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 ezetimibe / rosuvastatin, the scientific conclusions are as follows:

Based on review of literature data, the PRAC considered that the risk of drug interaction of ezetimibe/rosuvastatin with simeprevir, as well as with regorafenib should be reflected in section 4.5 of the Summary of Product Characteristics of ezetimibe/rosuvastatin containing products. The Package Leaflet should be updated 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 ezetimibe / rosuvastatin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing ezetimibe / 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 ezetimibe / 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 4.5 - Table of rosuvastatin interactions

The following interaction should be added as follows:

Table 1 Effect of co-administered medicinal products on rosuvastatin exposure (AUC; in order of decreasing magnitude) from published clinical trials

Interacting drug dose regimen	*Rosuvastatin dose regimen*	*Change in rosuvastatin AUC**
Regorafenib 160 mg, OD, 14 days	***5 mg single dose***	***3.8-fold*** ↑
Simeprevir 150 mg, OD, 7 days	***10 mg single dose***	***2.8-fold*** ↑

Package leaflet

- Section 2. Other medicines and ezetimibe/rosuvastatin

- regorafenib (used to treat cancer)

- simeprevir (used to treat chronic hepatitis C infection)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	March CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	5 May 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	4 July 2018