10 September 2024
EMA/183138/2024
European Medicines Agency

Guidance for industry on implementing Shortage Mitigation Plans (SMP)

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1. Introduction (background)

Medicine shortages are recognised as a growing issue across the EU and globally, and the COVID-19 pandemic has further increased their impact. They affect medicines of all classes and are increasingly affecting European countries. This may have a significant impact on patient care as they can lead to medicine rationing and delay of critical treatments and can require patients to use alternatives which may be less efficacious or may increase the risk of medication errors due to unfamiliarity with the new regimen.

Improving the availability of medicines authorised in the European Union (EU) is a key priority for the European Medicines Regulatory Network (EMRN). Since 2016, a task force set up by the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA), the HMA / EMA Task Force on the Availability of Authorised Medicines for Human and Veterinary Use (TFAAM), has been looking at availability issues, including supply chain disruptions , to improve the continuity of supply of human and veterinary medicines across Europe.

Availability issues with shortages in particular are recognised as a major area to tackle in the European Medicines Agencies Network Strategy to 2025 as well as in the European Commission's roadmap for its Pharmaceutical Strategy which has led to the release of the revision of the pharmaceutical legislation in April 2023. The revised pharmaceutical legislation envisages the obligation for Marketing Authorisation Holders (MAHs) to prepare a shortage mitigation plan for all potential and actual shortages.

The need to have a shortage mitigation plan to respond to shortages is also included as one of the recommendations (recommendation 5) of the good practices for industry for the prevention of human medicinal product shortages developed by the TFAAM in consultation with industry associations which was published in May 2023. The shortage mitigation plans are also recognised as one of the recommendations raised by the EC shortage study.

The implementation of shortage mitigation plans (SMP) will facilitate the MAH's compliance of their obligations to ensure, within the limits of their responsibilities, an adequate and continuous supply to the market (article 81 Directive 2001/83).

This guidance is intended to support Industry when implementing SMPs.

2. Scope and objective

Concerned MAHs should develop a SMP to address potential or actual shortages of medicines marketed by them with the aim to minimise any possible impact on patients in a timely and proportionate manner.

A SMP formally identifies signals and risks for the continued availability of the product and implements a procedure for their mitigation. The effectiveness of such mitigation plans and the controls intended to prevent supply interruptions should be formally evaluated for effectiveness.

The degree of effort, formalisation and documentation for each SMP should be proportionate to the identified level of risk for each medicine, for this purpose, ICH guideline Q9 on quality risk management should be applied.

It is highly recommended that the high-level hierarchy of the company (personnel with power and resources to solve the detected deficiencies in the supply chain) is involved in the development of the SMP.

3. ow to implement a SMP

Minimum requirements

MAHs should implement procedures describing the steps to manage a specific shortage, from the time a shortage (or potential shortage) is identified to its resolution, including measures taken to mitigate the impact of the shortage, notification to regulatory Authorities and follow up.

A record of root causes and mitigation measures taken should be kept after the resolution of shortages.

Submission

SMPs will be submitted to the Competent Authorities concerned (Competent Authority of the Member State where the medicinal product is marketed and, in addition, the EMA for a medicinal product covered by a centralised marketing authorisation) upon request according to timelines laid down in the pharmaceutical legislation and national regulations. SMPs may also be submitted directly to Competent Authorities when MAHs become aware of a shortage, in such case the shortage report and SMP might be submitted at the same time.

The MAH shall provide the information required and ensure that data provided are correct, accurate, not misleading and complete. The MAH shall update the information when necessary.

4. How to complete the SMP template

Some of the information listed below is extracted from the shortage reporting template and it is included for ease of reference.

4.1. Product information

Product information	
Product name(*) Pharmaceutical form(*) Strength(s) (*)	*Please note the complete trade name (speciality name), pharmaceutical form and strength(s)*
Active substance(s) name(*)	*Please note the active substance(s)*
Active substance(s) manufacturer(s) (*)	*Please note the active substance manufacturer of the concerned product*
Finished product manufacturer(s) (*)	*Please note the finished product manufacturer of the concerned product*
ATC code(*)	*Please note the ATC code*
Therapeutic indication(s) (*)	*Please note the authorized therapeutic indication(s)*
Route(s) of administration (*)	*Please note the route(s) of administration*
Affected pack size(s) (*)	*Please list the pack size(s) affected by the (potential) shortage*

Product information	
Pharmaceutical form, strength, route of administration or pack size, not affected by the supply disruption(*)	*Please list the product details of the medicines containing the same active substance(s) of your company that are still available*
Details of authorisation (procedure type (national (including Member State(s) involved)/ centralised marketing authorisation) and reference (*)	*Please note the procedure type (e.g., MRP, DCP, CAP) and reference (e.g., CAP number or MRP procedure number) : if it concerns a national procedure, please include the Member State(s) involved*
Member States in which the product is marketed (*)	*Please list the Member States in which the product is marketed*
MAH (name and address) (*)	*Please note the name and address of the Marketing Authorisation Holder. In case of NAP, MRP or DCP, the details of MAH can be included as an annex if needed.*
Contact person's details (*)	*Please note the contact details of the contact person, e.g., e-mail address , telephone*

4.2. Shortage details

<table>
<tr><th colspan="2">Shortage details</th></tr>
<tr><td>Shortage status (actual or potential) (*)</td><td>Please note if the shortage is ongoing (current) or anticipated (potential)</td></tr>
<tr><td>Impacted EU/EEA countries(*)</td><td>Please list all the EU/EEA countries that are or would be affected by the shortage</td></tr>
<tr><td>Other impacted countries - non EU/EEA countries (*)</td><td>Please list other (non EU/EEA) countries that are or would be affected by the shortage</td></tr>
<tr><td>Full description of the root cause (*)</td><td>Please provide details on the reason of the (potential) shortage</td></tr>
<tr><td>History details of shortages of the product over the last three years including record of root causes and any mitigation measures taken for those shortages(*)</td><td>Please list all shortages of the product over the last 3 years and include the root cause and mitigation measures per shortage, e.g.,
<table>
<tr><th>Start date</th><th>End date</th><th>MSs affected</th><th>Root cause</th><th>Mitigation measures taken</th></tr>
<tr><td>02/02/2022</td><td>02/03/2023</td><td>BE, ES, PT,GR</td><td>API shortage</td><td>Short-term: moved stocks amongst MSs

Mid-term: extra API manufacturer</td></tr>
</table></td></tr>
<tr><td>Expected start date of shortage (*)</td><td>Please note the expected start date of the shortage per pack size and affected Member State</td></tr>
<tr><td>Expected end date of shortage (*)</td><td>Please note the expected end date of the shortage per pack size and affected Member State</td></tr>
<tr><td>Monthly sales per Member State, in previous 12 months (*)</td><td>Please list the quantities that were delivered in the past 12 months, per month, per Member State and per marketed pack size, e.g.,

AT:
Feb 2024: 2.000 packages of 30 tablets of 500 mg
March 2024: 1.500 packages of 50 tablets of 500 mg
etc.</td></tr>
<tr><td>Actual demand at national level in previous 12 months (*)</td><td>Please list the actual demand per Member State for the last 12 months per marketed pack size, e.g.,

AT: 12.000 packs of 50 tablets of 500 mg

When relevant please provide separate rows containing information for hospital and community pharmacies.</td></tr>
</table>

<table>
<tr><th colspan="2">Shortage details</th></tr>
<tr><td>Manufacturing capacity globally per manufacturing site (*)</td><td>Please provide the maximum global manufacturing capacity for each active manufacturing site.</td></tr>
<tr><td>Forecast of supply per month and per Member State for the duration of the shortage (*)</td><td>Please list the current available stock and the stock that should be available in the next months (per month) for the duration of the shortage, per Member State and per marketed pack size e.g.,
<table>
<tr><th>MS</th><th>now</th><th>Month 1</th><th>Month 2</th><th>Month 3</th><th>Month 4</th></tr>
<tr><td>AT</td><td>1000 units of 100 mg tablets x30 = 30.000 tablets or 3 kg</td><td>3000 units of 100 mg tablets x30 = 90.000 tablets or 9 kg</td><td>2000 units of 100 mg tablets x30 = 60.000 tablets or 6 kg</td><td>0</td><td>…</td></tr>
<tr><td>AT</td><td>1000 units of 100 mg tablets x60 = 60.000 tablets or 6 kg</td><td>0</td><td>0</td><td>0</td><td>1000 units of 100 mg tablets x60 = 60.000 tablets or 6 kg</td></tr>
<tr><td>FR</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>SE</td><td></td><td></td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>Forecast of demand per month and per Member State for the duration of the shortage (*)</td><td>Please list the anticipated demand in the next months (per month) for the duration of the shortage, per Member State and per marketed pack size, e.g.,
<table>
<tr><th>MS</th><th>Month 1</th><th>Month 2</th><th>Month 3</th><th>Month 4</th></tr>
<tr><td>AT</td><td></td><td></td><td></td><td></td></tr>
<tr><td>BE</td><td></td><td></td><td></td><td></td></tr>
<tr><td>FR</td><td></td><td></td><td></td><td></td></tr>
<tr><td>SE</td><td></td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>Potential alternative products (*)</td><td>Please list potential alternative products to treat the authorized indications; this can be:

1.Same medicine with the same active substance:

a. the same or different strength or concentration or volume
b. the same or different pharmaceutical form
c. the same or different route of administration</td></tr>
</table>

Shortage details	
	2. Other medicinal product with the same active substance: *a. the same or different strength or concentration or volume* *b. the same or different pharmaceutical form* *c. the same or different route of administration* *3. Authorised medicinal products in the same class (therapeutic/pharmacological subgroup) with the same indications* *4. Authorised products in other class with the same approved indication*
Impact on the supply of other medicinal products from the same marketing authorisation holder (*)	*Please explain the impact of the shortage on the supply of other medicinal products of your company, e.g., lower production of product A or packsize X, need for controlled distribution of product B to avoid shortage as a consequence of increase in demand*
Potential impact on the consumption of or demand for other medicinal products (*)	

4.3. Shortage mitigating proposals

Any mitigating measures taken or planned by the marketing authorisation holder to address the shortage(*)

Shortage mitigating proposals	
Availability of alternatives:	
• Therapeutic alternative(s) marketed in the impacted country(1)	*Please list potential alternative products, available in the impacted country/ies. This can be:* *1.Same medicine with the same active substance:* *a. the same or different strength or concentration or volume* *b. the same or different pharmaceutical form* *c. the same or different route of administration* *2. Other medicinal product with the same active substance:* *a. the same or different strength or concentration or volume* *b. the same or different pharmaceutical form* *c. the same or different route of administration* *3. Authorised medicinal products in the same class (therapeutic/pharmacological subgroup) with the same indications* *4. Authorised products in other class with the same approved indication*

Shortage mitigating proposals	
• Therapeutic alternatives marketed in the EU/EEA[(1)]	*Please list potential alternative products, available in the EU/EEA. This can be:* *1.Same medicine with the same active substance:* *a. the same or different strength or concentration or volume* *b. the same or different pharmaceutical form* *c. the same or different route of administration* *2. Other medicinal product with the same active substance:* *a. the same or different strength or concentration or volume* *b. the same or different pharmaceutical form* *c. the same or different route of administration* *3. Authorised medicinal products in the same class (therapeutic/pharmacological subgroup) with the same indications* *4. Authorised products in other class with the same approved indication*
• Therapeutic alternatives marketed outside the EU/EEA (that could be imported from abroad)[(1)]	*Please list potential alternative products, available outside the EU/EEA that could be imported. This can be:* *1.Same medicine with the same active substance:* *a. the same or different strength or concentration or volume* *b. the same or different pharmaceutical form* *c. the same or different route of administration* *2. Other medicinal product with the same active substance:* *a. the same or different strength or concentration or volume* *b. the same or different pharmaceutical form* *c. the same or different route of administration* *3. Authorised medicinal products in the same class (therapeutic/pharmacological subgroup) with the same indications* *4. Authorised products in other class with the same approved indication*
Allocation of orders. If applicable, please provide details of criteria used to prioritise supply to countries and the clinical justification.	*Please indicate if you will or are prioritizing the supply to certain countries and if yes, please provide details of the criteria used and the clinical justification*
Request for support from Competent Authorities to solve/mitigate the impact of the shortage	*Please indicate if you would need support from Competent Authorities (NCAs or EMA) and which type of support*

Shortage mitigating proposals	
Reallocation of stock between markets. If applicable, please provide details on the justification for the reallocation of stock from one Member State to another and the mitigation measures if this results in a shortage.	*Please indicate reallocation of stocks between markets would be possible and if yes, please provide details on the mitigation measures if this action results in a shortage in the other market.*
Marketing of product in different language(2)	*Please indicate how many packages are available in a different language.* *Please be reminded that the use of these packages needs to be requested to the concerned NCA according to relevant national regulations*
Marketing of product with less than 6 months of expiry date	*Please indicate how many packages are available with an expiry date of less than 6 months* *Please be reminded that the use of these packages needs to be requested to the concerned NCA according to relevant national regulations*
Controlled distribution by the MAH	*Please explain how you apply controlled distribution, if applicable* *Please be reminded that the application of controlled distribution needs to be requested to the concerned NCA according to relevant national regulations*
Alternative distribution routes to expedite supply (site to country)	*Please note any alternative distribution route to expedite the supply (from site to country in need)*
Other	
• Supply plan proposal for member states including specific final presentations to maximize patient supply	*Please indicate if you will or are limiting production to one pack size or strength and if yes, please explain.*
• Other	*Please indicate any other activities you plan to implement to mitigate the impact of the shortage on patients*
Communication in collaboration with EMA/NCAs	*Please indicate if you plan a communication in collaboration with EMA/NCA. If yes, please include details of planned information for HCP, patients and press release if needed*