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European Medicines Agency

Methodology for the annual review of the Union list of critical medicines

1. Introduction

This document outlines the methodology, governance and criteria for identifying medicines to be added or removed from the Union list of critical medicines. Additionally, the document details the expected timelines and provides guidance on what information is needed to support a request for the review of a medicine to be added or removed from the Union list.

The Union list of critical medicines identifies medicines that are critical for health systems across the EU/EEA and for which continuity of supply should always be guaranteed for European patients.

In order to ensure the Union list remains relevant and aligned with the evolving needs of the EU/EEA healthcare systems, it is subject to review on an annual basis. The process is led by the Executive Steering Group on Medicines Shortages and Safety of Medicinal products (MSSG)[1], in collaboration with the MSSG Working Group on VSM and Policy, EMA, and relevant stakeholders including healthcare professional, patient, and industry organisations. The review will consider new scientific evidence, changes in public health priorities, emerging supply chain challenges, and updates to EU regulatory frameworks (including the proposed Reform of the Pharmaceutical Legislation and the proposed Critical Medicines Act). Through this collaborative and continuous process, the Union list will remain a dynamic tool for supporting the security of medicinal product supply across EU/EEA.

2. Overview of the Union list review

2.1. Governance and objectives

In 2025 MSSG and EMA established a draft methodology for the annual review of the Union list, including the procedures to be followed and the criteria to be met for a medicine to be considered for review during this procedure. This methodology has now been updated following completion of the first annual review and taking into account feedback received from member states, industry, healthcare professionals, and patient organisations.

[1] Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) | European Medicines Agency (EMA)

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2.2. Review process and frequency

This methodology establishes the procedure and criteria for the annual review of the Union list. Any amendment to the Union list takes effect upon its adoption and publication.

2.2.1. Review requests process

EU/EEA Member States and stakeholder groups (HCPs, patient organisations, learned societies and industry organisations) can submit review requests to EMA for review by the member states according to the Methodology to identify critical medicines [2].

A review request can be submitted for an active substance or a combination of active substances or for one or more routes of administration available for the respective active substance or its combination.

2.2.1.1. Grounds for inclusion or removal

Requests to consider the addition or removal of an active substance must be based on one or more of the specific grounds described below:

1) The active substance (or a combination of substances within its class) has been the subject of recurrent, historical critical shortages, with potential criticality already highlighted due to the lack of available alternatives (if request is to add a new active substance).
2) The active substance (or a combination of substances within its class) has stopped being the subject of recurrent, historical critical shortages, due to the number/abundance of available alternatives (if request is to remove a previously included active substance).
3) A change in market dynamics:
    a) Increasing the criticality of a medicine at EU level, i.e. new market development based on evidence that indicates that a medicine would become the predominant form of therapy or experience a significant increase in demand for an active substance (with limited or no alternative in the market), replacing other medicines that exit the market or occupy a diminished market share.
    b) Decreasing the criticality of a medicine at EU level, i.e., new market development based on evidence indicating market diversification due to an increasing number of available alternatives on the market.
4) A change in the indication of an authorised medicine that increases or decreases the criticality of the medicine to individual patients or to public health (linked to assessment criterion 1 of the criticality assessment "Therapeutic indication/importance").

2.2.1.2. Submission process and request periods

Requests for consideration of an active substance for addition or removal should be submitted using the template that will be circulated to all member states and stakeholders when the annual review procedure is launched. An example of this template is provided for reference in **Annex I**.

A specific template will be circulated for each annual review procedure. The template will specify the information necessary for a request for addition or removal to be considered and will list all active substance groups (ASGs) included in the most recently adopted version of the Union list.

[2] Methodology to identify critical medicines for the "Union List of critical medicines"

Review requests should be submitted to EMA as described in the procedure launch for each annual review and by the deadline specified.

MSSG and EMA will launch the annual review procedure in the first quarter of each year.

2.2.1.3. Review principles

EMA will consolidate all submissions received and circulate to member states for review based on the adopted methodology to identify critical medicines for the Union list of critical medicines[2].

- For active substances that have previously been categorised by the member states but ultimately not included in the Union list, member states will perform a targeted review of those substances based on the agreed methodology and the new information provided in the request for review.
- For active substances that have not previously been categorised by the member states, a criticality assessment will be performed by member states based on the agreed methodology, provided that the request is based on one or more of the specific grounds described above in section 2.2.1.1 and that sufficient supporting information has been provided in the request for review.
- For active substances currently included in the Union list that are proposed for removal, a criticality assessment will be performed by member states based on the agreed methodology, provided that the request is based on one or more of the specific grounds described above in section 2.2.1.1 and that sufficient supporting information has been provided in the request for review.

EMA will consolidate all requested changes, coordinate the review of all eligible requests by member states, and seek stakeholder feedback prior to finalisation and publication of the updated Union list.

2.2.1.4. High-level workflow

1. EMA launches the annual review procedure under the governance of the MSSG
2. Member states and stakeholders submit requests for review in parallel.
3. EMA reviews and validates the submitted requests for review, and prepares the list of active substance groups for criticality assessment by member states.
4. Member states perform a criticality assessment of all proposed additions or removals based on the adopted methodology.
5. EMA consults stakeholders on outcome of member states' criticality assessment.
6. EMA discusses with member states any remaining stakeholder comments and prepares final version for publication.
7. MSSG endorses the review outcome.
8. EMA notifies requesters about the substance review outcome.
9. EMA publishes the updated version on the EMA website, if applicable.

There may be a delay before EMA can respond due to the volume of requests and necessary processing time.

2.2.2. Maintenance activities

Annual maintenance tasks are scheduled to review the Union list. These tasks include reviewing:

- New ASGs authorised in Europe.
- ASGs that may exit the EU/EEA markets.
- ASGs that are becoming obsolete due to the new ASGs authorised and market shifts towards those ASGs.
- Editorial aspects of the published version, i.e., data artefacts on WHO ATC codes which may no longer be accurate, may also be addressed.

EMA annually plans these proactive activities in conjunction with SPOC WP/MSSG with support from the focal group on the Union list and the MSSG Working Group on VSM and Policy. EMA will consult with relevant Learned Societies on the criticality of molecules in the clinical domain as appropriate (per disease or therapeutic area).

3. Criteria for consideration for inclusion or removal of ASGs

3.1. Criteria for inclusion or removal

The criteria for inclusion or removal of ASGs is defined by the methodology to identify critical medicines for the Union list of critical medicines, adopted in June 2023 by the HMA/EMA TF-AAM Steering Committee[2]. Additional information can also be found in *section 2.2.1* of this document.

3.2. Supporting documentation

Member states and relevant stakeholder groups are required to provide a detailed reasoning for the request for inclusion or removal of the active ingredient in the Union list, supported by a strong clinical rationale and scientific evidence.

The parties are invited to consider the two criteria (therapeutic indication and availability of alternatives) for risk categorisation included in methodology of the Union list of critical medicines to strengthen their position.

An example of a clearly presented rationale received in the context of the 2025 annual update is provided below for reference*:*

> ***EXAMPLE:*** *A number of Marketing authorisation holders (MAHs) have decided to cease marketing some presentations of human insulins in all EU/EEA countries where they were previously marketed. Insulin treatment must be administered within regular dosing intervals and unavailability of these medicines can have serious implications for the health of patients. Human insulins are already included in the Union list, however considering the criticality of these medicines and the discontinuations of some human insulin products, analogue insulin medicines should be considered for inclusion in the Union list. Insulins must remain available to all patients who need them, and unavailability greatly impacts glycaemic control, risk of hypoglycaemia, and other serious complications for this patient group. Scientific evidence and strong clinical rationale that support this request for inclusion has been provided as part of this request.*

[2] Methodology to identify critical medicines for the "Union List of critical medicines"

4. Timelines at the glance

Time frame	Action	Who
Q1	EMA to launch procedure and circulate template. Member states and stakeholder groups to submit their requests for review/removal including a strong and detailed clinical rationale.	EMA Member states & Stakeholder groups
Q2	EMA to validate and process all requests for review/removal submitted. EMA to extract valid relevant data from Article 57 database and populate the list of active substance groups for MS classification.	EMA
Q2	Member States to complete the criticality categorisation exercise.	Member states
Q3	EMA to analyse the data on categorisation exercise submitted by member states	EMA
Q3	Stakeholder groups to provide input on the preliminary results following MS categorisation exercise.	EMA, Stakeholder groups
Q3/Q4	EMA to present and discuss the preliminary results with focal group, SPOC WP and MSSG WG for its adoption.	EMA, focal group, MSSG WG
Q4	MSSG adoption	MSSG
Q4/Q1 (next calendar year)	Notices to requester sent EMA to provide information on outcome of review to stakeholders who submitted a request for review/removal.	EMA
Q4	EMA to publish the annual review of Union list on EMA website.	EMA

5. Annex I: Template for request for review

The template will include two separate sheets: one for requests to include a new active substance, and another for requests to remove an active substance.

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International Nonproprietary Names (INN) **International Nonproprietary Names (INN) identify pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A nonproprietary name is also known as a generic name.**	**ATC level 5** **In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. Drugs are classified in groups at five different levels.** **ATC level 3 and 4 are chemical, pharmacological or therapeutic subgroups; level 5 is the chemical substance.**	**Route(s) of administration proposed for inclusion** *mandatory*	**Rationale for inclusion** **Please provide a detailed reasoning for the inclusion of the active ingredient in the Union list, supported by a strong clinical rationale and scientific evidence considering the grounds for inclusion described in section 2.2.1.1 above.** **Please consider the two criteria (therapeutic indication and availability of alternatives) for risk categorisation included in methodology of the Union list of critical medicines (EMA, 2023) to strengthen their position.** *mandatory*
INSULIN ASPART	*A10AB05*	*intravenous, subcutaneous use*	*Example: A number of Marketing authorisation holders (MAHs) have decided to cease marketing some presentations of human insulins in all EU/EEA countries where they were previously marketed. Insulin treatment must be administered within regular dosing intervals and unavailability of these medicines can have serious implications for the health of patients. Human insulins are already included in the Union list, however considering the criticality of these medicines and the discontinuations of some human insulin products, analogue insulin medicines should be considered for inclusion in the Union list. Insulins must remain available to all patients who need them, and unavailability greatly impacts glycaemic control, risk of hypoglycaemia, and other serious complications for this patient group. Scientific evidence and strong clinical rationale that support this request for inclusion has been provided as part of this request.*

ATC level 5 **In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. Drugs are classified in groups at five different levels. ATC level 3 and 4 are chemical, pharmacological or therapeutic subgroups; level 5 is the chemical substance.** *mandatory*	**ATC description** **The Anatomical Therapeutic Chemical code: a unique code assigned to a medicine according to the organ or system it works on and how it works. The classification system is maintained by the World Health Organization (WHO).** *mandatory*	**Route(s) of administration proposed for removal** *mandatory*	**Rationale for removal** **Please provide a detailed reasoning for the removal of this active ingredient from the Union list, supported by a strong clinical rationale and scientific evidence considering the grounds for removal described in section 2.2.1.1 above. Please take into account the two criteria (therapeutic indication and availability of alternatives) for risk categorisation included in methodology of the Union list of critical medicines to strengthen your position.** *mandatory*
ATC code level 5	*International Nonproprietary Names (INN)*	*Route of administration*	*Please include relevant information here to support the request as detailed in section 2.2.1 of this methodology.*