Summary of risk management plan for Thiotepa Riemser (thiotepa)

This is a summary of the risk management plan (RMP) for Thiotepa Riemser. The RMP details important risks of Thiotepa Riemser.

Thiotepa Riemser's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Thiotepa Riemser should be used.
This summary of the RMP for Thiotepa Riemser 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 Thiotepa Riemser's RMP.

I. The medicine and what it is used for

Thiotepa Riemser is authorised in combination with other chemotherapy medicinal products:
- with or without total body irradiation (TBI), as conditioning treatment prior to allogeneic or autologous haematopoietic progenitor cell transplantation (HPCT) in haematological diseases in adult and paediatric patients;
- when high dose chemotherapy with HPCT support is appropriate for the treatment of solid tumours in adult and paediatric patients.

(see SmPC for the full indication).
It contains thiotepa as the active substance and it is given by infusion.
Further information about the evaluation of Thiotepa Riemser's benefits can be found in Thiotepa Riemser'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/thiotepa-riemser.

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

Important risks of Thiotepa Riemser together with measures to minimise such 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 Thiotepa Riemser is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Thiotepa Riemser 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 Thiotepa Riemser. 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	Myelosuppression Hypersensitivity reactions Infection Treatment related secondary malignancy Graft Versus Host Disease Mucositis Confusion, delirium, hallucination Veno-occlusive liver disease Paediatric hepatic failure Pulmonary toxicity Nervous system disorders Cardiac failure Renal failure Embolism, haemorrhage Infertility
Important potential risks	Pulmonary arterial hypertension Toxic skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis Leukoencephalopathy
Missing information	Pregnant or lactating women Elderly patients Patients with clinically significant renal disease Patients with clinically significant hepatic disease Patients with impaired cardiac function Patients with impaired pulmonary function Patients with previous brain or craniospinal irradiation Data on ethnicity/race

II.B Summary of important risks

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

important identified risk: myelosuppression	
risk minimisation measures	routine risk minimisation measures: - warnings in SmPC section 4.4, 4.5, recommendation in section 4.4 and information in section 4.8 and 4.9 - warnings and recommendation in PIL section 2 and information in section 4 - prescription status
important identified risk: hypersensitivity reactions	
risk minimisation measures	routine risk minimisation measures: - instruction in SmPC section 4.3 to exclude patients at risk and information in section 4.8 - exclusion of patients at risk in PIL section 2 and information in section 4 - prescription status
important identified risk: infection	
risk minimisation measures	routine risk minimisation measures: - instructions to exclude patients at risk in SmPC sections 4.3 and 4.5, recommendation in section 4.4 and information in section 4.8 - exclusion of patients of risk and warnings as well as recommendation in PIL section 2 and information in section 4 - prescription status
important identified risk: treatment related secondary malignancy	
risk minimisation measures	routine risk minimisation measures: - warnings and information in SmPC sections 4.4 and 4.8 - warnings and information in PIL sections 2 and 4 - prescription status
important identified risk: graft versus host disease	
risk minimisation measures	routine risk minimisation measures: - information in SmPC section 4.8 and 5.1 - information in PIL section 4 - prescription status
important identified risk: mucositis	
risk minimisation measures	routine risk minimisation measures: - information in SmPC section 4.8 - information in PIL section 4 - prescription status
important identified risk: confusion, delirium, hallucination	
risk minimisation measures	routine risk minimisation measures: - information in SmPC section 4.8 - information in PIL section 4 - prescription status

important identified risk: veno-occlusive liver disease	
risk minimisation measures	routine risk minimisation measures: - warning in SmPC section 4.4 to indicate patients at risk and information in section 4.8 - information in PIL section 4 - prescription status
important identified risk: paediatric hepatic failure	
risk minimisation measures	routine risk minimisation measures: - information in SmPC sections 4.2, 4.4 and 4.8 - information in PIL sections 2 and 4 - prescription status
important identified risk: pulmonary toxicity	
risk minimisation measures	routine risk minimisation measures: - warnings in SmPC section 4.4 to indicate patients at risk and information in section 4.8 - information in PIL section 2 and 4 - prescription status
important identified risk: nervous system disorders	
risk minimisation measures	routine risk minimisation measures: - warnings and recommendation in SmPC section 4.4 and 4.5 for patients at risk and information in section 4.8 - warnings and recommendation in PIL section 2 and information in section 4 - prescription status
important identified risk: cardiac failure	
risk minimisation measures	routine risk minimisation measures: - warning and recommendation in SmPC section 4.4 and PIL section 2 for patients at risk and information in section 4.8 - information in PIL section 4 - prescription status
important identified risk: renal failure	
risk minimisation measures	routine risk minimisation measures: - recommendation in SmPC section 4.4 for patients at risk and information in section 4.8 - warning in PIL section 2 and information in section 4 - prescription status
important identified risk: embolism, haemorrhage	
risk minimisation measures	routine risk minimisation measures: - information in SmPC sections 4.5 and 4.8, recommendation for patients at risk in section 4.5 - recommendation in PIL section 2 for patients at risk and information in section 4 - prescription status

important identified risk: infertility	
risk minimisation measures	routine risk minimisation measures: - information in SmPC sections 4.4, 4.6, 4.8 and 5.3 as well as recommendation in section 4.6 - information and recommendation in PIL sections 2 and 4 - prescription status
important potential risk: pulmonary arterial hypertension	
risk minimisation measures	routine risk minimisation measures: - information in SmPC section 4.8 - information in PIL section 4 - prescription status
important potential risk: toxic skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis	
risk minimisation measures	routine risk minimisation measures: - information in SmPC section 4.8 - information in PIL section 4 - prescription status
important potential risk: leukoencephalopathy	
risk minimisation measures	routine risk minimisation measures: - information in SmPC section 4.8 - information in PIL section 4 - prescription status
missing information: pregnant or lactating women	
risk minimisation measures	routine risk minimisation measures: - instructions in SmPC section 4.3 to exclude patients at risk from the therapy, recommendation and information in sections 4.6 and 5.2 - instruction in PIL section 2 to exclude patients at risk as well as recommendation in section 2 - prescription status
missing information: elderly patients	
risk minimisation measures	routine risk minimisation measures: - information and recommendation in SmPC section 4.2 - prescription status
missing information: patients with clinically significant renal disease	
risk minimisation measures	routine risk minimisation measures: - information in SmPC sections 4.2, and 5.2 as well as warning in section 4.4 - warning in PIL section 2 - prescription status
missing information: patients with clinically significant hepatic disease	
risk minimisation measures	routine risk minimisation measures: - information and warnings in SmPC sections 4.2, 4.4, 4.8 and 5.2 as well as recommendation in section 4.4 - warning in PIL section 2 and information in section 4 - prescription status

missing information: patients with impaired cardiac function	
risk minimisation measures	routine risk minimisation measures: - warning and recommendation in SmPC section 4.4 for patients at risk - warning in PIL section 2 - prescription status
missing information: patients with impaired pulmonary function	
risk minimisation measures	routine risk minimisation measures: - information in SmPC section 4.4 - prescription status
missing information: patients with previous brain or craniospinal irradiation	
risk minimisation measures	routine risk minimisation measures: - warning in SmPC section 4.4 on the patients possibly at risk - prescription status
missing information: data on ethnicity/race	
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 Thiotepa Riemser.

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

There are no studies required for Thiotepa Riemser.