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 atorvastatin / ezetimibe, the scientific conclusions are as follows:

Based on the review of the PSUR data in relation to reported spontaneous cases of chromaturia associated with atorvastatin/ezetimibe use, and taking into account that hepatitis, hepatic failure and rhabdomyolysis which are listed as known side effected in section 4.8 of medicinal products containing statins including atorvastatin/ezetimibe, are known to cause urine discolouration, the PRAC considers that urine discolouration should be included in the Package Leaflet for patients. Patients who may not know that urine discolouration could be caused by atorvastatin, may be able to link it to the more serious disorders (liver disorders, rhabdomyolysis) listed in the SmPC and increase their chance of recognising the symptoms early as something more serious and as a result seek immediate medical advice.

In this context, it is also noted that other statins (i.e. pravastatin, simvastatin, rosuvastatin) have discoloured urine mentioned as symptom in their Package Leaflets.

The PRAC does not consider that a separate addition of chromaturia as a symptom of liver disorders or rhabdomyolysis in the SmPC is necessary.

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 atorvastatin / ezetimibe the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing atorvastatin / ezetimibes 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 atorvastatin / ezetimibe 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~~)>

Package Leaflet

4. Possible side effects

Like all medicines, <product name> can cause side effects, although not everybody gets them.

If you experience any of the following serious side effects or symptoms, stop taking your tablets and tell your doctor immediately or go to the nearest hospital accident and emergency department.

[..]

- muscle weakness, tenderness, ~~or~~ pain or **red-brown discolouration of urine** and particularly, if at the same time, you feel unwell or have a high temperature it may be caused by an abnormal muscle breakdown which can be life-threatening and lead to kidney problems

[..]

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	March / 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	11 May 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	10 July 2019