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:

The adverse drug reaction (ADR) hypersensitivity (encompassing anaphylaxis, angioedema, rash and urticaria) is considered as an important identified risk by one MAH. The reporting frequency of anaphylaxis is “very rare”. However, in the summary of product characteristics (SmPC) of simvastatin no mention to anaphylaxis exists.

Cases of anaphylactic reaction/shock have been reported with simvastatin in the clinical trials (total n=8) as well as post-marketing (total n=57). Of these, 4 cases were reported in this PSUR interval, and they have been evaluated to be causally related to simvastatin. Taking into account that anaphylaxis is considered as an important identified risk and its causal relationship with simvastatin, it is warranted to update the section 4.8 of the SmPC to include the ADR anaphylaxis under the system organ class (SOC) Immune system disorders with the frequency of very rare.

The Hypersensitivity subsection of ‘Section 4, Possible side effects’ of the current package leaflet (PL) does not contain adequate information to describe anaphylaxis. Therefore, the PL should also be updated to include this information.

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 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 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 simvastatin 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 4.8

The following adverse reaction(s) should be added under the SOC Immune system disorders with a frequency very rare:

anaphylaxis

Package Leaflet

To reflect the inclusion of anaphylaxis in the SmPC 'Section 4. Possible side effects' of the package leaflet should include the following bullet point within the hypersensitivity subsection:

The following rare serious side effects were reported.

If any of these serious side effects happen, stop taking the medicine and tell your doctor immediately or go to the emergency room at your nearest hospital.

• hypersensitivity (allergic) reactions including:

- swelling of the face, tongue and throat which may cause difficulty in breathing **(angioedema)**

The following very rare serious side effect was reported:

- a serious allergic reaction which causes difficulty in breathing or dizziness (anaphylaxis)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2017 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	27 January 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	28 March 2018