

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 acebutolol, the scientific conclusions are as follows:

In view of available data on **small-for-gestational-age newborns**, from the literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC considers a causal relationship between acebutolol and small-for-gestational-age is at least a reasonable possibility. The PRAC concluded that the product information of products containing acebutolol should be amended accordingly.

In view of available data on **alopecia** from the literature, spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and re-challenge, the PRAC considers a causal relationship between acebutolol and alopecia is at least a reasonable possibility. The PRAC concluded that the product information of products containing acebutolol should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for acebutolol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing acebutolol is unchanged subject to the proposed changes to the product information.

The CMDh recommends that the terms of the Marketing Authorisation(s) should be varied.

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 4.6 Fertility, pregnancy and lactation

Pregnancy

[...]

Beta-blockers can reduce placental perfusion, which can lead to premature delivery, **small-for-gestational-age newborn**, intrauterine foetal death and spontaneous abortion. [...]

Section 4.8 Undesirable effects:

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

Alopecia

Package Leaflet

2. What you need to know before you take acebutolol

Pregnancy and breast-feeding

[...]

Beta-blockers can reduce blood flow to the placenta, which can result in premature birth, **newborn smaller than expected**, intrauterine foetal death and abortion.

[...]

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

[...]

Other possible side effects:

Not known (frequency cannot be estimated from the available data)

- **Hair loss (Alopecia)**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	September 2023 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	29/10/2023
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	28/12/2023