SWISS SUMMARY OF THE RISK MANAGEMENT PLAN (RMP) FOR

SIVEXTRO®

(INN: tedizolid phosphate)

Based on EU RMP Version 5.0 (final sign off date: 02-Oct-2018)

Active substance(s): Tedizolid phosphate

Product(s) concerned: Sivextro® 200 mg film-coated tablets

Sivextro® 200 mg powder for concentrate for solution for infusion

Market Authorisation Holder: MSD Merck Sharp & Dohme AG, Lucerne

Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.
The RMP summary of Sivextro® is a concise document and does not claim to be exhaustive.
As the RMP is an international document, the summary might differ from the 'Arzneimittelinformation / Information sur le médicament' approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorisation.
Please note that the reference document which is valid and relevant for the effective and safe use of Sivextro in Switzerland is the 'Arzneimittelinformation / Information sur le médicament' (see www.swissmedicinfo.ch) approved and authorised by Swissmedic. MSD Merck Sharp & Dohme AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Sivextro.

PART VI SUMMARY OF THE RISK MANAGEMENT PLAN BY PRODUCT

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 (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 (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 http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/002846/WC500184803.pdf]

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	• Serotonin syndrome • Peripheral and optic nerve toxicity • Lactic acidosis • Emergence of drug resistance (cross-resistance to linezolid and tedizolid mediated by L3 or L4 ribosomal protein mutations)
Missing information	• Experience in pregnant or lactating women • 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 underrepresented 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 • Cardiac safety (ie, QT prolongation) in patients with pre-existing cardiovascular risk factors.

II.B Summary of Important Risks

The safety information in the proposed Prescribing Information is aligned to the reference medicinal product.

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

Study Title: Surveillance for emerging resistance (in vitro microbiology studies) Purpose of the study: Monitor the occurrence of resistance to linezolid and/or tedizolid in clinical Gram positive isolates (by either L3/L4 ribosomal protein mutations or cfr gene).