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 treprostinil, the scientific conclusions are as follows:

Literature suggests that arthralgia is known to be more commonly reported with the use of treprostinil and other prostacyclins than with placebo (CHEST guideline, Taichman, 2014). Although the mechanism by which prostacyclins may cause arthralgia is not known, cases have been reported in the post-marketing setting which suggest a causal association. This event is listed for another prostacyclin analogue and it is considered that arthralgia should also be listed in the product information of treprostinil. Based on pooled data from placebo-controlled clinical trials, the frequency of arthralgia with treprostinil is considered as common.

Data from clinical studies and literature suggest that treprostinil and other prostacyclin may induce myalgia. Pooled data from placebo-controlled clinical trials determine the frequency of myalgia as common. Although a limited number of relevant cases were reported in the post marketing setting, this is mostly due to the poor documentation of the cases and it is considered that myalgia should be listed in the product information.

Therefore, in view of the data presented in the reviewed PSUR(s), the PRAC considered that changes to the product information of medicinal products containing treprostinil, were warranted.

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 treprostinil the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing treprostinil 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 treprostinil are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that such marketing authorisations are varied accordingly.

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 reactions should be added under the SOC Musculoskeletal, connective tissue and bone disorders with a frequency **common**:

Myalgia, **Arthralgia**

Package Leaflet

- Section 4 Possible side effects

The following adverse reactions should be added as common side effects:

Common side effects (more than 1 in 100 cases)

Joint pain; **Muscle pain**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2017 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	11 March 2017
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	10 May 2017