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 dexketoprofen the scientific conclusions are as follows:

In view of available data on Kounis syndrome, and fixed drug eruption from literature and spontaneous reports including cases with a plausible temporal relationship, a positive re/de-challenge, confirmed diagnosis with laboratory tests, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between dexketoprofen and 'Kounis syndrome', and dexketoprofen and 'fixed drug eruption' is at least a reasonable possibility. The PRAC concluded that the product information of products containing dexketoprofen should be amended accordingly.

In view of available risks of use in pregnancy from the literature, spontaneous reports, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between dexketoprofen and risks of use in pregnancy is at least a reasonable possibility. The PRAC concluded that the product information of products containing dexketoprofen 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 dexketoprofen the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing dexketoprofen 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~~)

SYSTEMIC FORMULATIONS ONLY:

Summary of Product Characteristics

Section 4.4

A warning should be added as follows:

Cardiovascular and cerebrovascular effects

(…)

Cases of Kounis syndrome have been reported in patients treated with dexketoprofen. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

Section 4.8

The following adverse reaction(s) should be added under the SOC Cardiac Disorders with a frequency **not known**:

Kounis syndrome

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

Fixed drug eruption

Package Leaflet

Kounis Syndrome

Section 2

What you need to know before you take [product]

Signs of an allergic reaction to this medicine, including breathing problems, swelling of the face and neck region (angioedema), chest pain have been reported with dexketoprofen. Stop immediately [product name] and contact immediately your doctor or medical emergencies if you notice any of these signs.

Section 4

Not known : frequency cannot be estimated from the available data

Chest pain, which can be a sign of a potentially serious allergic reaction called Kounis syndrome.

Fixed drug eruption

An allergic skin reaction known as fixed drug eruption that may include round or oval patches of redness and swelling of the skin, blistering, and itching. Darkening of the skin in affected areas, which might persist after healing, may also occur. Fixed drug eruption usually reoccurs at the same site(s) if the medication is taken again.

TOPICAL FORMULATIONS ONLY:

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 added as follows:

[…] 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/fetus. 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 fetus. 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 dexketoprofen can cause adverse effects in your unborn baby. It is not known if the same risk applies to [product name] when it is used in 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 using 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:	June 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	03 August 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	02 October 2025