Part VI: Summary of the risk management plan

Summary of risk management plan for Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion

This is a summary of the risk management plan (RMP) for Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion.

The RMP details important risks of Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion, how these risks can be minimized, and how more information will be obtained about Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion 's risks and uncertainties (missing information).

Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion should be used.

Important new concerns or changes to the current ones will be included in updates of Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion's RMP.

I. The medicine and what it is used for

Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion are authorised for (see SmPC for the full indication):

Adults, adolescents ≥ 16 years of age and elderly:

- Treatment of invasive candidiasis.
- Treatment of oesophageal candidiasis in patients for whom intravenous therapy is appropriate.
- Prophylaxis of Candida infection in patients undergoing allogeneic haematopoietic stem cell transplantation or patients who are expected to have neutropenia (absolute neutrophil count < 500 cells / µl) for 10 or more days.

Children (including neonates) and adolescents < 16 years of age:

- Treatment of invasive candidiasis.
- Prophylaxis of Candida infection in patients undergoing allogeneic haematopoietic stem cell transplantation or patients who are expected to have neutropenia (absolute neutrophil count < 500 cells / µl) for 10 or more days.

The decision to use Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion should take into account a potential risk for the development of liver tumours (see section 4.4 of proposed SmPC). Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion should therefore only be used if other antifungals are not appropriate.

Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion contain Micafungin) as the active substance and are given by intravenous use.

II. Risk associated with the medicine and activities to minimize or further characterize the risks

Important risks of Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion, together with measures to minimize such risks and the proposed studies for learning more about Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion 's 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 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 minimize its risks.

Together, these measures constitute *routine risk minimization* measures.

In the case of Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion, these measures are supplemented with *additional risk minimization measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including Periodic Safety Update Report (PSUR) 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 Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion are risks that need special risk management activities to further investigate or minimize 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 Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion. 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	- Hemolytic AEs including DIC - Hepatic AEs - Renal AEs
Important potential risks	- Relevance in humans of the development of liver tumors in rats - Development of resistant strains
Missing information	- None

AEs: adverse events; DIC: disseminated intravascular coagulation

II.B Summary of important risks

Important identified risk: Hemolytic AEs including DIC	
Risk minimization measures	**Routine risk minimisation measures:** − SmPC section 4.4, 4.8 − PL section 2 and 4 − Recommendation to monitor closely patients who develop clinical or laboratory evidence of haemolysis to notice evidence of worsening of these conditions and to evaluate the risk/benefit of continuing micafungin therapy (SmPC section 4.4). − Pack size: Packs of 1 vial. − Legal status: Prescription only. Treatment with Micafungin should be initiated by a physician experienced in the management of fungal infections. Additional risk minimization measures: Prescriber checklist

Important identified risk: Hepatic AEs	
Risk minimization measures	**Routine risk minimisation measures:** − SmPC section 4.4, 4.8 − PIL section 2 and 4 − Recommendation that “Liver function should be carefully monitored during micafungin treatment." (SmPC section 4.4). − Pack size: Packs of 1 vial. − Legal status: Prescription only. Treatment with Micafungin should be initiated by a physician experienced in the management of fungal infections. Additional risk minimization measures: Prescriber checklist

Important identified risk: Renal AEs	
Risk minimization measures	**Routine risk minimisation measures:** − SmPC section 4.4, 4.8 − PL section 2 and 4 − Recommendation to closely monitor patients for worsening renal function (SmPC section 4.4). − Pack size: Packs of 1 vial. − Legal status: Prescription only. Treatment with Micafungin should be initiated by a physician experienced in the management of fungal infections. Additional risk minimization measures: Prescriber checklist

Important potential risk: Relevance in humans of the development of liver tumors in rats	
Risk minimization measures	**Routine risk minimisation measures:** − SmPC section 4.4, 5.3 − PL section 2 − Recommendation that “Liver function should be carefully monitored during micafungin treatment. To minimise the risk of adaptive regeneration and potentially subsequent liver tumour formation, early discontinuation in the presence of significant and persistent elevation of ALT/AST is recommended." (SmPC section 4.4). − Warning that “In rats, long-term treatment with micafungin led to liver damage and subsequent liver tumours. The potential risk of developing liver tumours in humans is not known, and your doctor will assess the benefits and risks of Micafungin treatment before starting your medicine. Please tell your doctor if you have severe liver problems (e.g. liver failure or hepatitis) or have had abnormal liver function tests. During treatment your liver functions will be monitored more closely.” (PL section 2). − Pack size: Packs of 1 vial.

	− Legal status: Prescription only. Treatment with Micafungin should be initiated by a physician experienced in the management of fungal infections. Additional risk minimization measures: Prescriber checklist

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 Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion.

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

There are no studies required for Micafungin Lorien 50 mg powder for concentrate for solution for infusion and Micafungin Lorien 100 mg powder for concentrate for solution for infusion.