Technical recommendations of the European Drug Shortages Formulary Working Party

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Framework

General considerations

The preparation of unlicensed pharmaceutical preparations is, in certain situations an efficient tool to mitigate the negative effects of the shortage of licensed medicines. However, in the event of a medicine shortage and before considering the use of unlicensed pharmaceutical preparations – as defined in the European Pharmacopoeia (Ph. Eur.) general monograph on *Pharmaceutical preparations* (*2619*) – preference should always be given to:

1. Licensed medicinal products that have been assessed by a regulatory agency
2. Licensed medicinal products that have been assessed by a foreign regulatory agency and have been imported
3. Alternative licensed medicinal products that have been assessed by a regulatory agency

As per Resolution CM/Res (2016)1 of the Council of Europe on quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients, it is crucial that:

"*All pharmacy-prepared medicinal products should be prepared using an appropriate quality assurance system. Before preparation, a risk assessment should always be carried out in order to define the level of the quality assurance system which should be applied to the preparation of the medicinal product.*"

"Premises, facilities and pharmaceutical knowledge should be appropriate for the preparation of the medicinal product."

"For extemporaneous preparations, […], the pharmacist and the prescriber should always consider the risks for the patient, which include the risks posed by a medicinal product without documentation specifying the added value of the pharmacy preparation and the quality assurance system applied to its production, versus the risks related to the unavailability of this medicinal product."

Unlicensed pharmaceutical preparations are defined according to the European Pharmacopoeia (Ph. Eur.) general monograph on Pharmaceutical preparations (2619).

About the technical recommendations of the EDSForm WP

Technical recommendations of the European Drug Shortages working party (EDSForm WP) are elaborated at the initiative of the EDSForm WP or upon proposal or request by stakeholders. They are elaborated to mitigate shortages of licensed medicines for which there is no suitable EDSForm monograph and when the preparation of extemporaneous or stock unlicensed pharmaceutical preparations is deemed relevant by the EDSForm WP. The technical recommendations support pharmacists and healthcare professionals in the member states in their decision-making process when considering the preparation of unlicensed medicines during a shortage. To this end, the technical recommendations are intended to serve as a source of evaluated products, formulations and relevant guidelines, including reference to the source of data, evidence ranking and guidance information.

Data included in the technical recommendations are assessed against several criteria to determine the confidence level and to ensure that the end user is aware of the general evidence related to that formulation. Formulations described in each entry should then be assigned a confidence level, e.g. using a colour coding system.

Criteria for the elaboration of a technical recommendation of the EDSForm WP

The appropriateness of elaborating a technical recommendation in response to a medicine shortage should be evaluated in the light of factors such as:

- duration and criticality of the shortage of one or several form(s) of a medicine;
- availability of the import of alternative licensed products;
- availability of e.g. the active pharmaceutical substance, excipients or licensed products that could be used as a starting material;
- feasability of unlicensed pharmaceutical preparations for the substitution of the missing licensed product;
- availability of bibliographic sources describing unlicensed pharmaceutical preparation that could be used for the substitution of the missing licensed product.

Use of the technical recommendations of the EDSForm WP

The technical recommendations are intended to support the decision-making process of healthcare professionals faced with a currently on-going shortage of a specific licensed medicine or group of licensed medicines.
However, it is ultimately up to the pharmacist or responsible person to decide how to best use the content of the technical recommendations, depending on the medicine shortage situation they face and national or supranational regulations.
It is wholly the responsibility up to the pharmacist or the responsible person using part or all of a formulation or the guidance given in a technical recommendation to ensure that the resulting pharmaceutical preparations comply with the requirements of the Ph. Eur. (e.g. Ph. Eur. monograph *2619*, *Pharmaceutical preparations*) and national or supranational regulations.

Overview of the technical recommendations of the EDSForm WP

Technical recommendations generally contain:

- an introduction providing the scope of the document and how to use it;
- information on existing licensed products that could be used either as a an alternative or as a starting material for unlicensed pharmaceutical preparations;
- information related to the use of unlicensed pharmaceutical preparations (e.g. specific risks posed by the substance(s), BCS class, information on cross-contamination, general information related to the handling and stability of the substance(s));
- an overview of selected unlicensed pharmaceutical preparations, with their assigned confidence level;
- bibliographical references to guidelines and other information that might be helpful during the on-going shortage;
- appendices containing further information on the formulations presented (e.g. guidance on preparation steps, composition and stability);

Other data or information that is considered relevant in a specific situation would be added on a case-by-case basis.

Lifecycle of the technical recommendations of the EDSForm WP

Technical recommendations are published on a dedicated webpage of the EDQM Website.

Once no reports of the respective medicine shortage are received anymore, the document should be removed or appropriately archived.

Published technical recommendations should be revised when information regarding the following cases is received:

- safety signals other than from EMA's Pharmacovigilance Risk Assessment Committee (PRAC),
- quality issues,
- new evidence-based clinical use,
- follow-up from questions received by the EDQM.

Current version, date of revision and reason of revision should be clearly indicated in the technical recommendations.