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 nimesulide (topical formulations), the scientific conclusions are as follows:

In view of available information about medicines of the same therapeutic class, on a plausible mechanism, the Lead Member State considers that PI should be amended to include a contraindication for use during the last trimester, as well as recommendations to avoid usage during the first and second trimester of pregnancy, unless clearly necessary, and if so use of the lowest possible dose, and for the shortest treatment duration.

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 nimesulide (topical formulations) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing nimesulide (topical formulations) 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~~)

This text is to be adapted, at a national level, to the existing wordings in the product information. In case the product information already includes a similar or stricter advice on use in pregnancy, the similar or stricter advice remains valid and should remain.

In case the product information contains statements indicating no teratogenic effects or no relevant systemic exposure, this text should be deleted.

Summary of Product Characteristics

• Section 4.3

[…]

- third trimester of pregnancy

• Section 4.6

[…] **Pregnancy**

There are no clinical data from the use of [product name] during pregnancy. Even if systemic exposure is 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 [product name] can cause adverse effects in your unborn baby. It is not known if the same risk applies to [product name] when it is used on the skin.

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:	February CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	7 April 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	6 June 2024