OpoPharma Vertriebs AG
Riedmattstrasse 9
CH-8153 Rümlang

Summary of the Risk Management Plan (RMP) for Trecondi® (Treosulfan)

TRECONDI 1 G / 5 G POWDER FOR SOLUTION FOR INFUSION

EU Risk Management Plan Version 0.3 dated 06-Nov-2018

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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 minimise them.

The RMP summary of Trecondi 1 g / 5 g powder for solution for infusion 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 authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Trecondi 1 g / 5 g powder for solution for infusion in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. OpoPharma Vertriebs AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Trecondi 1 g / 5 g powder for solution for infusion.

Summary of risk management plan for Trecondi (INN: treosulfan)

This is a summary of the risk management plan (RMP) for Trecondi 1 g / 5 g powder for solution for infusion. The RMP details important risks of Trecondi, how these risks can be minimised, and how more information will be obtained about Trecondi's risks and uncertainties (missing information).

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

This summary of the RMP for Trecondi should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Trecondi's RMP.

I. The medicine and what it is used for

Trecondi is authorised as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT) in adult patients with malignant and non-malignant diseases and in paediatric patients older than one month with malignant diseases (see SmPC for the full indication). It contains treosulfan as the active substance and it is given in by intravenous infusion over two hours.

Further information about the evaluation of Trecondi's benefits can be found in Trecondi's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage https://www.ema.europa.eu/en/medicines/human/EPAR/trecondi.

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

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

II.A List of important risks and missing information

Important risks of Trecondi 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 Trecondi. 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).

List of important risks and missing information	
Important identified risks	– Treatment-related second malignancy
Important potential risks	– Seizures in small infants
Missing information	– Effect on fertility – Use in patients with prior alloHSCT

II.B Summary of important risks

Important identified risk: Treatment-related second malignancy	
Evidence for linking the risk to the medicine	Secondary malignancies are well established complications in long-term survivors after alloHSCT. They occur rarely after TREO-based conditioning.
Risk factors and risk groups	Prior treatment with alkylating medicinal products and extensive post-transplant immunosuppressive treatment. TBI-containing conditioning regimens.
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4, and 4.8 PL sections 2, and 4 Legal status: prescription only medicine Additional risk minimisation measures: None

Important potential risk: Seizures in small infants	
Evidence for linking the risk to the medicine	Seizures are commonly observed after busulfan-containing conditioning regimens. Busulfan freely crosses the blood-brain barrier to achieve significant concentrations in the CNS. Busulfan concentrations in the CNS are similar to plasma concentrations, which most likely accounts for the neurotoxicity seen with high-dose busulfan. In contrast to busulfan, TREO is not able to penetrate the blood-brain barrier. However, the blood-brain barrier might not yet be fully developed in infants.

Important potential risk: Seizures in small infants	
Risk factors and risk groups	Small infants (< 1 year of age) .
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 Legal status: prescription only medicine Additional risk minimisation measures: None

Missing information: Effect on fertility	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4, and 4.6 PL section 2 Legal status: prescription only medicine Additional risk minimisation measures: None

Missing information: Use in patients with prior alloHSCT	
Risk minimisation measures	Routine risk minimisation measures: Legal status: prescription only medicine Additional risk minimisation measures: None

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 Trecondi.

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

There are no studies required for Trecondi.