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 vinorelbine the scientific conclusions are as follows:

In view of available data on risks of Pulmonary embolism, Posterior reversible encephalopathy syndrome and Skin hyperpigmentation (serpentine supravenous hyperpigmentation) from the clinical trials, the literature, spontaneous reports including in some cases a close temporal relationship, a positive re-challenge, the PRAC considers a causal relationship between vinorelbine and Pulmonary embolism, Posterior reversible encephalopathy syndrome and Skin hyperpigmentation (serpentine supravenous hyperpigmentation) is at least a reasonable possibility. The PRAC concluded that the product information of products containing vinorelbine should be amended accordingly.

The CMDh agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

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

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing vinorelbine are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

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~~)

Both forms of vinorelbine (iv, oral):

Summary of Product Characteristics

Section 4.8

The following adverse reaction should be added under the SOC Respiratory, thoracic and mediastinal disorders with a frequency not known:

Pulmonary embolism

Package Leaflet

Section 4:

Immediately contact your doctor, while you are given (product name), if you develop any of the following symptoms

…..

a chest pain, breathlessness and fainting, which can be a symptom of a clot in a blood vessel in the lungs (pulmonary embolism)

Both forms of vinorelbine (iv, oral):

Summary of Product Characteristics

Section 4.8

The following adverse reactions should be added under the SOC Nervous system disorders with a frequency not known:

Posterior reversible encephalopathy syndrome

Package Leaflet

Section 4:

Immediately contact your doctor, while you are given (product name), if you develop any of the following symptoms

….

headaches, changed mental state which may lead to confusion and coma, convulsions, blurred vision and high blood pressure, which could be sign of a neurological disorder such as posterior reversible encephalopathy syndrome

IV form of vinorelbine:

Summary of Product Characteristics

Section 4.8

The following adverse reactions should be added under the SOC Skin and subcutaneous tissue disorders with a frequency not known:

Skin hyperpigmentation (serpentine supravenous hyperpigmentation)

Package Leaflet

Section 4:

Not known:

Darker colour of skin that follows the path of veins

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 15 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	January 29 2023
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	March 30 2023