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 meropenem, the scientific conclusions are as follows:

In view of available data on risks from clinical trials, the literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC considers that a causal relationship between meropenem and hypokalaemia and drug-induced liver injury is at least a reasonable possibility. The PRAC concluded that the product information of products containing meropenem 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 meropenem, the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing meropenem 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 amended as follows:

[…]

~~Hepatic function monitoring~~ **Drug-induced liver injury (DILI)**

Hepatic function should be closely monitored during treatment with meropenem due to the risk of ~~hepatic toxicity (hepatic dysfunction with cholestasis and cytolysis~~ **DILI** (see section 4.8). **If severe DILI occurs, treatment discontinuation should be considered as clinically appropriate. Meropenem should be reintroduced only if assessed as essential for treatment.**

Use in patients with liver disease: patients with pre-existing liver disorders should have liver function monitored during treatment with meropenem. There is no dose adjustment necessary (see section 4.2).

[…]

- Section 4.8

The following adverse reaction should be added under the SOC Metabolism and nutrition disorders with a frequency "uncommon": **Hypokalaemia**

The following adverse reaction should be added under the SOC Hepatobiliary disorders with a frequency "uncommon": **Drug-induced liver injury** with the following footnote **DILI includes hepatitis and liver failure**.

Package Leaflet

- Section 2

  A warning should be added as follows under "warnings and precautions"":

  Liver problems

  If you notice yellowing of the skin and eyes, itchy skin, dark-coloured urine or light-coloured stool tell your doctor. This may be a sign of liver problems which your doctor needs to check.

- Section 4

  The following adverse drug reactions should be added under "Uncommon":

  - **Reduced levels of potassium in your blood (which can cause weakness, muscle cramps, tingling and heart rhythm disturbances).**
  - **Liver problems. Yellowing of the skin and eyes, itchy skin, dark-coloured urine or light-coloured stool. If you notice these signs or symptoms, see a doctor straight away.**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	25 April 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	09 June 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	08 August 2025