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 cefditoren, the scientific conclusions are as follows:

In view of available data on acute generalised exanthematous pustulosis (AGEP), pseudomembranous colitis and tubulointerstitial nephritis from the literature, spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between cefditoren pivoxil and AGEP, pseudomembranous colitis and tubulointerstitial nephritis is at least a reasonable possibility. The PRAC concluded that the product information of products containing cefditoren pivoxil 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 cefditoren the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing cefditoren 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

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN) and acute generalised exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported post-marketing in association with cefditoren treatment (see section 4.8).

Patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, cefditoren should be withdrawn immediately, and an alternative treatment considered (as appropriate). If the patient has developed a serious reaction such as SJS, TEN or AGEP with the use of cefditoren, treatment with cefditoren must not be restarted in this patient at any time.

Interference with neonatal screening tests: The intake of cefditoren shortly before delivery may cause a false positive test for isovaleric acidemia in the newborn as part of neonatal screening. It is therefore recommended to include a second-tier screening test for each sample obtained from newborns tested positive for isovaleric acidaemia if those findings are suspected of being cefditoren-related false positive (see section 4.6).

- Section 4.6

On Pregnancy section:

The intake of cefditoren shortly before delivery may cause a false positive test for isovaleric acidaemia in the newborn as part of neonatal screening (see section 4.4).

- Section 4.8

The following adverse reactions should be added:

- **Pseudomembranous colitis,** under the SOC Infections and Infestations, with a frequency not known.
- **Tubulointerstitial nephritis**, under the SOC Renal disorders, with a frequency not known.
- **Acute Generalised Exanthematous Pustulosis**, under the SOC Skin and subcutaneous tissue disorders, with frequency not known.

Package Leaflet

Section 2:

You may develop signs and symptoms of severe skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis and acute generalised exanthematous pustulosis. Stop using [Product name] and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

On section Pregnancy, breast-feeding and fertility

Pregnancy

The intake of [Product name] shortly before delivery may interfere with the results of the neonatal screening tests for metabolic disorders. You should tell the health care professional performing the test if you have taken this medicine shortly before delivery.

Section 4

Tell your doctor straight away if you get these symptoms as you may need urgent medical treatment:

Severe skin reactions (not known, frequency cannot be estimated from the available data)

- [--- existing section on Stevens-Johnson syndrome and toxic epidermal necrolysis for which the exact wording can be different in the package leaflet in each member state ---]
- **a red, scaly widespread rash with bumps under the skin and blisters accompanied by fever. The symptoms usually appear at the initiation of treatment (acute generalised exanthematous pustulosis)**.

(frequency not known)

Inflammation of the large bowel (colon). The signs included diarrhoea, usually with blood and mucus, stomach pain and fever.

Inflammation of the kidneys (tubulointerstitial nephritis)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	25 January 2026
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	26 March 2026