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 cefpodoxim, the scientific conclusions are as follows:

In view of available data on severe cutaneous adverse reactions (SCARs) and particularly for acute generalized exanthematous pustulosis (AGEP) and drug reaction with eosinophilia and systemic symptoms (DRESS) from the literature and spontaneous reports including some AGEP and DRESS cases with a close temporal relationship and a positive de-challenge, the PRAC considers a causal relationship between cefpodoxim and AGEP and DRESS is at least a reasonable possibility. The PRAC concluded that the product information of products containing cefpodoxim 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 cefpodoxim the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing cefpodoxim 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

A warning should be added/amended as follows:

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported with unknown frequency in association with cefpodoxime treatment.

Patients should be advised of the signs and symptoms and monitored closely for skin reactions.

If signs and symptoms suggestive of these reactions appear, cefpodoxime should be withdrawn immediately, and an alternative treatment considered.

If the patient has developed a serious reaction such as SJS, TEN, DRESS or AGEP with the use of cefpodoxime, treatment with cefpodoxime must not be restarted in this patient at any time.

- Section 4.8

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

acute generalized exanthematous pustulosis (AGEP)

drug reaction with eosinophilia and systemic symptoms (DRESS)

Package Leaflet

- Section 2

Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP) have been reported in association with cefpodoxime treatment. Stop using cefpodoxime and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

- Section 4 (beginning of the section)

Stop using cefpodoxime and seek medical attention immediately if you notice any of the following symptoms:

• Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).

• 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).

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	8 September 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	7 November 2024

APPENDIX I

PRAC PSUR Assessment Report