



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Inspections and Human Medicines Pharmacovigilance

## Criteria for classification of critical medicinal products for human and veterinary use

Shortages due to GMP non-compliance/quality defects

### 1. Introduction

GMP non-compliance/quality defects may lead to shortage of a product, if it is decided not to release a batch or even to withdraw batches from the market. Though in general such action based on GMP issues/quality defects is good precautionary practice, there might be situations where withdrawing a product or not releasing it might do more harm to public and animal health than allowing a product to remain on the market.

The classification of a medicinal product as critical should be performed by Member States for centrally authorized products (CAPs) and for non-CAPs taking into account the criteria expressed in this document and supply situations at a national level.

At the moment there is no harmonized approach to the classification of critical products, as the importance of a particular product might vary between Member States depending on factors such as the availability of alternative products (including capacity to meet demand), a worsening disease situation or the requirements of a national disease control program (for example, vaccination campaign). In the following a proposal is made for a more harmonized way of handling the classification of a medicinal product as 'critical'.

The principles set out in this paper may also apply when shortages due to other reasons are encountered, at the Member States' discretion.

### 2. Criteria for classification

When defining a product as critical, two criteria are of importance: therapeutic use and availability



of alternatives.

#### *A. Therapeutic use*

The medicinal product is an integral part of the treatment for or prevention of a disease, which is life-threatening or irreversibly progressive, or without which the public and animal health could be severely harmed.

This could be in acute situations (e.g. emergency situations), or chronic situations/maintenance of stable conditions, or disease with a fatal outcome where the product has been shown to affect the progression of the disease or survival.

In the case of veterinary medicinal products, a product may be classified as critical where its non-availability may have a negative impact on disease control programs or threaten sustainability of livestock production at a regional or national level.

#### *B. Availability of alternatives*

While a product may satisfy the criteria for therapeutic use (defined above), it would not be classified as being critical in case appropriate alternatives are available. These could be:

- Alternative manufacturing site for the same product; caveat: manufacturing capacity and technical and regulatory times to switch.
- Different strength/formulations of the same product; caveat: need for formulations suitable for use in special populations.
- Alternative dosing (lower dose/temporary break from treatment) or limiting the use to high risk patients/animals could be explored; caveat: this might depend on the expected duration.
- Generics; caveat, the availability and volume should be checked.
- Other products in the same class or even other classes; caveat: adverse events, or narrow therapeutic range or contra-indications.

### **3. Assessment and justification of a product being critical**

A product should be manufactured following GMP and to the quality standards specified in the marketing authorization and deviating from GMP and the marketing authorization may be harmful for public and animal health. Therefore, classifying a product as critical to allow continuity of supply should be thoroughly discussed, analysed from a benefit risk perspective and justified in an assessment report. A template for such an assessment report is available.

Whether a product would fulfil the therapeutic use criteria should be supported by literature and EU treatment guidelines and/or recommendations of physicians'/veterinarians'/other healthcare professionals' organizations, if available.

When assessing the alternatives, the caveats should be explicitly taken into account.

When assessing the need to keep a product on the market even in case of GMP issues, the expected duration of the shortage must be taken into account, as the utilization of a GMP non-compliant/quality defect product may only be allowed, by definition, on an extraordinary and, therefore, temporary, basis. It is also of importance to know the exact number of batches involved, the risk to the public

and animal health and the time lines for addressing the deficiencies.

Additionally, the situation may change over time, as for instance, other manufacturing sites become available or generics are approved. The assessment should mention timelines and number of units of product approved to be released and criteria for re-evaluation of the situation.

Also, at the start the situation might be different in the various Member States, as certain alternatives might not be available, or not to the same extent, everywhere. This will have to be addressed in the assessment report and ways forward to solve this and to re-evaluate this should be part of the assessment.