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 aceclofenac, the scientific conclusions are as follows:

In view of available data and the recommendation regarding use of systemic nonsteroidal anti-inflammatory drugs (NSAIDs - including aceclofenac) during pregnancy, and in the absence of clinical data for the use of topical aceclofenac formulation during pregnancy (in particular, uncertainty of systemic plasma levels and lack of a known threshold of plasma level below which NSAID exposure during pregnancy does not result in adverse effects to the foetus), the PRAC concluded that the product information of topical aceclofenac-containing medicinal products should be updated. This includes highlighting the contraindication for use during the last trimester, as well as recommendation to avoid usage during the first and second trimester of pregnancy, unless clearly necessary. If use during pregnancy is justified, the lowest possible dose for the shortest treatment duration should be applied.

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 aceclofenac the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing aceclofenac 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 4.3**

The contraindication should be added as follows:

Third trimester of pregnancy

- **Section 4.6**

The recommendations for use in pregnancy should be amended as follows:

Pregnancy

There are no clinical data from the use of [product name] during pregnancy. Even if systemic exposure is presumably lower compared with oral administration, it is not known if the systemic [product name] exposure reached after topical administration can be harmful to an embryo/foetus. During the first and second trimester of pregnancy, [product name] should not be used unless clearly necessary. If used, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, systemic use of prostaglandin synthetase inhibitors including [product name] may induce cardiopulmonary and renal toxicity in the foetus. At the end of the pregnancy prolonged bleeding time in both mother and child may occur, and labour can be delayed. Therefore, [product name] is contraindicated during the last trimester of pregnancy (see section 4.3).

Package Leaflet

Section 2. What you need to know before you <take/use> [product name]

Do not use <product>

If you are in the last 3 months of pregnancy.

Pregnancy, breast-feeding and fertility

[…]

Oral forms (e.g., tablets) of aceclofenac can cause adverse effects in your unborn baby. It is not known if the same risk applies to [product name].

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Do not use [product name] if you are in the last 3 months of pregnancy. You should not use [product name] during the first 6 months of pregnancy unless clearly necessary and advised by your doctor. If you need treatment during this period, the lowest dose for the shortest time possible should be used.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2023 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	28 January 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	28 March 2024