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 levobunolol (ophthalmic indication), the scientific conclusions are as follows:

During the reporting interval, the MAH reviewed and considered confirmed signals of foreign body sensation in eyes, alopecia and hypersensitivity reaction including symptoms or signs of eye allergy and skin allergy. Based on their close temporal relationship, positive de-challenge or rechallenge in some cases and plausible mode of action, the PRAC agreed with the MAH conclusion that these adverse reactions should be included in the product information for levobunolol-containing products authorised in ophthalmic indications. In addition, to avoid duplication, where alopecia is already listed as an adverse reaction for other ophthalmic beta-blockers to indicate reactions that may possibly occur with levobunolol, it should be deleted from that section.

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 levobunolol (ophthalmic indication) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing levobunolol (ophthalmic indication) 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 levobunolol (ophthalmic indication) 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 Eye disorders with a frequency not known] **foreign body sensation in eyes**

[The following adverse reaction(s) should be added under the SOC Skin and subcutaneous tissue disorders with a frequency not known] **alopecia**

[The following adverse reaction(s) should be added under the SOC Immune system disorders with a frequency not known] **hypersensitivity reaction including symptoms or signs of eye allergy and skin allergy**

[…]

Additional adverse reactions have been observed with other ophthalmic beta-blockers, which may potentially occur in use of <invented name>:

[The following adverse reaction(s) should be deleted under the SOC Skin and subcutaneous tissue disorders] ~~alopecia~~

[…]

Package Leaflet

- Section 4

[The following adverse reactions should be added with a frequency not known]

Hair loss

Sensation of a foreign body in the eye

Symptoms of allergic reaction (such as swelling, redness of the eye and rash of the skin)

[…]

Reactions seen within the class of beta-blockers when used for treating eye conditions:

[The following adverse reactions should be deleted]

~~Hair loss~~

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

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