Summary of risk management plan for tedizolid phosphate

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

The Summary of product characteristics (SmPC) for Sivextro and its package leaflet give essential information to healthcare professionals and patients on how tedizolid phosphate should be used.

I. The Medicine and What it is Used For

Sivextro 200 mg film-coated tablet is authorised for the treatment of acute bacterial skin and soft structure infections (ABSSSI) in adults and adolescents 12 years of age and older (see SmPC for the full indication). It contains tedizolid phosphate as the active substance and it is given by oral administration once daily for 6 days.

Sivextro 200 mg powder for concentration for solution for infusion is authorised for the treatment of acute bacterial skin and soft structure infections (ABSSSI) in adults and adolescents 12 years of age and older (see SmPC for the full indication). It contains tedizolid phosphate as the active substance and it is given by intravenous infusion over 60 minutes once daily for 6 days.

Further information about the evaluation of the benefits of Sivextro can be found in the EPAR for Sivextro, including in its plain-language summary, available on the EMA website, under the medicine's webpage [link to product's EPAR summary landing page on the EMA webpage https://www.ema.europa.eu/en/medicines/human/EPAR/sivextro]

II. Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Sivextro, together with measures to minimise such risks and the proposed studies for learning more about the risks of Sivextro, 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 as 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 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 Sivextro is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Sivextro 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 evidence of a link with the use of Sivextro. 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. 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).

Table II.A.1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	• Myelosuppression (e.g., decreased platelets, decreased haemoglobin, decreased neutrophils)
Important potential risks	• Peripheral and optic nerve toxicity • Lactic acidosis
Missing information	• Prolonged treatment >7 days • Treatment of ABSSSI in severely immunocompromised patients (eg, patients with neutropenia, transplant recipients, HIV/AIDS) • Treatment of ABSSSI in patient populations/conditions that were under-represented in pivotal studies (eg, elderly patients, diabetic patients, and patients with acute polymicrobial infections such as major abscesses or traumatic wounds) and potential need for longer course of treatment and/or adjunctive gram-negative antimicrobial therapy

II.B Summary of Important Risks

Important identified risk: Myelosuppression (e.g., decreased platelets, decreased haemoglobin, decreased neutrophils)	
Evidence for linking the risk to the medicine	Integrated Analysis of Safety for Tedizolid Phosphate Tedizolid Global Safety Database Clinical Study Reports
Risk factors and risk groups	The risk groups (based on published data for linezolid) include patients with severe renal disease, patients with pre-existing myelosuppression due to underlying haematological or other malignancy, and the elderly
Risk minimisation measures	Routine risk minimisation measures: This item is communicated through the EU SmPC, Sections 4.2 (Posology) and 4.4
Important potential risk: Peripheral Neuropathy	
Evidence for linking the risk to the medicine	Integrated Analysis of Safety for Tedizolid Phosphate Tedizolid Global Safety Database Clinical Study Reports
Risk factors and risk groups	Unknown
Risk minimisation measures	Routine risk minimisation measures: This item is communicated through the EU SmPC, Section 4.4
Important potential risk: Optic nerve toxicity	
Evidence for linking the risk to the medicine	Integrated Analysis of Safety for Tedizolid Phosphate Tedizolid Global safety database
Risk factors and risk groups	Unknown
Risk minimisation measures	Routine risk minimisation measures: This item is communicated through the EU SmPC, Section 4.4
Important potential risk: Lactic acidosis	
Evidence for linking the risk to the medicine	Integrated Analysis of Safety for Tedizolid Phosphate Clincial study reports Tedizolid Global safety database
Risk factors and risk groups	Unknown
Risk minimisation measures	Routine risk minimisation measures: This item is communicated through the EU SmPC, Section 4.4.

Important identified risk: Myelosuppression (e.g., decreased platelets, decreased haemoglobin, decreased neutrophils)	
Missing Information: Prolonged treatment >7 days	
Risk minimisation measures	Routine risk minimisation measures: The SmPC (Section 4.2) outlines that the recommended dose is 200 mg once daily for 6 days. The safety and efficacy of tedizolid phosphate when administered for periods longer than 6 days have not been established. The risks associated with prolonged treatment are addressed in the SmPC Sections 4.2 and 4.4.
Missing Information: Treatment of ABSSSI in severely immunocompromised patients (eg, patients with neutropenia, transplant recipients, HIV/AIDS)	
Risk minimisation measures	Routine risk minimisation measures: This item is communicated through the EU SmPC, Section 4.4 on the limitations of clinical trial data.
Missing Information: Treatment of ABSSSI in patient populations/conditions that were under-represented in pivotal studies (eg, elderly patients, diabetic patients, and patients with acute polymicrobial infections such as major abscesses or traumatic wounds) and potential need for longer course of treatment and/or adjunctive gram-negative antimicrobial therapy	
Risk minimisation measures	Routine risk minimisation measures: Section 4.4 of the SmPC contains information on the limitations of clinical trial data.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Sivextro.

II.C.2 Other Studies in Post-Authorisation Development Plan

All studies sponsored by the MAH have been completed.