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Shortage Prevention Plan (SPP)

1. Introduction

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 prevention plan. In addition, the development of the SPP is one of the elements of the upcoming revised pharmaceutical legislation that could be anticipated according to the Communication on addressing medicine shortages in the EU published by the European Commission on 24 October 2023.

The need to have shortage prevention plans is also included as one of the recommendations (*recommendation 4*) 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 prevention plans are also recognised as one of the recommendations raised by the EC shortage study.

The implementation of shortage prevention plans (SPP) 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).

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2. Scope

In case of a crisis (public health emergency or major event) SPPs are mandatory for medicines included in the list of critical medicines for that specific crisis according to article 9.3.k of the Regulation 2022/123.

MAHs should have in place a SPP for any medicinal product for human use they place on the market of the EU/EEA according to the good practices for industry for the prevention of human medicinal product shortages.

The SPP should be part of the annual product quality review and updated accordingly on an annual basis or if relevant changes occur such as critical shortage occurrence or a variation of the supply chain.

SPPs aim to collect information on the product, the marketing status at both EU/EEA and international level, their vulnerabilities in the supply chain, measures to prevent shortages and, where appropriate, to reduce their impact in terms of public health. Their ultimate objective is to reduce the likelihood of shortages by analysing the risks in the supply chain and defining measures to be taken to mitigate the impact of the shortage by identifying particular existing vulnerabilities in the supply chain and addressing these risks.

The degree of effort, formalization and documentation 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 SPP. It is key that the company considers the SPPs not as an administrative document but as a useful tool that is beneficial, first and foremost for them to identify any potential risk and be prepared if shortages occur.

The document should be written in English and translated into the language of the Member State when requested by the NCA. National specifications, if any, should be indicated in the risk assessment (variations of markets, production cycle) if requested by the NCA.

The SPP should be part of the company pharmaceutical quality system, should be subject to continuous evaluation.

3. Shortage Prevention Plan

3.1. Minimum requirements

Each medicinal product should have a prevention plan which contains information on the MAH, the supply and manufacturing chain, key data on stock, sales, consumption and manufacturing and, an analysis of the history of supply problems.

When developing a medicinal product shortage prevention plan MAHs should:

- Identify any vulnerabilities in the supply chain and assess the robustness of any arrangements and controls that are in place to prevent shortages. This could include that the MAH requests its manufacturers have effective prevention plans.
- Identify and evaluate the risks of an interruption in supply for patients.

- Develop a medicine shortage risk register in particular to identify products of clinical importance based on therapeutic use and availability of alternatives.
- Assess whether corrective and preventive action or any revalidation should be undertaken, both at national and international level, based on information available to the MAH, such as root cause analysis of shortages. This could include the analysis of supply and demand to guarantee the continuous supply of the market, identify any potential risk and be prepared in case of shortages.
- Identify and guarantee the maintenance of minimum stock levels at national levels, when applicable.
- Once established, regularly review the effectiveness of the controls in place to prevent shortages for patients.

A proposed template is included as Annex I.

3.2. Submission

SPPs should be readily available for submission to the Competent Authorities concerned (Competent Authority of the Member State where the medicinal product has been placed on the market and, in addition, the EMA for a medicinal product covered by a centralised marketing authorisation) upon request.

SPPs can be subject to inspection during GMP and/or GDP inspections or inspections of MAHs, in accordance with national regulations.

The information included in the SPP will be used only by Competent Authorities. Information will not be disclosed with third parties.

Annex I – SPP template

Product information

Product information	
Product name(*)	
Active substance(s) name(*)	
Active substance(s) manufacturer(s) (*)	
Finished product manufacturer(s) (*)	
ATC code(*)	
Therapeutic indication(s) (*)	
Pharmaceutical form(*)	
Strength(s) (*)	
Route(s) of administration(*)	
Pack size(s) (*)	
Details of authorisation (procedure type (national (including Member State(s) involved)/ centralised marketing authorisation) and reference(*)	
Member States in which the product is marketed(*)	
MAH (name and address)[1] (*)	
Contact person's details(*)	

Risk assessment

Impact on patient (3 different risk levels: high, medium, low)	
Classification of the therapeutic indication (**)	
Alternative marketed medicinal products per Member State(*) (**) (***)	
Annual sales data over the last year (number of batches, monthly sales) per Member State	
Final impact on patients classification:	

[1] In case of NAP, MRP or DCP, the details of MAH can be included as an annex if needed

Supply chain risk assessment. Risk level of likelihood of shortages: high, medium, low	
Supply chain map with risk identification and analysis with particular attention to supply chain vulnerabilities(*)	
• Active substance(s): Identification, analysis and risk assessment on the manufacture and supply	
• Critical raw materials: Identification, analysis and risk assessment on the manufacture and supply	
• Finished product: Identification, analysis and risk assessment of the manufacture, control and supply	
History details of batch rejections, quality defects, recalls from the market over the last three years in the EU/EEA[2]	
History details of delays from critical suppliers over the last 3 years	
Average led production time and lead time for restarting supply	
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(*)	
Bottlenecks in the supply and manufacturing process	
Other factors to be taken into account such as seasonality	
National specifications, when requested by NCAs	
Final supply chain risk assessment classification	

[2] According to the Compilation of Union Procedures on Inspections and Exchange of Information a Quality defects is 'any defect in a medicinal product within the scope of their authorisation that could result in a recall or abnormal restriction in supply'

Risk classification

The final risk level is the result of the combination of the impact on patients and the risk of disruption in the supply chain. There are three categories of risk:

- Low risk
- Medium risk
- High risk

The level of detail for each SPP and consequent proposed shortage management measures should be proportionate to the identified level of risk for each medicine.

Shortage management measures

Measures	
Risk control strategy in place, i.e. strategies to minimise risks of shortages and how these are implemented(*)	
• Existence of safety stocks, including minimum stocks at national level	
• Existence of any other active manufacturing sites of critical raw materials registered in the dossier or under evaluation. For non-active sites, time to activate	
• Existence of any other active manufacturing sites of API registered in the dossier or under evaluation. For non-active sites, time to activate	
• Existence of any other active manufacturing sites of finished medicinal product registered in the dossier or under evaluation. For non-active sites, time to activate.	
• Other measures	
Existence of any specific processes for the detection of supply disruptions	
• Monitoring of stocks	
• Monitoring of demand	
• …….	

Measures	
Company's internal procedures for communication/reporting	
• Existence of specific processes for communication of availability issues within different departments of the company	
• Existence of specific processes for the reporting of availability issues with the actors in the supply chain to allow early detection (wholesaler distributors, pharmacies)	
• Existence of specific processes for the notification of supply disruptions to regulatory authorities	
Process for checking of effectiveness, review and update of the shortage prevention plan (*)	

[ii](*) Data required in Annex IV-part V- the shortage prevention plan of the proposal of Regulation.
(**) risk levels according to the methodology published for the development of the Union list of critical medicines.
[ii](**) Alternatives marketed by the same and different MAHs.