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 simvastatin, the scientific conclusions are as follows:

In view of available data on drug-drug interaction between simvastatin and palbociclib, and between simvastatin and ribociclib, from the literature, spontaneous reports including cases with a close temporal relationship, a positive de-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship of drug-drug interaction between simvastatin and palbociclib, as well as between simvastatin and ribociclib, is at least a reasonable possibility. The PRAC concluded that the product information of products containing simvastatin 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 simvastatin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing simvastatin 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 4.5

Palbociclib and ribociclib should be added to the table Drug Interactions Associated with Increased Risk of Myopathy/Rhabdomyolysis

Interacting agents: **Palbociclib**

Ribociclib

Prescribing recommendation for palbociclib: **concomitant administration is not recommended**

Prescribing recommendation for ribociclib: **concomitant administration should be avoided**

MAHs who do not present this information in a table should consider presenting this information in a table. However, other ways of presenting the information may be acceptable. If the information is not tabulated, the following wording should be used:

[**…] concomitant use of simvastatin with** […] **and ribociclib should be avoided. Concomitant administration of simvastatin with palbociclib is not recommended, because it may increase the risk of rhabdomyolysis.**

Package Leaflet

Other medicines and simvastatin

Tell your doctor if you are taking, have recently taken or might take any other medicine(s) with any of the following active ingredients:
[…]

Ribociclib (used to treat breast cancer)

Palbociclib (used to treat breast cancer)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	25 January 2026
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	26 March 2026