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) amlodipine/rosuvastatin, perindopril/amlodipine/rosuvastatin, the scientific conclusions are as follows:

Non-cardiogenic pulmonary oedema in amlodipine overdose

In view of available data on non-cardiogenic pulmonary oedema from the literature, spontaneous reports including cases with a compatible temporal relationship, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between amlodipine and non-cardiogenic pulmonary oedema is at least a reasonable possibility. The PRAC concluded that the product information of products containing perindopril / amlodipine / rosuvastatin and amlodipine / rosuvastatin 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 amlodipine/rosuvastatin, perindopril/amlodipine/rosuvastatin), the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing amlodipine / rosuvastatin, perindopril/amlodipine/rosuvastatin 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 amlodipine/rosuvastatin, perindopril/amlodipine/rosuvastatin 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~~)

Summary of Product Characteristics

Section 4.9

Available data for amlodipine suggest that gross overdosage could result in excessive peripheral vasodilatation and possibly reflex tachycardia. Marked and probably prolonged systemic hypotension up to and including shock with fatal outcome have been reported.

Non-cardiogenic pulmonary oedema has rarely been reported as a consequence of amlodipine overdose that may manifest with a delayed onset (24-48 hours post-ingestion) and require ventilatory support. Early resuscitative measures (including fluid overload) to maintain perfusion and cardiac output may be precipitating factors.

Package Leaflet

3. How to take <perindopril /amlodipine / rosuvastatin>, <amlodipine / rosuvastatin>

If you take more <perindopril /amlodipine / rosuvastatin>, <amlodipine / rosuvastatin> than you should

[…]

Excess fluid may accumulate in your lungs (pulmonary oedema) causing shortness of breath that may develop up to 24-48 hours after intake.

[…]

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	March 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	8 May 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	7 July 2022