

Risk Management Plan

Part VI: Summary of the Risk Management Plan**Summary of Risk Management Plan for Cladribine Sandoz 10 mg, Tabletten (Cladribine)**

This is a summary of the risk management plan (RMP) for Cladribine Sandoz 10 mg, Tabletten. The RMP details important risks of Cladribine Sandoz 10 mg, Tabletten, how these risks can be minimised, and how more information will be obtained about Cladribine Sandoz 10 mg, Tabletten's risks and uncertainties (missing information).

Cladribine Sandoz 10 mg, Tabletten's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Cladribine Sandoz 10 mg, Tabletten should be used.

Important new concerns or changes to the current ones will be included in updates of Cladribine Sandoz 10 mg, Tabletten RMP.

I. The Medicine and What It is used for

Cladribine Sandoz 10 mg, Tabletten is indicated for the treatment of adult patients with highly active relapsing multiple sclerosis (MS) as defined by clinical or imaging features.

It contains cladribine as the active substance and it is taken orally.

II. Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of Cladribine Sandoz 10 mg, Tabletten, together with measures to minimize such risks are outlined below.

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

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorized 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 HCP can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including periodic safety update report assessment, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

II.A List of Important Risks and Missing Information

Important risks of Cladribine Sandoz 10 mg, Tabletten are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks

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are concerns for which there is sufficient proof of a link with the use of Cladribine Sandoz 10 mg, Tabletten. 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	• Severe (Grade ≥ 3) lymphopenia • Herpes zoster • Tuberculosis • Liver injury
Important potential risks	• Severe infections • Progressive Multifocal Leukoencephalopathy (PML) • Opportunistic infections (other than tuberculosis and PML) • Malignancies • Teratogenicity/adverse pregnancy outcomes • Seizures
Missing information	• Sequential use of other immunosuppressive or immunomodulatory agents after cladribine treatment • Impact of exposure to prior immunomodulatory/immunosuppressive agents on subsequent risks following cladribine exposure • Long-term safety data in particular for malignancy risk

II.B Summary of Important Risks

Important identified risks	
Severe (Grade ≥ 3) lymphopenia	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC sections 4.2, 4.4, 4.5 and 4.8. PIL sections 2 and 4. Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u>

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	• Prescriber Guide • Patient Alert Card
Herpes zoster	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.3, 4.4 and 4.8. PIL section 2 & 4 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> • Prescriber Guide • Patient Alert Card
Tuberculosis	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.2, 4.3, 4.4 and 4.8. PIL sections 2 and 4 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> • Prescriber Guide • Patient Alert Card
Liver injury	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.4 and 4.8. PIL sections 2 & 4 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> • Prescriber Guide

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	• Patient Alert Card
<u>Important potential risks</u>	
Severe infections	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.3 and 4.4 PL section 2 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> • Prescriber Guide • Patient Alert Card
Progressive Multifocal Leukoencephalopathy (PML)	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.3 & 4.4 PIL section 2 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> • Prescriber Guide • Patient Alert Card
Opportunistic infections (other than tuberculosis and PML)	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.2, 4.3, 4.4 PIL section 2 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> • Prescriber Guide

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	• Patient Alert Card
Malignancies	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.3, 4.4, 4.8 PIL section 2 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> • Prescriber Guide • Patient Alert Card
Teratogenicity/adverse pregnancy outcomes	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.3, 4.4, 4.6, 5.3 PIL section 2 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> • Prescriber Guide • Patient Alert Card
Seizures	
Risk minimization measures	<u>Routine risk minimization measures:</u> Prescription only medicine <u>Additional risk minimisation measures:</u> None
<u>Missing information</u>	
Sequential use of other immunosuppressive or immunomodulatory agents after cladribine treatment	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.4 PIL section 2

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	Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> None
Impact of exposure to prior immunomodulatory/immunosuppressive agents on subsequent risks following cladribine exposure	
Risk minimization measures	<u>Routine risk minimization measures:</u> SmPC section 4.4 PIL section 2 Other routine risk minimisation measures beyond the Product Information: Prescription only medicine <u>Additional risk minimisation measures:</u> None
Long-term safety data in particular for malignancy risk	
Risk minimization measures	<u>Routine risk minimization measures:</u> Prescription only medicine <u>Additional risk minimisation measures:</u> None

II.C Post-Authorization Development Plan**II.C.1 Studies Which Are Conditions of the Marketing Authorization**

There are no studies which are conditions of the marketing authorization or specific obligation of Cladribine Sandoz 10 mg, Tabletten.

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

There are no studies required for Cladribine Sandoz 10 mg, Tabletten.