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 diclofenac (systemic formulations), the scientific conclusions are as follows:

In view of available data on fixed drug eruptions from the literature, and spontaneous reports including in some cases a close temporal relationship, and a positive de-challenge and/or re-challenge, the PRAC considers a causal relationship between diclofenac (systemic formulations) and fixed drug eruptions is at least a reasonable possibility.

The PRAC concluded that the product information of products containing diclofenac (systemic formulations) 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 diclofenac (systemic formulations) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing diclofenac (systemic 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~~)

Summary of Product Characteristics

- Section 4.4

The following text should be added to the existing place(s) where severe skin reactions (e.g. SJS and TEN) are listed in the existing paragraph regarding skin reactions in section 4.4 of the SmPC. If a similar wording is not already in place, it should be entirely implemented. In case the product information already includes a similar or stricter advice on skin reactions, the similar or stricter advice remains valid and should remain.

Skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome**,** ~~and~~ toxic epidermal necrolysis**, and generalised bullous fixed drug eruption** have been reported very rarely in association with the use of **diclofenac** ~~NSAIDs, including [Product name]~~ (see section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. [Product name] should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

- Section 4.8

If 'fixed drug eruption' or 'generalised bullous fixed drug eruption' is already included in section 4.8 with other frequency, the existing frequency should be maintained.

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

Fixed drug eruption

Generalised bullous fixed drug eruption

Package Leaflet

The following warnings should be added if no other corresponding warnings regarding serious skin reactions are already in place. In case of existing warnings regarding serious skin reactions, these should remain.

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

Talk to your doctor before <taking><using> [product name]:

- **If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after <taking><using> [Product name] or other pain medications.**

Section 4. Possible side effects

Stop <taking><using> [product name] and see a doctor straight away if you notice any of the following serious side effects – you may need urgent medical treatment:

- **A serious allergic skin reaction which may include large widespread red and/or dark patches, swelling of the skin, blisters, and itching (Generalised bullous fixed drug eruption).**

Other side effects:

If 'fixed drug eruption' is already included in the Package Leaflet section 4 with other frequency, the existing frequency should be maintained.

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

- **An allergic skin reaction, that may include round or oval patches of redness and swelling of the skin, blistering, and itching (Fixed drug eruption). 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><used> again.**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	May 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	7 July 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	4 September 2025