



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH



# HMA/EMA workshop on availability of authorised medicines

Report from a multi-stakeholder meeting  
held at EMA on 9th November 2018





# 1. Introduction

Shortages or problems with availability of medicines in the wider sense have been a global problem for the past decade and are increasingly affecting the EU. They have been increasing in severity in recent years and are affecting many commonly used medicines including antibiotics, anaesthetics and oncology medicines. They affect not only the supply chain but also healthcare systems themselves with a significant impact on public health. They can lead to failure to treat, delayed treatment, use of less desirable and more costly alternative medicines and an increased risk of medication errors and adverse events.

Causes vary widely and are broadly linked to economic, manufacturing or quality issues. Dealing with problems of medicines availability is an EU priority which has been recognised by HMA and EMA as an area of great concern.<sup>1</sup> Improving availability of medicines is included as a priority in the EMA/HMA strategy to 2020 and EMA/HMA multiannual work plan. In fact, the EU network has been improving processes for handling shortages caused by GMP compliance problems since 2012.<sup>2</sup> This work, together with actions stemming from two previous workshops, paved the way for the HMA/EMA taskforce on availability of authorised medicines for human

and veterinary use in 2016. The Task Force looks at availability issues in the wider context and is tasked with the coordination of actions to improve continuity of supply of human and veterinary medicines across the EU. In the context of Brexit, the taskforce is also acting as a platform to facilitate and coordinate actions between Member States, EMA and the European Commission to ensure the continuity of supply of medicines.

Because availability issues are multifactorial and there is no single solution, coordinated actions from all stakeholders are needed, including from patients and healthcare professionals, in order to raise awareness and find plausible long-term solutions.

Acknowledging the important role stakeholders play in the prevention and management of medicines availability issues, a multi-stakeholders workshop took place on 9 November 2018 at EMA in London to gather stakeholder perspectives on how to better address potential problems with the supply of medicines and how to avoid shortages. The focus of the workshop was on human medicines. However, issues common to both human and veterinary

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1 EU Medicines Agencies Network Strategy to 2020: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2015/12/WC500199060.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/12/WC500199060.pdf)

2 Reflection paper on medicinal product supply shortages caused by manufacturing/Good Manufacturing Practice Compliance problems; accessed on 07/12/2018 on: [https://www.ema.europa.eu/documents/other/reflection-paper-medicinal-product-supply-shortages-caused-manufacturing/good-manufacturing-practice-compliance-problems\\_en.pdf](https://www.ema.europa.eu/documents/other/reflection-paper-medicinal-product-supply-shortages-caused-manufacturing/good-manufacturing-practice-compliance-problems_en.pdf)

medicines were addressed in the context of Brexit (session 2).

Before the workshop, a meeting took place on 8 November with representatives from industry associations (professional and trade) and representatives from national competent authorities to discuss the deliverables of the task force and to get an update on industry's preparedness for the

UK's withdrawal from the EU. These topics were then further explored during the workshop with all stakeholders. The meeting and the workshop were chaired by the co-chairs of the taskforce, Kristin Raudsepp from HMA and Noël Wathion from EMA.

Input obtained from stakeholders at the workshop will be incorporated into the deliverables of the taskforce.

## 2. Objectives

1. Inform stakeholders about activities of the HMA/EMA taskforce and expected deliverables, including how these may be affected by Brexit.
2. Update stakeholders on progress with deliverables and identify areas of agreement as well as areas for further discussion.
3. Share stakeholders' perspectives and (ongoing/planned) initiatives to address availability issues and discuss how these can contribute to the deliverables of the taskforce.

### 2.1. Session 1: Availability of authorised medicines — setting the scene

Key messages:

- ▶ Shortages and problems with the availability of medicines are complex and longstanding problems which have a significant impact on public health and can contribute to health inequalities.
- ▶ There are no quick solutions and the issues need to be addressed in close collaboration with all stakeholders.
- ▶ Pharmaceutical industry plays an important active role in the prevention and management of medicines' availability issues.

Shortages continue to have a significant impact on public health and contribute to health inequalities

across the world. They are therefore a high priority in the EU and worldwide. The European Commission (EC) fully endorses the work of the taskforce and Agnes Mathieu-Mendes, the EC's representative, gave an overview of its initiatives aimed at improving accessibility and availability of medicines throughout the EU. In this context, the EC recently issued clarification of relevant European legislation (Article 81 [and 23a] of Directive 2001/83/EC) to facilitate its implementation. The guidance describes the responsibilities and the limits of manufacturers and distributors.<sup>3</sup>

Health Technology Assessments (HTA) are another powerful tool supporting health policy decisions by enabling policy-makers to assess the added value of a medicine. In January 2018, the EC adopted a legislative proposal for sustainable EU cooperation on HTAs. This proposal aims to improve business predictability and availability of medicines. Finally, the EC presented a study on access to medicines carried out by the EC expert group on Safe and Timely Access to Medicines for Patients (STAMP).<sup>4</sup> Results

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3 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 [https://ec.europa.eu/health/sites/health/files/files/committee/ev\\_20180525\\_rd01\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/committee/ev_20180525_rd01_en.pdf)

4 [https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp\\_en](https://ec.europa.eu/health/documents/pharmaceutical-committee/stamp_en)

showed a great variability between member states in the time between authorisation and launch of a medicine which can lead to large health inequalities between countries. During the facilitated discussion, a suggestion was made to review the provision of the sunset clause and its impact on supply of medicines. Agnes Mathieu-Mendes reinforced the need for commitment from all players in order to address shortages.

At a global level, availability issues also pose a significant risk to public health, especially in middle or lower income countries. Access to medicines and the continuous supply of affordable medicines with acceptable quality, safety and efficacy are requisites for achieving universal health cover. Francisco Blanco from the World Health Organization (WHO) gave an update on the ongoing efforts at WHO to address shortages of medicines and vaccines. In 2016, the World Health Assembly agreed a range of measures aimed at addressing the global shortage of medicines and vaccines by improving notification systems and finding better ways of monitoring supply and demand. WHO was asked to develop a definition of a shortage and a global notification system to better detect and understand causes of shortages. As part of this work, a WHO review in 2016 identified 56 definitions of a medicine's shortage and led to two draft definitions being proposed.<sup>5</sup> Consultations on introducing a global reporting system have started in 2018 with a mapping of existing notification systems and which countries would be interested in participating. In addition, there are a number of collaborative programmes in specific disease areas (HIV, TB, malaria, reproductive health and immunization and vaccines) to increase availability of medicines.

The impact of shortages on patients was illustrated by Francois Houyez from Eurordis using real-life examples. Full transparency and more involvement of patients in the handling of shortages were proposed. There is an urgent need to better inform patients about shortages and how shortages can affect their care. Improvement of inter-pharmacy communication was suggested so that patients can be better informed about pharmacies holding remaining supplies of a medicine when supply has been disrupted. Francois Houyez also suggested enabling pharmacists to make substitutions without the need for new prescriptions

for medicines that are temporarily unavailable. In order to better understand the impact of shortages, he called for indicators and tools to measure health consequences of shortages.

From a healthcare professional's point of view, oncologists are a key group who frequently experience shortages of medicines. Elisabeth de Vries from ESMO illustrated how frequently shortages affect cancer medicines, stating that it is often cheaper medicines that are affected. To tackle shortages within the oncology sector in Europe, ESMO carried out a literature review and consultation which led to six policy recommendations for countries across Europe.<sup>6</sup> They include a call for:

- ▶ Introduction of legislation for early notification requirements for shortages
- ▶ Strategic plans for medicines shortages
- ▶ Development of catalogues of shortages
- ▶ Development of essential medicines lists
- ▶ Introduction of incentives for production infrastructure improvements
- ▶ Procurement models designed to prevent medicines shortages

The lack of a common definition of shortages was highlighted as an obstacle for developing a common EU-approach and ESMO gave its assurance to continue its dialogue with policy makers to keep this issue high on their agenda.

The pharmaceutical industry plays an important role in the prevention and management of medicines availability issues and efforts to improve this are ongoing. Adrian van den Hoven, from Medicines for Europe, elaborated on the multifactorial causes of shortages and how important it is to address availability issues from different sides. In the view of Medicines for Europe, shortages can be an unwanted effect of cost-containment measures (e.g. tender practices leading to decreased competition in the market) or other cost-cutting measures that can lead to unwanted consequences (e.g.

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5 WHO Meeting Report: Technical Definitions of Shortages and Stockouts of Medicines and Vaccines accessed on 07/12/2018: [https://www.who.int/medicines/areas/access/Meeting\\_report\\_October\\_Shortages.pdf](https://www.who.int/medicines/areas/access/Meeting_report_October_Shortages.pdf)

6 <http://www.eiu.com/graphics/marketing/pdf/ESMO-Cancer-medicines-shortages.pdf>





withdrawals of marketing authorisations). It was noted that availability issues due to delays of medicines coming to market must be distinguished from shortages. Vaccines were highlighted as being particularly susceptible to shortages due to their long manufacturing lead times which make it particularly difficult to respond to short-term unexpected changes in the demand. In order to manage shortages effectively, it is important to involve all stakeholders in addressing the root causes. Full transparency with efficient communication between stakeholders and simplified and harmonised reporting procedures are key for success.

## 2.2. Session 2: Impact of Brexit on medicines availability

Key messages:

- ▶ Human as well as veterinary medicines with an important regulatory step in the UK face potential supply challenges due to the regulatory changes needed after Brexit.
- ▶ Work is ongoing at central level and at national level to minimise any disruptions in supply.
- ▶ EMA and national competent authorities (NCAs) continue to work with companies on regulatory preparedness to minimise any supply disruption after Brexit.

- ▶ Ensuring continuous supply of medicines is a collective responsibility. Although there is enough capacity in the regulatory network to deal with the regulatory changes required by Brexit it is essential that requests for regulatory changes are made in time.
- ▶ Pragmatism, preparedness and communication are key to minimise future supply disruptions.

Monica Dias from EMA and the Thematic Working Group 1 of the taskforce summarised the ongoing efforts at EMA to help industry make the necessary regulatory changes to minimise the potential impact on the supply of medicines following UK's withdrawal from the EU. The current advice is based on the assumption that the UK becomes a third country after Brexit. As marketing authorisation holders must be located within the EU/EEA in order to be able to market a medicine in the EU, companies with medicines where some of the regulatory processes take place in the UK are required to make changes to ensure that their marketing authorisations remain valid. The outcome of EMA's latest assessment of industry's preparedness for Brexit shows that although marketing authorisation holders are taking actions, there are concerns at the moment that for a number of centrally authorised medicines (19 human medicines and 12 for veterinary medicines) the necessary actions will not be carried out in time. This is an evolving picture and EMA continues to monitor the situation. For any medicines considered at risk, EMA is carefully analysing how to minimise supply disruptions and any resulting impact on public and animal health.

For nationally authorised products the picture is more complex due to the larger number of nationally authorised medicines and difficulties in carrying out a common criticality assessment. Hugo Hurts on behalf of CMDh chair Laura Oliviera informed the workshop participants that authorities have however identified affected national medicines and are considering measures to minimize the impact. CMDh is where information is shared among NCAs about the medicines and the measures to be taken. In addition, CMDh gives marketing authorisation holders the opportunity for an oral hearing to discuss specific Brexit contingency plans. For veterinary products the picture is similar and CMDv chair Laetitia Le Letty explained that CMDv is assisting marketing authorisation holders by providing advice on measures needed in relation to individual veterinary medicines. She pointed out that it is essential that the marketing authorisation holders are proactive in planning and reporting any issues they face due to Brexit to CMDv.

Yvonne Stewart from the European Trade Association representing biopharmaceutical companies described the regulatory arrangements required and the potential risks if this is not done in time. Despite current efforts, the requirements are significant and the timeframe is very constraining. The obligation to re-test medicines manufactured in the UK upon importation into the EU was highlighted as a particular burden. In this regard more flexibility and pragmatism was requested by industry stakeholders for both, veterinary and human medicines. Withdrawals of marketing authorisations due to commercial reasons represent a particular risk for medicines in the veterinary sector. Rick Clayton on behalf of Animal Health Europe gave an update on the current situation and noted that companies were stepping up their efforts to ensure continuous medicines' supply post-Brexit. In order to ensure supply, a transition period for the implementation of batch testing upon importation and more flexibility in the use of multilingual packaging were considered beneficial. He spoke about article 55(2) of Directive 2001/82 on the importation of medicines from a third country and the possibility of flexibility in interpreting this article.

In the facilitated discussions, it was noted that continuous supply of medicines is a collective responsibility. Although there is enough capacity in the regulatory network to deal with the required regulatory changes and the additional workload due to the redistribution of the UK portfolio, it is essential

that requests for regulatory changes are made in time. Industry stakeholders highlighted the fact that for nationally authorised medicines requests for variations cannot be made for medicines with ongoing procedures. There was a call to highlight any such cases to CMDh and CMDv. The issue of the requirement for re-testing and the possibility of flexibility in interpreting Article 55(2) of Directive 2001/82/EC for the supply of veterinary medicines needs further consideration. In the meantime, industry stakeholders should make the required arrangements for batch re-testing upon importation. Transparency and communication with healthcare professionals and patients was also raised as key in ensuring continued supply of medicines post-Brexit.

## 2.3. Session 3: Addressing shortages caused by supply chain disruptions

Key messages:

- ▶ Harmonised EU-wide shortage definition and metrics are needed to improve reporting.
- ▶ Further discussion is needed to decide whether a minimum period for time-out and information on pack sizes should be included in the definition of a shortage.
- ▶ Good collaboration and communication with stakeholders are needed for good management of shortages.
- ▶ Further discussion is needed on how to incorporate healthcare professionals and patients in the reporting process.

The lack of a European-wide definition for shortages has long been a factor hampering a harmonised European-wide approach to managing shortages. One of the main deliverables of the taskforce is therefore to deliver a harmonised definition of a shortage.

Annette Byrholt Hansen from the Danish medicines Agency and Working Group 2 of the taskforce presented a draft proposal for a harmonised definition. The definition ("A shortage of a medicinal product for human and veterinary use occurs when supply cannot meet demand at a national level") has been developed taking into account existing



definitions and reporting systems. While being simple, short and concise it includes the necessary and measurable elements identified by the taskforce to qualify as a shortage such as “demand” rather than “need”. A harmonised definition will facilitate data comparisons across countries. In this context, Brendan Cuddy from EMA presented the outcome of a recent survey of national competent authorities which showed that a third of EU/EEA member states already collect and evaluate information on shortages (so-called metrics). However, the type of data gathered varies from one member state to another. The survey identified key information necessary to adequately describe shortages which was used to design a template for marketing authorisation holders to notify national competent authorities of shortages. The layout is simple, allowing for collection of the minimum amount of information required for assessment. It is hoped that with the feedback gathered through the survey a European-wide unit of measure for shortages can be found to facilitate measurement of supply chain performance and comparison across the EU.

Workshop participants welcomed a common definition and notification system, however they also highlighted the need for a notification system to be well balanced allowing the collection of sufficient information on shortages and at the same time avoiding information overload. Stakeholders made suggestions to consider a risk-based approach when reporting shortages, taking into account the probability of a shortage occurring, criticality of a medicine and the number of manufacturing sources for the medicine. Requirements for a minimum period of time-out before qualifying a disruption of supply as a shortage should also be further explored. There were opposing views on whether pack sizes should be considered for the classification of shortages, as reimbursement may vary for individual pack sizes. This was identified as an area for further discussion.

Belen Escribano and Esther Martinez from Working Group 2 provided further information on the notification process as detailed in the draft guidance to industry. Using a case study, where supply of a critical cancer medicine was disrupted leading to the importation of an alternative medicine from outside the EU, they illustrated how good collaboration and communication led to a resolution with minimal disruption for patients. Stakeholders highlighted the importance of transparency throughout the supply chain, timely reporting and the need for healthcare

professionals and patients to be involved in the notification system.

## **2.4. Session 4: Public communication – improving access to information on availability issues**

In the EU, most medicine shortages are dealt with at national level by the national competent authorities. However, EMA can be involved in certain situations, for example when a medicine shortage is linked to a safety or quality concern or affects several Member States. Processes for communicating to the public are already in place at EU and national level. The results of a recent mapping of public communication practices by EU regulators was presented by Yngvil Knudsen from the Norwegian medicines agency and Thematic Working Group 3 of the taskforce. The survey found that public communication practices of member states have improved considerably over the last few years with most member states now communicating to the public on shortages. In fact, the survey found that 23 out of 30 EU regulatory authorities publish information on shortages targeting patients and healthcare professionals. Despite some differences in the content and criteria for publication, the majority of member states publish on all shortages and ensure that the information is updated as the situation changes. Although engagement with stakeholders was considered to be key, the level of involvement within member states is variable. In addition to the publication of a dedicated catalogue, member states use a wide range of communication tools to communicate on shortages and other availability issues, from press releases to social media as well as electronic prescribing systems. Better internal cooperation with communication colleagues and more engagement with external target audiences to ensure that communication fulfils the needs of the target audience were some of the main recommendations of the survey.

The panellists and the participants emphasized that transparency and public communication are crucial for good shortage management. In order to be comprehensive public communication should reflect the expected duration of the shortage, any recommended or suitable alternatives and any other relevant clinical advice. It is important that



communication is updated as needed to reflect the current status of a shortage. The points raised were further addressed by Juan Garcia-Burgos from EMA and Thematic Working Group 3 of the taskforce who presented the draft best practice guide for public communication to the public. The guidance highlights the catalogue format as the ideal tool to provide information to the public on shortages. However other tools should also be used, such as social media and electronic prescribing systems. All availability issues should be accessible through a single page on the website of the national regulatory authority. In addition Juan Garcia- Burgos described how shortage communication at EMA is interlinked with the communication to the public at individual member states level, providing a single point of reference for EU shortages. As shortages affect all stakeholders it is important to be fully transparent and to involve them when communicating to the public. Involvement is needed to obtain advice and feed-back on potential suitable alternatives and to ensure that all parties

are duly informed. In addition, Juan Garcia described a proposal to improve EU cooperation by optimising the current system for sharing of information within the EU network. The proposed new system aims for better monitoring, prevention, management and public communication on shortages.

In order to facilitate access and usage of the taskforce's output (i.e. new tools and guidance), an EU regulator's manual is being drafted and is expected to be published in 2019. The manual is intended as a single source of reference for assessors and stakeholders.

Panellists noted that although member states may publish information, it is not always easy to find. In addition to increasing visibility, dissemination channels need to be further explored and alternative communication tools need to be used to ensure that the target audience is reached.

### 3. Conclusion

The workshop illustrated the complexity of availability problems and their multifactorial causes. Availability problems can affect all medicines and are a growing issue not only in the EU but also globally. There are no quick solutions but firm steps are being taken to tackle the problem from different sides with the collaboration of all stakeholders. The workshop provided a forum for stakeholders to share

experiences on how availability issues impact them and allowed them to give their views on the work of the taskforce. Their perspectives have provided rich input into the deliverables of the taskforce.

There was consensus that an EU-wide harmonised definition of a shortage is essential for good shortage management. However, in order to address the



needs of all stakeholder groups it is important that the definition strikes the right balance to be able to capture all relevant shortages without overburdening the system. There were also some views that the definition should incorporate additional elements to make it more specific (such as pack sizes, a minimum period of time-out).

There was a call to harmonise and simplify the reporting process and avoid duplication.

Healthcare professionals and patients should be incorporated in the reporting process.

In relation to Brexit, all stakeholders agreed that there are challenges ahead in order to ensure continuous supply during the post-Brexit period and therefore early planning and communication are key. A call was made to implement any regulatory changes timely to allow smooth transition post-Brexit in order to minimise impact in medicines supply.

## 4. Next steps

Noël Wathion informed workshop participants that the deliverables of the taskforce will be updated taking into account feedback received at the workshop. In addition, stakeholders were invited to submit comments in writing by 23 November 2018. Comments will be consolidated and discussed within the taskforce as well as with all member states.

In relation to public communication, patients and healthcare professionals asked for more transparency and accessibility. Stakeholders welcomed proposed guidance on public communication practices across the EU, raising the profile of communication by defining common standards for timing, content, tools, involvement of stakeholders and dissemination practices.

In addition, a multidisciplinary approach within individual agencies and more interaction with target audiences was welcomed to improve public communication.

EMA together with HMA and the European Commission will provide regular updates on the work of the taskforce and will consult stakeholders as needed.

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