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 pitavastatin, the scientific conclusions are as follows:

Angioedema

Based on reported post-marketing cases of angioedema, including face, lip, oropharyngeal and laryngeal swelling, for which some cases had positive dechallenges (n=37) and even positive rechallenges (n=3), the PRAC considers a causal relationship between pitavastatin and angioedema can be established and concluded that the product information of products containing pitavastatin should be amended accordingly.

Lupus-like syndrome

Based on the presented safety information from literature in other statin procedures regarding lupus-like syndrome and product information from other statins, pointing towards a class-effect, and the evidence from the pitavastatin case in the Eudravigilance database, the PRAC considers that a causal association between pitavastatin and lupus-like syndrome is at least a reasonable possibility and concluded that the product information of products containing pitavastatin should be amended accordingly.

Gynaecomastia

Based on reported post-marketing cases of gynaecomastia, for which 2 cases had positive dechallenge and even 1 of them positive rechallenge and no alternative cause could be identified, the PRAC considers that a causal association between pitavastatin and gynaecomastia is at least a reasonable possibility and concluded that the product information of products containing pitavastatin 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 pitavastatin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing pitavastatin 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 pitavastatin 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 Skin and subcutaneous tissue disorders with a frequency not known:

Angioedema

The following adverse reaction(s) should be added under the SOC Musculoskeletal and connective tissue disorders with a frequency not known:

Lupus-like syndrome

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

Gynaecomastia

Package Leaflet

Section 4

Heading describing serious side effects which needs treatment discontinuation and immediate medical attention

Under Side effects of unknown frequency:

- **Lupus-like syndrome (including rash, joint disorders and effects on blood cells)**

Under Rare (affects less than 1 in 1,000 people):

- **Breast enlargement in men (gynaecomastia)**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	February 2020 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	12 April 2020
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	11 June 2020