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 etoposide, the scientific conclusions are as follows:

In view of available data on opportunistic infections from clinical trial(s), the literature, spontaneous reports including in some cases a close temporal relationship, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between etoposide and opportunistic infections like *pneumocystis jirovecii* pneumonia is at least a reasonable possibility. The PRAC concluded that the product information of products containing etoposide should be amended accordingly.

In view of available data on an increased risk of hypersensitivity reactions if an in-line filter is used for administration from the literature, the PRAC considers a causal relationship between etoposide (not etoposide phosphate) administered with an in-line filter and this increased risk is at least a reasonable possibility. The PRAC concluded that the product information of products containing etoposide (not etoposide phosphate) for i.v. administration 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 etoposide the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing etoposide 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 (for products for injection/infusion only, not for etoposide phosphate containing products):

Hypersensitivity

Physicians should be aware of the possible occurrence of an anaphylactic reaction with <product>, manifested by chills, pyrexia, tachycardia, bronchospasm, dyspnoea and hypotension, which can be fatal. Treatment is symptomatic. <product> should be terminated immediately, followed by the administration of pressor agents, corticosteroids, antihistamines, or volume expanders at the discretion of the physician. **An increased risk for infusion-related hypersensitivity reactions was observed when in-line filters were used during etoposide administration. In-line filters should not be used.**

- Section 4.8

The following adverse reaction(s) should be amended for all etoposide or etoposide phosphate containing products under the SOC Infections and infestations:

- Infection*****

***including opportunistic infections like *pneumocystis jirovecii* pneumonia**

Package Leaflet

4. Possible side effects

- Infection **(including infections seen in patients with a weakened immune system, e.g. a lung infection called *pneumocystis jirovecii* pneumonia)**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	October 2023 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	27/11/2023
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	25/01/2024