COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion (micafungin sodium)

NL/H/6426/001-002/DC

Date: 22 July 2025

This module reflects the scientific discussion for the approval of Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion. The procedure was finalised at 11th of June 2020 in Malta (MT/H/0393/001-002/DC). After a transfer on 25 April 2025, the current RMS is the Netherlands. For information on changes after the finalisation date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion (Micafungin Sodium), from Viatris Limited, Ireland.

The product is indicated for:

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.

A comprehensive description of the indications and posology is given in the current SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC. A condition to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC in section V has been issued, namely the addressing of additional risk minimisations via a Prescriber's Checklist.

II. QUALITY ASPECTS

II.1 Introduction

The active substance, Micafungin sodium, is not described in the Ph. Eur. Micafungin belongs to the pharmacotherapeutic group: antimycotics for systemic use, other antimycotics for systemic use, ATC Code: J02AX05. The pharmaceutical form is Concentrate for powder for solution for infusion 100mg. It is presented in a 10ml clear glass vial (Type 1), a red plastic flip-off cap and wrapped in a UV protective film.

II.2 Drug Substance

The active substance, Micafungin sodium, is not described in the Ph. Eur. Micafungin belongs to the pharmacotherapeutic group: antimycotics for systemic use, other antimycotics for systemic use, ATC Code: J02AX05.

II.3 Medicinal Product

Pharmaceutical development

The pharmaceutical drug product has been developed as a freeze-dried powder intended for intravenous infusion after reconstitution in vial or dilution with either, 0.9% Sodium Chloride solution for infusion or 5 % Glucose solution, for infusion.

The pharmaceutical and manufacturing development work is described in detail. Micafungine Viatris 50 mg and 100 mg – powder for concentrate for solution for infusion was developed as a generic to the reference medicinal product, Mycamine (Micafungin) powder for solution for infusion (50 mg/vial and 100 mg/vial). The reference medicinal product Mycamine is manufactured by Astellas Pharma Tech Co. Ltd. The finished product contains the same active substance as the reference product Mycamine and the same excipients.

Manufacturing process

The manufacturing process has been described and justified by production of exhibit batches. The manufacturing process is considered as standard based considered on the basis of the finished product manufacturer's experience with similar sterile lyophilised products. The applicant has however provided commitment to perform process validation on the first three commercial scale batches before the larger batch size is placed onto the market.

Quality control of drug product

The choice of parameters to be tested in the release and shelf-life specifications is in agreement with the Ph. Eur. monograph on parenteral preparations. Method descriptions and validations of the analytical methods have been presented. Batch analysis has been performed on three exhibit batches of each strength (50 mg and 100 mg). The batch analysis results show that the finished products meet the specifications proposed.

Stability of drug product

The conditions used in the stability studies are according to the ICH stability guideline. Results of stability studies for 6 months under accelerated conditions have been provided. Results from the 24-month time point under long-term conditions for 2 batches of Micafungine Viatris 50 mg and 1 batch of Micafungine Viatris 50 mg and 100 mg are provided. Results from an additional Micafungine Viatris 100 mg batch is also provided at the 18-month time point. A shelf life of 36 months is therefore approvable for the Micafungine Viatris 50 mg strength and a 30-month shelf life is approvable for the Micafungine Viatris 100 mg strength.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of Micafungin Sodium are well known. As Micafungin Sodium is a widely used, well-known active substance, the

applicant has not provided additional studies and further studies are not required. Overview based on literature review is, thus, appropriate.

The non-clinical overview has been written by Angelyne Benavides, Ph.D., Pharmacist, EU Qualified Person Responsible for Pharmacovigilance (QPPV) Medical Writer and dated September 2018. Report refers 57 publications up to year 2018.

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate.

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

No additional non-clinical data are required because the product is a generic and is therefore acceptable.
This generic product contains well-established excipients and has an impurity profile that is adequately controlled in line with current ICH guidelines. There are no toxicological concerns.

IV. CLINICAL ASPECTS

IV.1 Introduction

Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion is presented as a powder for solution for infusion. It should be administered as an intravenous infusion. Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion contain the active substance in the same concentration as the European originator Mycamine 50 mg and 50 mg and 100 mg (MAH: Astellas Pharma Europe B.V.). The active substance of Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion is micafungin sodium.

IV.2 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Micafungine Viatris 50 mg and 100 mg, powder for solution for infusion.

Summary of safety concerns	
Important identified risks	• Hemolytic AEs including disseminated intravascular coagulation • 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

Risk minimisation measures

Routine risk minimisation is suggested and additional risk minimisation activities are proposed by the applicant. The additional risk minimisation measure consists of Prescriber checklist. This is endorsed.

Summary of the RMP

The following RMPs are considered acceptable:

- Micafungin 50mg & 100mg powder for solution for infusion, MT/H/0393/001-002/DC: version 1.1 dated 18-11-2019.

- Summary of Safety Concerns and Planned Risk Minimisation Activities as approved in RMP

Safety Concern	Routine Risk Minimisation Measures	Additional Risk Minimisation Measures
Important Identified Risks		
Haemolytic AEs including disseminated intravascular coagulation	Warning in section 4.4 of the SmPC Listed in section 4.8 of the SmPC	Prescriber Checklist
Hepatic AEs	Warning in section 4.4 of the SMPC Listed in section 4.8 of the SmPC	Prescriber Checklist Administration and monitoring guide
Renal AEs	Warning in section 4.4 of the SmPC Listed in section 4.8 of the SmPC	Prescriber Checklist Administration and monitoring guide
Important Potential Risks		
Relevance in humans of the development of liver tumours in rats	Description in section 5.3 of the SmPC	Prescriber Checklist Administration and monitoring guide
Development of resistant strains	Description in section 5.1 of the SmPC	

Safety Concern	Routine Risk Minimisation Measures	Additional Risk Minimisation Measures
Missing Information		
None		

IV.3 Discussion on the clinical aspects

Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion was developed as a generic version of the reference product Mycamine 100 mg. During formulation it was decided to keep the excipients in the formulation as similar as possible to the reference product excipients. The excipients are well-established and do not interact with the drug substance.
All of the proposed excipients are present in the reference product. In addition, the excipients used are of Ph. Eur. quality, commonly used for this type of dosage form.
According to the Guideline On The Investigation Of Bioequivalence CPMP/EWP/QWP/ 1401/98 Rev. 1/ Corr **: *"Parenteral solutions: Bioequivalence studies are generally not required if the test product is to be administered as an aqueous intravenous solution containing the same active substance as the currently approved product".*
Therefore, based on all mentioned above, Micafungine Viatris 50 mg and 100 mg, powder for concentrate for solution for infusion is considered bioequivalent to the innovator Mycamine 100 mg

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Micafungin 50 mg & 50mg and 100 mg powder for solution for infusion (MT/H/0388). The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

In conclusion, from a quality, clinical and non-clinical point of view, the benefit/risk ratio for the product is positive.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
MT/H/0393/1-2/IA/001	Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product Secondary packaging site	No	24 March 2021	Approved	N.A.
MT/H/0393/1-2/II/002	Change in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer (including where relevant quality control testing sites) of the active substance, where no Ph. Eur. Certificate of Suitability is part of the approved dossier Introduction of a manufacturer of the active substance supported by an ASMF	No	4 September 2021	Approved	N.A.
MT/H/0393/1-2/IA/003	Deletion of manufacturing sites (including for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place, or supplier of a starting material, reagent or excipient (when mentioned in the dossier))	Yes	3 June 2021	Approved	N.A.
MT/H/0393/1-2/IB/004/G	Change in the name and/or address of the marketing authorisation holder + Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes Yes	3 June 2022	Approved	N.A.
MT/H/0393/1-2/IA/005	Change in the name and/or address of a manufacturer/importer of the finished product	No	15 March 2023	Approved	N.A.

	(including batch release or quality control testing sites) Name change of the finished product batch testing site				
MT/H/0393/2/IB/006	Change in the shelf-life or storage conditions of the finished product Extension of the shelf life of the finished product – As packaged for sale (supported by real time data)	Yes	7 December 2023	Approved	N.A.
MT/H/0393/1-2/IB/007	Change in the shelf-life or storage conditions of the finished product Extension of the shelf life of the finished product – After dilution or reconstitution (supported by real time data)	Yes	17 November 2023	Approved	N.A.
MT/H/0393/1/IA/008/G	Change in the name and/or address of a manufacturer/importer of the finished product (including batch release or quality control testing sites) + Change to importer, batch release arrangements and quality control testing of the finished product Replacement or addition of a site where batch control/testing takes place + Replacement or addition of a manufacturer responsible for importation and/or batch release – Including batch control/testing	No No Yes	9 October 2023	Approved	N.A.
MT/H/0393/1-2/IB/009	Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan Update to risk management plan	No	18 March 2024	Approved	N.A.

MT/H/0393/1-2/IB/010	Change in the (invented) name of the medicinal product for Nationally Authorised Products	Yes	28 April 2024	Approved	N.A.
MT/h/0393/1-2/R/001	Renewal	No	20 March 2025	Approved	N.A.
MT/H/0393/1-2/IB/011/G	Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product Secondary packaging site + Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) manufactured using an aseptic method excluding biological/ immunological medicinal products + Change to importer, batch release arrangements and quality control testing of the finished product Replacement or addition of a site where batch control/testing takes place + Change in the manufacturing process of the finished product , including an intermediate used in the manufacture of the finished product Minor change in the manufacturing process + Change to in-process tests or limits applied during the	No No No No No	23 October 2024	Approved	N.A.

	manufacture of the finished product Addition of a new test(s) and limits				