Summary of risk management plan for Zevtera® 500 mg powder for concentrate for solution for infusion (ceftobiprole)

This is a summary of the risk management plan (RMP) for Zevtera. The RMP details important risks of Zevtera®, how these risks can be minimised, and how more information will be obtained about Zevtera's risks and uncertainties (missing information).

Zevtera's summary of product characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals and patients on how Zevtera should be used.

I. The medicine and what it is used for

Zevtera is authorised for the treatment of the following infections in adults:

- Hospital-acquired pneumonia (HAP), excluding ventilator-associated pneumonia (VAP)
- Community-acquired pneumonia (CAP)

It contains ceftobiprole (as ceftobiprole medocaril) as the active substance and it is given by intravenous infusion.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Zevtera, together with measures to minimise such risks and the proposed studies for learning more about Zevtera's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation measures*.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report (PSUR) assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Zevtera is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Zevtera are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Zevtera. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. There are no important identified or important potential risks associated to Zevtera. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	*None*
Important potential risks	*None*
Missing information	• Use in patients with hepatic impairment • Use in HIV-positive patients, patients with neutropenia immunocompromised patients, and patients with myelosuppression • Use in patients with severe renal impairment or end-stage renal disease

II.B Summary of important risks

Important identified risks

None.

Important potential risks

None.

Missing information

Missing information: USE IN PATIENTS WITH HEPATIC IMPAIRMENT	
Risk minimisation measures	*Routine risk minimisation measures*: • SmPC Sections 4.2 • Legal status: Prescription only medicine *Additional risk minimisation measures*: • None
Additional pharmacovigilance activities	*Additional pharmacovigilance activities*: • BPR-PAS-001 See Section II.C of this summary for an overview of the post-authorisation development plan.

Missing information: USE IN HIV-POSITIVE PATIENTS, PATIENTS WITH NEUTROPENIA, IMMUNOCOMPROMISED PATIENTS, AND PATIENTS WITH MYELOSUPPRESSION	
Risk minimisation measures	*Routine risk minimisation measures*: • SmPC Section 4.4 • PL Section 2 • Legal status: Prescription only medicine *Additional risk minimisation measures*: • None
Additional pharmacovigilance activities	*Additional pharmacovigilance activities*: • BPR-PAS-001 See Section II.C of this summary for an overview of the post-authorisation development plan.

Missing information: USE IN PATIENTS WITH SEVERE RENAL IMPAIRMENT OR END-STAGE RENAL DISEASE	
Risk minimisation measures	*Routine risk minimisation measures*: • SmPC Sections 4.2 and 5.2 • Legal status: Prescription only medicine *Additional risk minimisation measures*: • None
Additional pharmacovigilance activities	*Additional pharmacovigilance activities*: • BPR-PAS-001 See Section II.C of this summary for an overview of the post-authorisation development plan.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There is no study which is a condition of the marketing authorisation or specific obligation of Zevtera.

II.C.2 Other studies in post-authorisation development plan

Non-interventional post-authorisation safety study

- *BPR-PAS-001 - Retrospective chart review to evaluate the safety profile of ceftobiprole in patients with impaired hepatic or renal function or immunosuppression*

Purpose of the study:

Rationale: To estimate the incidence rate of treatment-emergent adverse events in patients treated with ceftobiprole, who have at least one of the following conditions:

- impaired renal function
- impaired hepatic function
- immunosuppression

Objectives: The objective of this study is to further characterise the safety profile of ceftobiprole, with particular emphasis on the following groups of patients:

- patients with severe renal impairment / end-stage renal disease
- patients with impaired baseline hepatic function
- patients with immunosuppression, including HIV-positive patients, immunocompromised patients (any type or aetiology), patients with baseline neutropenia, and/or patients with baseline myelosuppression