Minister of Health

ORDER No. 662
of 28 February 2025
on approval of the methodology for elaboration of the list of critical medicinal products of Romania

Published in: the Official Gazette of Romania no. 202 of 7 March 2025

On seeing approval report no. R.662 of 28.02.2025 of the Pharmaceutical and Medical Devices Directorate and notification no. 124.551E of 18.09.2024, of the National Agency for Medicines and Medical Devices of Romania, registered at the Ministry of Health with no. Reg2/28.040 of 18.09.2024,

taking into account the following provisions:

- Art. 5 a) of Law no. 95/2006 on healthcare reform, republished, as further amended and supplemented,
- Art. 3 a) and Art. 4 (3) points 1, 33 and 34 of Law no. 134/2019 on reorganisation of the National Agency for Medicines and Medical Devices and amendment of further ruling provisions, as further amended and supplemented,

pursuant to Article 7 (4) of Government Decision no. 144/2010 on the organisation and operation of the Ministry of Health, as further amended and supplemented,

the minister of health hereby issues the following order:

Art. 1 - The methodology for elaboration of the list of critical medicinal products of Romania, mentioned in the Annex which is integral part of this Order, is approved.

Art. 2 - The National Agency for Medicines and Medical Devices of Romania, as the competent authority in the field of medicinal products for human use, according to the provisions of Art. 699 point 29 of Law no. 95/2006 on healthcare reform, republished, as further amended and supplemented, shall carry out the provisions of this Order.

Art. 3 - On this Order's entry into force, Order of the Minister of Health no. 6.120/2024 on approval of the methodological rules for elaboration of the list of critical medicinal products of Romania, published in the Official Gazette of Romania, Part I, no. 1329 of December 31, 2024, shall be repealed.

Art. 4 - This Order shall be published in the Official Gazette of Romania, Part I.

Minister of health,
Alexandru Rafila

Annex

METHODOLOGY
for elaboration of the list of critical medicinal products of Romania

Chapter I
General provisions

Art. 1 - The current methodology establishes the general criteria for elaboration of the list of critical medicinal products of Romania, hereinafter referred to as the List, as well as classification of these medicinal products, according to the risk level that the lack of these products on the market can determine, at population health level.

Art. 2 - For the purpose of the provisions of this methodology, the terms and notions used have the following meanings:

1. ***ATC classification*** - the anatomical, therapeutic and chemical classification of the medicinal product;
2. ***INN*** – International Non-proprietary Name recommended by the World Health Organisation;
3. ***The Union list of critical medicines*** - the list of critical medicinal products, elaborated by the European Medicines Agency in collaboration with the national medicines agencies in the European Union, posted on www.ema.europa.eu;
4. ***GTLMPF*** – the multidisciplinary technical group for pharmaceutical policies, set up through Order of the Minister of Health;
5. ***MAH*** – Marketing Authorisation Holder – holder of the marketing authorisation of a medicinal product;
6. ***Permanent discontinuation*** - definitive cessation of the marketing of a medicinal product;
7. ***temporary discontinuation*** - cessation of marketing of a medicinal product for a limited period, with or without an estimated date of resumption of marketing. The temporary discontinuation can be prolonged or repeated, by delaying the initial date of resuming the marketing or repeating the discontinuation during the same year;
8. ***limited quantities*** – the quantities placed on the market by the MAH are considered insufficient to cover the treatment of patients.

Chapter II
Elaboration of the list

Art. 3 - (1) The list includes the INNs corresponding to medicinal products for human use considered critical for the national healthcare system, whose lack of continuation of the supply may generate risks to the population health.

(2) The National Agency for Medicines and Medical Devices of Romania, hereinafter referred to as **the NAMMDR**, evaluates the medicinal products associated with the INNs included in the list of critical medicinal products of the European Union, as well as the medicinal products corresponding to INNs for which, for a 2-year period, prior to the date of the evaluation, have been recorded at national level.

Art. 4 - (1) The NAMMDR performs the assessment of the risk of a medicinal product of being unavailable to the population, taking into account its relevance to public health, depending on the INN/ATC classification/pharmaceutical form/strength/specific indication, and classifies this risk according to the following criteria:

a) the product's therapeutic indication;

b) the availability of appropriate therapeutic alternatives;

c) Discontinuations notified to the NAMMDR by the MAH.

(2) The medicinal products associated to the INN analysed by the NAMMDR are evaluated according to the criteria provided in paragraph (1), each criterion being assigned a score between 0 and 3 points.

Art. 5 - (1) For the evaluation according to the criterion of the therapeutic indication, the importance of the indication from a clinical viewpoint is appreciated.

(2) If a medicinal product has several therapeutic indications, the indication for the condition with the most serious consequences for patients determines the risk level.

Art. 6 - The criterion of the availability of the appropriate therapeutic alternative aims to estimate whether a potential shortage of a medicinal product can be managed with appropriate therapeutic alternatives, namely if the medicinal products can be substituted without any negative impact on the patient's health by providing the same quality of care standard.

Art. 7 - The evaluation based on the criterion of discontinuation takes into account the NAMMDR evaluation of the discontinuations notified by the MAH in accordance with the provisions of Art. 737 (2) of Law no. 95/2006 on healthcare reform, republished, as further amended and supplemented.

Art. 8 - (1) The list proposed by the NAMMDR, as well as its changes are

subject to the multidisciplinary technical group for pharmaceutical policies (GTLMPF).

(2) In order to set up this List, in the context of the evaluation process carried out according to the present methodology, the NAMMDR may consult the GTLMPF, whenever it deems necessary.

Art. 9 - The NAMMDR carries out a yearly assessment in accordance with Art. 4, following which it can propose to maintain, add, exclude or reclassify some INNs from the List.

Chapter III
Approval of the list

Art. 10 - (1) The NAMMDR evaluates the analysed medicinal products in line with the criteria provided in Art. 4 and calculates the score of criticism in accordance with this methodology.

(2) The NAMMDR proposes the inclusion in the List of INNs corresponding to medicinal products having obtained a score of criticism greater than or equal to 2, which the NAMMDR classifies as one of the 3 risk levels: high, medium or low.

Art. 11 - (1) The proposal of a List set up by the NAMMDR is forwarded to the GTLMPF for analysis and approval.

(2) Within maximum 20 calendar days from receipt of the analysis of the list proposal, the GTLMPF formulates favourable opinion or notice with observations, which is forwarded to the NAMMDR. The notice with observations must be accompanied by their substantiation from the viewpoint of applying the criteria provided in Art. 4.

(3) In case of formulating a notice with observations, the NAMMDR analyses and takes over the observations or motivates their rejection.

(4)The NAMMDR sends the Pharmaceuticals and Medical Devices Directorate of the Ministry of Health the final List, within maximum 10 working days from receipt of GTLMPF's opinion.

Art. 12 - (1) The List of critical medicinal products of Romania is approved through Order of the Minister of Health and is published in the Official Gazette of Romania, Part I.

(2) The List provided in paragraph (1) is also posted on the webpages of the NAMMDR and the Ministry of Health.

Chapter IV
Classification of medicinal products included in the list according to the risk level

Section 1
The therapeutic indication criterion

Art. 13 - (1) The high-risk level, for which 3 points are awarded, is assigned to a medicinal product if at least one of the following conditions is met:

a) the medicinal product has a therapeutic indication for a condition with very serious consequences for the health of individual patients or public health: medicinal products or classes of medicinal products used to treat patients with general life-threatening acute conditions, specific life-threatening acute conditions, or irreversibly progressive conditions;

b) the medicinal product has a therapeutic indication for a disease which is potentially fatal, irreversibly progressive or, if left untreated, will pose an immediate threat, or cause severe impairment to the patient. This applies similarly to acute situations (emergencies), chronic situations or situations with potentially fatal outcomes.

c) If the treatment is unavailable or interrupted, it will jeopardise the vital prognosis of patients in the short or medium term;

d) the medicinal product is part of national public health programs.

(2) The medium risk level, for which 2 points are awarded, is assigned to a medicinal product if at least one of the following conditions is met:

a)the medicinal product is indicated for treatment of chronic, severely limiting diseases.

b) the medicinal product is indicated for the treatment of the following patient groups: minors, persons with disabilities, pregnant or breastfeeding women;

c) the medicinal product is indicated for the treatment of patients for whom replacing the treatment, according to the summary of product characteristics, may raise tolerability problems or difficulties in administration;

d) the medicinal product is indicated for the prevention or treatment of notifiable diseases, according to the provisions of Government Decision No. 657/2022 on approval of the content and methodology for reporting and collecting data for the surveillance of communicable diseases in the Romanian Register of Communicable Diseases, with the exception of medicinal products provided under national public health programs;

e) If the disease is left untreated, it may induce potentially irreversible disease progression, hospitalisation or intensified treatment, but no fatality is expected.

f) the medicinal product prevents relapses of a condition, and if no longer administered, the disease will relapse even if the disease progression is slow.

(3) The low risk level, for which 0 points are awarded, is attributed to a medicinal product which does not fulfil the high or medium risk conditions specified in paragraphs (1) and (2).

Section 2
The criterion of availability of appropriate alternatives

Art. 14 - An alternative is appropriate if it fulfils all the following criteria:

a) The alternative medicine is authorised for the same therapeutic indication and is marketed in Romania;

b) the alternative treatment is clinically possible;

c) The use of alternative treatment does not have a negative impact on the patient's health and provides the same quality of care standard.

Art. 15 - The risk level assessment, according to the criterion of availability of the appropriate alternative is carried out qualitatively and quantitatively, by reporting to the number of appropriate alternatives identified as being placed on the Romanian market.

Art. 16 - The high risk level, for which 3 points are awarded, takes into account the fact that there is no appropriate alternative or there is only one appropriate alternative available on ATC level 4 or 5, which is in one of the following situations:

1. alternative treatment is not clinically possible, and the active substance or combination of active substances has unique pharmacology and no alternative treatment options exist;
2. switching to an alternative treatment cannot be made in a timely manner due to the need for additional specialist medical consultations or requires a switch from self-administration to administration under medical supervision;
3. the alternative treatment does not meet the clinical needs of the entire target patient population, a subgroup of patients who are not in the majority cannot use the alternative treatment or it is contraindicated and requires additional clinical consultations;
4. the alternative treatment is available in limited quantities and a possible shortage is expected due to increased demand.

Art. 17 - The medium risk level, for which 2 points are awarded, is considered when at most two appropriate alternatives are available on ATC level 4 or 5, the same INN, in one of the following situations:

1. the alternative treatment may only be achieved by using alternative pharmaceutical forms or different routes of administration, alternative strengths, or alternative dosing regimens;
2. the alternative treatment is available in limited quantities and a shortage is expected due to increased demand.

Art. 18 - The low risk level, for which 0 points are awarded, is attributed to a medicinal product which does not meet the high or medium risk conditions specified in Articles 16 and 17.

Section 3
The discontinuation criterion

Art. 19 - (1) The discontinuation criterion takes into account the assessment performed by the NAMMDR of the discontinuations notified by the MAH in a 2-year period prior to the date on which the assessment is performed, in accordance with the provisions of Art. 737 paragraph (2) of Law no. 95/2006, republished, as further amended and supplemented, taking into account:

a) the negative impact on ensuring the availability of necessary treatments for patients;

b) the frequency and periods in which the discontinuation of a medicinal product had a negative impact at patient level;

c) the availability of marketed pharmaceutical equivalents, also considering the location of the supply source.

(2) A negative impact on ensuring availability at patient level, during the period notified with "discontinuation", is considered to be the decrease in the stock of a medicinal product at national level below the average monthly turnover, if the need was not covered by the use of medicinal products which are pharmaceutical equivalents. The average monthly turnover is calculated as the monthly average of the turnover of the respective medicinal product for the last three months prior to the notification of discontinuation, according to the consumption history recorded in the Electronic Reporting System provided for in Art. 804^1 of Law no. 95/2006, republished, as further amended and supplemented.

(3) A medicinal product which cumulatively meets the following conditions is considered a pharmaceutical equivalent:

a) it contains the same active substance(s);

b) it contains the same amount of active substance(s) or the same strength, for liquid pharmaceutical forms;

c) it has the same pharmaceutical form;

d) it meets the same/equivalent standards as regards the patient's clinical needs at the moment of product administration.

Art. 20 - The awarding of the score provided for in Art. 4 paragraph (2) is done as follows:

a) for permanent discontinuation or temporary discontinuation which had a negative impact on ensuring the availability of treatments at patient level for a cumulative period longer than 6 months, 3 points are awarded;

b) for temporary discontinuation which had a negative impact on ensuring the availability of treatments at patient level for a cumulative period shorter than 6 months, 2 points are awarded;

c) for discontinuation caused by limited quantities, 1 point is awarded;

d) for discontinuation which did not have a negative impact on ensuring the availability of treatments at patient level, 0 points are awarded.

Chapter V
Calculation of the score of criticism

Art. 21 - (1) The sum of the scores corresponding to each criterion constitutes the score of criticism for a medicinal product whose INN is proposed for inclusion in the List.

(2) The classification by risk category is based on the score of criticism, as follows:

a) 2 - 4 points – low risk;

b) 5 - 7 points – medium risk;

c) 8 - 9 points – high risk.