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 verapamil, the scientific conclusions are as follows:

In view of available data on drug-drug interaction between verapamil and metformin from the literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC considers that causal relationship between verapamil and reduced hypoglycemic effect of metformin is at least a reasonable possibility.

In view of available data on the risk of acute respiratory distress syndrome from the literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC considers that a causal relationship between verapamil overdose and acute respiratory distress syndrome is at least a reasonable possibility.

The PRAC concluded that the product information of products containing verapamil 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 verapamil the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing verapamil 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 verapamil 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 4.5

The interactions/s should be added as follows:

Co-administration of verapamil with metformin may reduce the efficacy of metformin.

- Section 4.9

Acute respiratory distress syndrome should be added along with other clinical manifestations of verapamil overdose

Package Leaflet

- Section 2

Other medicines and verapamil
<Tell your <doctor> <or> <pharmacist> if you are <taking> <using>, have recently <taken> <used>or might <take> <use> any other medicines.>
Verapamil may decrease the glucose-lowering effect of metformin.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	10/2020 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	29/11/2020
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	20/01/2021