there is an alternative with the same ingredients available, the unavailability could still be reported as a suspected shortage by healthcare professionals or wholesalers. This is because wholesalers are not allowed to substitute orders and, in some cases, pharmacists require proof of a shortage in order to enable substitution and, in the case of the OTC medication, the information held on the database (for example the expected duration of delay) could be used to inform their patients when their preferred proprietary OTC medicine will be available again for purchase. As such, this could facilitate the work of pharmacists in finding the appropriate replacement therapy or action, and treatment of patients will not be interrupted. Pharmacists, with their knowledge of medicines and products, may be in position to offer training or support to other professionals on the correct selection and use of substituted products.

5 Alternative Treatments

The effects of shortages can be mitigated if patients have access to suitable alternatives, either by way of generic substitution or the use of therapeutic alternatives as appropriate. Generic substitution, where possible, has been demonstrated to be an important solution to medicines shortages. KNMP's "Farmanco" system reports that 62% of shortages in the Netherlands are effectively managed through substitution with generic medicines[xxiii]. The multi-source nature of generic medicines means that this might entail substitution of a branded medicine for a generic, a generic for a branded medicine or one generic for another.

In order to respect

(i) Member State's competencies in regulating the dispensing of medicines,

[4] Where permitted by national rules

(ii) the professional autonomy of the healthcare professionals involved and
(iii) the desire for patients to be involved in their own care,

we believe that information systems should not suggest specific alternative products, whether they are multi-source substitutes or therapeutic alternatives. Instead, the systems should simply indicate whether alternatives are available from one or more suppliers, allowing decisions regarding substitution and therapeutic alternatives to be made at practice (pharmacy and prescriber) level.

6 Governance

Supply Chain Actors are fundamental to the provision of information. As argued above, we believe Supply Chain Actors have a duty to mitigate the effects of shortages. Where information systems are not in place at national level, we believe that Supply Chain Actors should be proactive in cooperating to develop and/or advocating for such systems.

Supply Chain Actors' involvement in the governance of information systems – including the participation of patients – would help to ensure that systems are broadly based, responsive, efficient, user-friendly and ultimately meeting primary needs. Ideally, systems should have a level of coordination with each other in order to enable improved understanding of the international nature of medicines shortages. We recognise that national competent authorities have a role in the governance of information systems for medicines shortages (as cited in the examples below). Partnership between authorities and Supply Chain Actors may be preferred in some Member States, and is strongly welcomed by Supply Chain Actors. In order to facilitate the flow of information and reporting we recommend that definitions are harmonised both nationally and at European level. We believe that for an effective system, there should not be any barriers to reporting of suspected shortages by healthcare professionals and wholesalers.

However, we believe that the principles laid out in this statement are essential to ensure that information systems are truly effective, and therefore should also be respected by national competent authorities.

7. Competition Rules

We recognise that collaboration between Supply Chain Actors potentially gives rise to competition law issues, especially in the market based manufacturing sector. Supply Chain Actors should be aware of their obligations in this respect, and should seek legal counsel where appropriate. It is of paramount importance that any initiatives by Supply Chain Actors are undertaken in the public interest with the sole objective of improving the provision of information on shortages.

8. A Supply Chain Actors Code

Given the potential consequences for patients of an inability to access medication, shortages of medicines are both a practical and a moral problem.

Collaboration between national Supply Chain Actors to provide information systems should be underpinned by a Code of collaborative action. The Code should address, as a minimum:

(i) the provision of information to the system;
(ii) removal of information from the system;
(iii) advisory timeframes;
(iv) verification of information;
(v) procedure of assessment of suspected shortages;
(vi) withholding of information from the system which may have detrimental effects;
(vii) making information on medicine shortages public;
(viii) mutual assistance to mitigate the effect of shortages; and,
(ix) resolution of disputes between Supply Chain Actors.

Recommendations

European associations representing manufacturers of medicinal products, parallel distributors, pharmaceutical wholesalers and pharmacists have come together and are in agreement that reliable information systems are an essential step in communicating shortages. While it is recognised that such systems need to be implemented at national level, and therefore to be responsive to specific national concerns and regulation, a number of principles underpin efficient, effective and reliable information systems:

1. **Transparency** in the supply chain is crucial to mitigate shortages before they arise. Supply chain actors on national level should therefore have a tool to communicate openly and without barriers.
2. **Detection and Assessment of Medicine Shortage**: Reporting of suspected medicine shortages is encouraged in a similar spirit to the reporting of suspected adverse drug reactions. 'Signals' of medicine shortages can then be periodically assessed by, for example, a national Supply Chain Actor stakeholder panel to establish if signals are suspected or actual shortages.
3. **Information Source:** In order to aid clear and consistent reporting of suspected shortages, a standardised reporting template is suggested. Information systems should be open to reports from manufacturers, wholesalers, parallel traders, pharmacists and other healthcare professionals, with reference to the origin of reports of suspected shortages. Reports, where possible, could be verified with relevant Supply Chain Actors, but in any case, have to be confirmed prior to considering any form of publication.
4. **Level of Access:** In order to aid mitigation of shortages, access to information on suspected shortages should be made available to all Supply Chain Actors. Access to information on verified shortages should be generally available to the public where appropriate and meaningful and restricted access imposed only on reasonable and justifiable grounds, on an *ad hoc* basis, and in accordance with a national Supply Chain Actors Code. Information should be collated and verified, non-alarmist, non-prescriptive,

meaningful and made available to all who provided it. Patient organisations, may be involved in mitigating potential risks and help to support patients with information and advice.

5. **Content of Information System**: Information systems should be as reliable, up-to-date and as comprehensive as possible. They should allow identification of the medicinal product in short supply (by brand where appropriate), and where possible state the cause and likely duration of the shortage (also causes arising from outside the supply chain such as pricing and reimbursement issues). The systems should indicate (where appropriate) whether alternatives are available from one or more suppliers, allowing decisions regarding substitution and therapeutic alternatives to be made at practice level.
6. **Governance:** Supply Chain Actors should be proactive in cooperating to develop and/or advocating for such systems at national level. Partnership between authorities and Supply Chain Actors is strongly encouraged by Supply Chain Actors. Collaboration between Supply Chain Actors to provide information systems should be underpinned by **a national Code of collaborative action**.
7. **Competition Rules:** Supply Chain Actors should be aware of their obligations in this respect, and should seek legal counsel where appropriate.

Annex I: Examples of Best Practice

Full practice examples are provided below. There are traditionally two types of Information systems available namely ones lead and set up by stakeholders and government lead systems.

Note: information based on the state of affairs at the date of the publication of this joint statement

A. Stakeholder lead system examples

Austria

There are two information systems in Austria.

System1

1. **Detection and Assessment of Medicine Shortage**: The system is operated by Datacare and provides a web based interface which facilitates communication between pharmaceutical manufacturers and wholesale distributors for making wholesale distributors aware of the likelihood of a shortage and / or reporting effective medicine shortages to pharmaceutical wholesalers.
2. **Information Source:** In the event of a wholesale distributor experiencing a stock-out, the concerned wholesaler initiates a request for the manufacturer to upload information onto the database. Manufacturers can proactively upload information onto the database.
3. **Level of Access:** It is accessible to wholesale distributors and pharmaceutical manufacturers. Information is passed to pharmacies in the event of a stock out at the level of the wholesale distributor.
4. **Content of Information System**: The following content appears in the system – reason for delivery problem; explanation for shortage; estimated duration of supply disruption; contact person (if possible), and helpful information for healthcare professionals.
5. **Governance:** The system is operated by Datacare a company owned by the wholesale distributor association PHAGO in conjunction with pharmaceutical manufacturers (Pharmig).

System 2:

1. **Detection and Assessment of Medicine Shortage**: The system is based on the online publication called "index of medicines" to which a 'box' was added for the purpose of informing about shortage. The box is populated by the manufacturer – including probable length of shortages, potential replacement, cause, and contact person for additional questions.
2. **Information Source:** Information is provided by pharmaceutical manufacturers.
3. **Level of Access:** System is accessible to all health professionals and supply chain operators in the case that they are customers of the publishing company of "index of medicines".

4. **Content of Information System**: The following content appears in the system – product name; probable duration of the shortage; potential replacement; cause of the shortage and a contact person for questions.
5. **Governance:** The system is operated by pharmacies (hosted by Österreichischer Apothekerverlag) in-conjunction with pharmaceutical industry (Pharmig).

<u>France</u>

1. **Legal basis:** Supply chain operators have the following obligations due to Health Law 2016-41, decree 2012-1096 and decree 2016-993:
   - Manufacturer / MAH must inform ANSM (L'Agence nationale de sécurité du médicament et des produits de santé) of any stock out or risk of stock out for medicinal products of major therapeutic interest,
   - MAH informs the supply chain actors in case of stock out for medicinal products of major therapeutic interest
   - ANSM publishes the information available on its own website. The information remains visible for the duration of the shortage
   - Full-line wholesalers must inform manufacturers of any shortages not notified by the ANSM,
   - MAHs have to make available a call-centre (or an equivalent organisation, e.g. 'DP-Ruptures system") in order to manage the shortages and supply medicines in case of emergency.

   A shortage is defined as the impossibility for a pharmacist, after asking two wholesalers, to dispense a medicine for the 3 consecutive days.

2. **Information Source:** All supply chain actors (manufacturers, wholesalers, community or hospital pharmacists) can notify shortages experienced at their level, both top-down and bottom-up to the 'DP-Ruptures' system. Pharmacists are encouraged to notify shortages through an automated system.
3. **Level of Access:** System allows:
   • Communication with the Medicines Agency: for manufacturers, notification of a shortage or risk of shortage; dialogue with the Agency in terms of shortage management and traceability.
   • Communication with customers: top-down information dissemination in relation to anticipated shortage management; upward transmission of information allowing centralisation of notifications of observed shortages; reactive information in answer to the notification of an observed shortage.
4. **Content of Information System**: Company, Product name, type of medicine ("of major therapeutic interest" or not), foreseeable date of shortage, cause of the shortage, expected date of availability, possible alternatives; in addition, in the communication with the French Medicines Agency (ANSM) only: market share, stocks available, measures

included in the Shortage Management Plan (if applicable) including corrective solutions (such as generics, alternative treatments, importation etc.).

5. **Governance:** The French regulatory body for all pharmacists (Ordre national des pharmaciens) uses and hosts an existing IT network connecting all supply chain actors (community pharmacies, hospital pharmacies, full-line wholesalers, manufacturers) and health authorities. This network, originally developed to support shared medication records, has since come to support rapid information exchange systems on batch recalls and safety alerts. The build-on system called "DP-Ruptures", was launched in February 2013 by the Ordre, followed by a pilot phase from August 2013 onwards. Since October 2014, the service is being gradually deployed. In September 2015, around 3000 community pharmacies and hundreds of hospital pharmacists are involved in the system, as well as 55 manufacturers and health authorities (Medicines Agency, plus 8 Regional Health Agencies). As the "DP-Ruptures" system is usable on a voluntary basis, the exchanges with ANSM can be made by e-mail (Rupture-stock@ansm.sante.fr) and the information with customers can be made through the call-center. Completing the system, the agency publishes its notification on its own website.

The Netherlands

1. **Detection and Assessment of Medicine Shortage**: Submissions are usually made by pharmacies and each submission is checked by the respective MAH.
2. **Information Source:** The submission system is open to reports from manufacturers, wholesalers, pharmacists, other healthcare professionals and patients.
3. **Level of Access:** The Dutch system allows for public access to the information.
4. **Content of Information System**: The following content is contained in the system: product name; reason for shortage; expected data of availability, and possible solution for patients (substitution; compounding; importing, and possible alternatives). The information remains visible in the system for the duration of the shortage plus one additional month.
5. **Governance:** The system operating in the Netherlands ("Farmanco") is hosted and governed by KNMP – the Royal Dutch Pharmacists Association.

Portugal

1. **Detection and Assessment of Medicine Shortage**: The system automatically registers the information on medicines not delivered to pharmacies by wholesalers. This automatic registry is done during the process of reception and verification of orders delivered to pharmacies. The information is used by CEFAR (centre for health research and evaluation) to produce a report every month.

2. **Information Source:** Shortages notifications by pharmacies to the National Association of Pharmacies (ANF) are on a voluntary basis although 65% of pharmacies participate in the system daily.
3. **Level of Access:** ANF keeps the history of shortages from the beginning of the system. The information is sent by CEFAR to the national agency (Infarmed).
4. **Content of Information System**: The file created in the process by Sifarma (pharmacy stock management and dispensing software) is sent to ANF where the daily information is collected including name, strength, pharmaceutical form, package size and price, name of the market authorization older, name of the supplier (wholesaler), number of units in shortage.
5. **Governance:** System is developed and supported by ANF. The pharmacy system is hosted at the IT department of ANF.

Spain

1. **Detection and Assessment of Medicine Shortage**: Information Center on Supply of Medicines (CISMED) established by the Spanish General Pharmaceutical Council manages the information sent directly by pharmacies to the regional pharmaceutical councils. The information is communicated through the application of pharmacy order management system. Information is registered in the system when order of goods has been denied by all wholesalers that pharmacy works with and pharmacy gets response message "There are no stocks".
2. **Information Source:** All pharmacies are connected to the information system.
3. **Level of Access:** Regional pharmaceutical councils receive information about supply disruptions in the province and refer aggregated information to the General Council. The data is then consolidated, analysed and processes. Report is then sent to the competent authority, the National Medicines Agency.
4. **Content of Information System**: Information contained in the system is: the national product number; the number of units of each medicine within an order that has not been supplied to a pharmacy; name of wholesalers that have not been able to serve the orders; any other information about the activity of the pharmacy.
5. **Governance:** CISMED is an information system set up by community pharmacists that allows to detect in real time, general situations of supply disruptions based on the reports from community pharmacies. It provides information to the Spanish supply chain actors and health authorities on availability of medicines in pharmacies and allows pharmacists to know about potential supply disruptions and provide timely solutions to the patients and ensure continuity of treatment.
6. **Outline of the Process:**

B. Government led system examples

Belgium

1. **Detection and Assessment of Medicine Shortage**: In line with the EU legislation MAHs are legally obliged to notify all shortages lasting for at least two weeks no later than the first week of the shortage. Since July 2016, the legislation has been modified in a way that a temporary stop of commercialisation of a medicine needs to be notified at least 2 months in advance to the Famhp (the Federal Agency of Medicines). The legislative modification contains exceptions to the obligation of notification in cases where notification on beforehand is not possible. The stock breaches still need to be notified as soon as possible. Additionally, other Supply Chain Actors (pharmacies, wholesaler-distributors, etc.) can notify the Agency of (potential) shortages. On the basis of these notifications, the Agency will check with the MAH whether or not it consists of a real out of stock, and if yes, will request the company to complete a formal notification. All notified shortages are published on the Agency's website. For those shortages that hold an immediate risk for public health, substitution possibilities are also published. In the case where the company received a MA derogation and is allowed to import a batch of the medicine destined for another Member State, this information is made available on the website.
2. **Information Source:** All supply chain actors can notify the Agency of potential medicine shortages.
   Level of Access: All Supply Chain Actors have access to the data on the medicines shortages system. The list of medicine shortages is publicly available.
3. **Content of Information System**: The published list of shortages contains following information: human or veterinary medicines, product name, pharmaceutical form, pack size, national product code, beginning date of a shortage, expected date of return to the stock and reason(s) of the shortage. The information is made available on notifications

(daily update) and remains visible until the end of the out of stock period is confirmed by the MAH.

4. **Governance**: In Belgium the federal medicines agency (*Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten* (FAGG)/ Federal Agency for Medicines and Health Products (FAMHP*)/ L'Agence Fédérale des Médicaments et des Produits de Santé* (AFMPS)) publishes on a daily basis a list of medicines experiencing shortages which is established on the basis of information received from Marketing Authorisation Holders. The notifications and publication are managed by the Agency and the setup and general policy is guided through a Supply Chain Actors platform "medicines (un)availability".

Portugal

Reports on shortages of medicines to the national agency (Infarmed) are governed by legislation and follows the pathways below:

a) Information is submitted by the pharmaceutical manufacturers through an online application designed specifically for this purpose, "Shortages Notification System" and is available on www.infarmed.pt

b) Information can be submitted by other supply chain operators and healthcare professionals – in a two-step approach. Doctors and / or patients are considered as sources of information for the purpose of reporting a medicine shortage. However, the report of the shortage is made in a second step by the manufacturer, in the same way as above, after confirming stock levels with wholesale distributors.

Italy

Since 2014 a full list of products not available due to supply disruption is available on the Italian Medicines Agency (AIFA) website and updated weekly and provided by MAHs.

AIFA, the Ministry of Health, the Regions and the interested stakeholders are working together on a pilot project that sets up a monitoring system for products not available for non-regulatory reasons (for instance parallel trade): to check the presence of the products in the internal market.

Germany

German authorities (BfArM, PEI) publish data that is voluntarily provided by pharmaceutical companies. Additional reporting obligations are currently under discussion in a draft legislation as follow up from the "Pharmadialog".

EU level

In November 2013 the European Medicines Agency established a public catalogue for supply shortages of medicines that have been assessed by the Agency to affect more than one Member State, and for which recommendations have been provided. The aim of the catalogue is to offer

stakeholders, healthcare professionals and patients updated information on the reason, the status and the extent of the shortage, while also providing material on relevant related website links and documents. The information is public.

Annex II:EU Legal Framework

Marketing Authorisation Holders (MAHs) obligations, as laid down in Directive 2001/83 as amended

Article 23a: 'If the product ceases to be placed on the market of a Member State, either temporarily or permanently, the marketing authorisation holder shall notify the competent authority of that Member State. Such notification shall, other than in exceptional circumstances, be made no less than two months before the interruption in the placing on the market of the product. The marketing authorisation holder shall inform the competent authority of the reasons for such action in accordance with Article 123(2).'

Article 81: 'The holder of a marketing authorisation for a medicinal product and the distributors of the said medicinal product actually placed on the market in a Member State shall, within the limits of their responsibilities, ensure appropriate and continued supplies of that medicinal product to pharmacies and persons authorised to supply medicinal products so that the needs of patients in the Member State in question are covered.'

Article 123(2): 'The marketing authorisation holder shall be obliged to notify Member States forthwith of any action taken by him to suspend the marketing of a medicinal product, to withdraw a medicinal product from the market, to request the withdrawal of a marketing authorisation or not to apply for the renewal of a marketing authorisation, together with the reasons for such action. The marketing authorisation holder shall in particular declare if such action is linked to any of the grounds set out in Articles 116 and 117. In such case, Member States shall ensure that this information is brought to the attention of the Agency.'

Manufacturing Authorisation Holder obligations, as laid down in Directive 2003/94

Article 13: 'The manufacturer shall inform the competent authority of any defect that could result in a recall or abnormal restriction on supply and, in so far as is possible, indicate the countries of destination.'

Under the auspices of the work led by EMA, industry trade associations including EFPIA, Medicines for Europe, AESGP and PPTA (plasma products) have developed a set of communication principles in order to streamline in a harmonised and risk proportionate framework the diversity in data packages and expectations from the 28 EU member states' competent authorities and EMA[xvi]. This framework encompasses the following elements:

- An identical trigger point for notification based on an agreed definition of a meaningful disruption, and a triaging process based on an evaluation of the level of risk associated with a potential supply chain disruption;
- A harmonised reporting content;

- An agreed time point and recipient of the information for all nationally and centrally approved products.

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The Association of the European Self-Medication Industry (AESGP) is the official representation of manufacturers of non-prescription medicines, food supplements and self-care medical devices in Europe. AESGP was founded in 1964 to contribute to the improvement of responsible self-medication at the European level and to ensure that the value of responsible self-care is recognised in pharmaceutical, food and health matters.

The European Association of Euro-Pharmaceutical Companies (EAEPC) is the representative voice of pharmaceutical parallel distribution in Europe. Through national association or individual company membership it encompasses over 85 firms from 22 countries in the European Economic Area (EEA). The EAEPC's primary aims are to safeguard the free movement of medicines, as laid down in the EU treaty, and to counteract any attempts to restrict the freedom of choice for the consumer through trading patterns in breach of European competition law. The Association believes that free trade will lead to improvements in health standards through the provision of innovative medicines at lower cost, benefiting statutory healthcare systems, other third-party payers, and the public as both patients and taxpayers, as well as assisting the EU to achieve its objective of a single, internal market. More information www.eaepc.org

The European Association of Hospital Pharmacists (EAHP) represents c. 21,000 hospital pharmacists across 35 European countries. More information about its activities in respect to medicines shortages is available at http://www.eahp.eu/practice-and-policy/medicines-shortages

The European Industrial Pharmacists Group (EIPG) is a European association representing the national, professional organizations of pharmacists employed in the pharmaceutical or allied industries of the Member States of the European Union, the European Economic Area, or European countries having a mutual recognition agreement with the European Union on compliance control of regulated medicines.

The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the pharmaceutical industry operating in Europe. EFPIA is the voice on the EU scene of 1,900 companies committed to researching, developing and bringing to patients new medicines that will improve health and the quality of life around the world.

The European Healthcare Distribution Association (GIRP) is the umbrella organisation for pharmaceutical full-line wholesalers and distributors of healthcare products and services in Europe. It represents the national associations of over 750 pharmaceutical wholesalers serving 32 European countries, as well as major international and pan-European healthcare distribution companies. GIRP members employ over 140,000 people and distribute around 15 billion packs of medicines as well as a wide range of healthcare products per year. As the vital link in healthcare, they are committed to developing and providing innovative and efficient healthcare products and services to improve health and wellbeing of patients across Europe.

Medicines for Europe (formerly EGA) represents the generic, biosimilar and value added medicines industries across Europe. Its vision is to provide sustainable access to high quality medicines, based on 5 important pillars: patients, quality, value, sustainability and partnership. Its members employ 160,000 people at over 350 manufacturing and R&D sites in Europe, and invest up to 17% of their turnover in medical innovation.

The Pharmaceutical Group of the European Union (PGEU) is the association representing community pharmacists in 32 European countries. In Europe over 400.000 community pharmacists provide services through a network of more than 160.000 pharmacies, to an estimated 46 million European citizens daily. PGEU's objective is to promote the role of pharmacists as key players in healthcare systems throughout Europe and to ensure that the views of the pharmacy profession are taken into account in the EU decision-making process.

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