Annex I

Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisation(s)

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for isoniazid, the scientific conclusions are as follows:

In view of the available data on acute generalised exanthematous pustulosis (AGEP) with a case of close temporal relationship, a positive de-challenge and re-challenge and a positive patch test, and in view of the data on drug-induced lupus, the PRAC considers a causal relationship between isoniazid and AGEP, and between isoniazid and lupus-like syndrome, is at least a reasonable possibility. The PRAC concluded that the product information of products containing isoniazid should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for isoniazid the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing isoniazid is unchanged subject to the proposed changes to the product information

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

Annex II

Amendments to the product information of the nationally authorised medicinal product(s)

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike through~~)

Summary of Product Characteristics

- Section 4.4

A warning should be added as follows (to be adapted at national level):

Severe cutaneous adverse reactions (SCARs) such as <include all SCARs already listed in the SmPC section 4.8: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS)> and acute generalised exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with <medicine> treatment.

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions.

If signs and symptoms suggestive of these reactions appear, <medicine> should be withdrawn immediately and an alternative treatment considered.

If the patient has developed a serious reaction such as SJS, TEN, DRESS or AGEP with the use of <medicine>, treatment with <medicine> must not be restarted in this patient at any time.

- Section 4.8

The following adverse reaction should be added under the SOC Skin and subcutaneous tissue disorders with a frequency unknown:

Acute generalised exanthematous pustulosis

The following adverse reaction should be added under the SOC Musculoskeletal and connective tissue disorders with a frequency unknown:

Lupus-like syndrome

Package Leaflet

- Section 2

A contraindication and warning related to SCARs should be added to the PL section 2:

Do not take <medicine>:

- **If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking <medicine>.**

Warnings and precautions - Take special care with <medicine>:

Serious skin reactions such as <include all SCARs already listed in the PL section 4: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS)> <and> acute generalised exanthematous pustulosis (AGEP)

have been reported in association with <medicine> treatment. Stop using <medicine> and seek medical attention immediately if you notice any of the symptoms described in section 4.

- Section 4

The following adverse reactions should be added as a serious side effect with a frequency unknown:

A red, scaly widespread rash with bumps under the skin and blisters accompanied by fever. The symptoms usually appear at the initiation of treatment (acute generalised exanthematous pustulosis).

[…]

Lupus-like syndrome, causing symptoms such as swollen joints, tiredness and rashes.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	June 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	3 August 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	2 October 2025