PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

ECALTA (ANIDULAFUNGIN)

Marketing Authorization Number 58325

POWDER FOR SOLUTION FOR INFUSION

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LIST OF ABBREVIATIONS

AE	Adverse Event
CNS	Central nervous system
CSR	Clinical Study Report
DLP	Data-Lock Point
EMA	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
MedDRA	Medical Dictionary for Regulatory Activities
PhV	Pharmacovigilance
PS80	Polysorbate 80
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics (Europe)

OVERVIEW

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 for Ecalta 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 marketing authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Ecalta in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic. Pfizer AG is fully responsible for the accuracy and correctness of the content of the published RMP summary of Ecalta.

SUMMARY OF RISK MANAGEMENT PLAN FOR ECALTA (ANIDULAFUNGIN)

This is a summary of the Risk Management Plan (RMP) for Ecalta. The RMP details important risks of Ecalta, how these risks can be minimised, and how more information will be obtained about Ecalta's risks and uncertainties (missing information).

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

This summary of the RMP for Ecalta 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).

New concerns or changes to the current ones will be included in updates of Ecalta's RMP.

I. The Medicine and What It Is Used For

Ecalta is authorised for treatment of invasive candidiasis in adults and paediatric patients aged 1 month to < 18 years. It contains anidulafungin as the active substance and it is given by IV route of administration.

Further information about the evaluation of Ecalta's benefits can be found in Ecalta's EPAR, including in its plain-language summary, available on the EMA website.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

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

II.A. List of Important Risks and Missing Information

Important risks of Ecalta 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 Ecalta. 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).

The MAH reclassified all potential and identified risks to risks 'not important' and added a new important potential risk i.e., Hepatic impairment and other serious toxicities in neonates < 1 month of age. In addition, the MAH removed the following safety concerns which were classified as Missing information: Children/adolescents, Elderly, Pregnant women and Resistance.

Table 1. List of important risks and missing information

Important identified risks	None
Important potential risks	Hepatic impairment and other serious toxicities in neonates < 1 month of age
Missing information	None

II.B. Summary of Important Risks

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

Table 2. Important Potential Risk: Hepatic impairment and other serious toxicities in neonates (< 1 month of age)

Evidence for linking the risk to the medicine	*Candida* meningitis is a serious life-threatening consequence of *Candida* infection in neonates and is associated with high morbidity (i.e., neurologic sequelae) and mortality. In neonates with invasive candidiasis, it has been estimated that 15-20% of cases may have CNS involvement[1]. Owing to the difficulty in rapidly diagnosing CNS infection, neonates with invasive candidiasis are often presumed to have CNS involvement unless proven otherwise. Therefore, when treating neonates with invasive candidiasis, it is often necessary to select an antifungal agent known to have adequate CNS penetration and activity. PS80 is a solubilizing agent used in the current anidulafungin formulation. As described in literature, clinical[1] and non-clinical studies[2 3 4] suggest that an approximately 3-fold higher dose than the standard dose of anidulafungin may be needed to achieve the target exposure to treat neonatal candidiasis with CNS involvement. Based on the available data there are concerns regarding the potential risk of hepatic-related adverse events and other possible unknown toxicities resulting from the administration of higher doses of PS80[5].
Risk factors and risk groups	Treating neonates requires consideration for coverage of disseminated candidiasis including CNS; nonclinical infection models indicate that higher doses of anidulafungin are needed to achieve adequate CNS penetration, resulting in higher doses of PS80. Given the potential risk of hepatotoxicity associated with polysorbate 80 when an increased amount is used in neonates, there is a theoretical risk of additive or synergistic hepatic effects in neonates when exposed to anidulafungin and polysorbate 80 at higher doses.
Risk minimisation measures	Routine risk minimisation measures The risk is communicated through the label (SmPC Section 4.4 Special warnings and precautions for use) 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 Ecalta.

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

There are no studies required for Ecalta.

REFERENCES

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