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 rosuvastatin, the scientific conclusions are as follows:

Based on a review of literature data provided within the reporting period of this PSUR showing interaction of rosuvastatin with regorafenib and protease inhibitors leading to an increased AUC of rosuvastatin, muscle related adverse drug reactions being dose dependent, and having considered the PRAC recommendation and the PRAC assessment report of the PSUSA for ezetimibe/rosuvastatin (PSUSA/00010271/201707), the PRAC considers that the risk of drug interaction of rosuvastatin with regorafenib and protease inhibitors should be reflected in section 4.5 of the Summary of Product Characteristics of 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 rosuvastatin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing 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 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

The following interactions 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*** ↑
Velpatasvir 100 mg OD	***10 mg, single dose***	***2.7-fold*** ↑
Ombitasvir 25 mg/paritaprevir 150 mg/ Ritonavir 100 mg OD/ dasabuvir 400 mg BID, 14 days	***5 mg, single dose***	***2.6-fold*** ↑
Grazoprevir 200 mg/elbasvir 50mg OD, 11 days	***10 mg, single dose***	***2.3-fold*** ↑
Glecaprevir 400 mg/pibrentasvir 120 mg OD, 7 days	***5 mg OD, 7 days***	***2.2-fold*** ↑

Package Leaflet

- Section 2. Other medicines and rosuvastatin

- regorafenib (used to treat cancer)

- any of the following drugs used to treat viral infections, including HIV or hepatitis C infection, alone or in combination (please see Warnings and precautions): ritonavir, lopinavir, atazanavir, simeprevir, ombitasvir, paritaprevir, dasabuvir, velpatasvir, grazoprevir, elbasvir, glecaprevir, pibrentasvir.

Annex III

Timetable for the implementation of this position>

Timetable for the implementation of this position

Adoption of CMDh position:	July 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position :	8 September 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	7 November 2018