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 ceftazidime, 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) from the literature and spontaneous reports including some AGEP cases with a close temporal relationship and a positive de-challenge, the PRAC considers a causal relationship between ceftazidime and AGEP is at least a reasonable possibility. The PRAC concluded that the product information of products containing ceftazidime 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 ceftazidime the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing ceftazidime 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~~)

Section 4.4:

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 ceftazidime 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If signs and symptoms suggestive of these reactions appear, ceftazidime should be withdrawn immediately, and an alternative treatment considered.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 ceftazidime, treatment with ceftazidime must not be restarted in this patient at any time.

Section 4.8:

Skin and subcutaneous tissue disorders SOC, Frequency: (Not known)

acute generalized exanthematous pustulosis (AGEP)

In the PL, the following addition should be made under section 2, Warnings and precautions:

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 ceftazidime treatment. Seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

Unless no corresponding information is already present under section 4 the following information should be added under section 4 (beginning of the section):

Seek medical attention immediately if you notice any of the following symptoms:

● reddish patches on the trunk, the patches are target-like macules or circular, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome, toxic epidermal necrolysis).

● 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:	June 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	11 August 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	10 October 2024