Swiss Summary of the Risk Management Plan (RMP)
(Based on EU RMP version 9.0 of 30 April 2021)

CRESEMBA 100 mg Capsules, hard
CRESEMBA 200 mg Powder for Concentrate for Solution for Infusion

Isavuconazole (as Isavuconazonium sulfate)

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Disclaimer

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 of "Cresemba" 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 authorization.

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

Note: This is an electronically controlled document.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

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

Cresemba's Summary of Product Characteristics (SmPC) and its Package Leaflet (PL) give essential information to healthcare professionals and patients on how Cresemba should be used.

This summary of the RMP for Cresemba 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 Cresemba's RMP.

VI.I The medicine and what it is used for

Cresemba is authorised for the treatment of:

- Invasive aspergillosis
- Mucormycosis in patients for whom amphotericin B is inappropriate

It contains isavuconazonium sulfate, which is the prodrug for the active substance isavuconazole, and it is given either orally or intravenously.

Further information about the evaluation of Cresemba's benefits can be found in Cresemba's EPAR, including in its plain-language summary.

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

Important risks for Cresemba, together with measures to minimise such risks and the proposed studies for learning more about Cresemba's risks, are outlined below.

Measures to minimise the risks identified for medicinal products:

- 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 public (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 Cresemba is not yet available, it is listed under 'missing information' below.

VI.II.A List of important risks and missing information

Important risks of Cresemba 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 Cresemba. 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	• Infusion-related reactions
Important potential risks	• Teratogenicity
Missing information	None

VI.II.B Summary of important risks

Important identified risk: Infusion-related reactions	
Evidence for linking the risk to the medicine	During clinical trials, infusion-related reactions e.g., hypotension, dyspnoea, dizziness, paraesthesia, nausea, and headache were reported. Infusion related reactions are therefore considered an identified risk for isavuconazole. Clinical study data from the development programme provide the evidence for this risk.
Risk factors and risk groups	A history of allergic conditions appears to be associated with higher risk of infusion-related reactions. Risk factors for allergic drug reaction include the following: female gender, being an adult, HIV infection, concomitant viral infection, asthma, use of beta blockers, systemic lupus erythematosus, specific genetic polymorphisms, and previous hypersensitivity to a chemically-related drug.
Risk minimisation measures	Routine risk minimisation measures: SmPC Sections 4.2 and 4.4 Section 2 of the PL Recommendation to administer by intravenous infusion over a minimum of 1 hour to reduce the risk of infusion-related reactions is warranted in Section 4.2 of the SmPC. Recommendation to stop the infusion, when infusion-related reactions suggestive of systemic hypersensitivity occur (such as hypotension, dyspnoea, dizziness, paraesthesia, nausea, and headache) is presented in Section 4.4 and PL Section 2. Additional risk minimisation measures: None.

Important Potential Risk: Teratogenicity	
Evidence for linking the risk to the medicine	Teratogenicity is considered to be an important potential risk based on non-clinical findings (skeletal anomalies in rats and rabbits). There is no clinical data on the use of isavuconazole in pregnancy.
Risk factors and risk groups	No specific risk factors or risk groups, other than exposure in pregnant women have yet been identified.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.6 PL Section 2 Isavuconazole is not recommended for women of childbearing potential who are not using contraception, as specified in Section 4.6 of the SmPC. In pregnant women, isavuconazole should be used only if he anticipated benefits outweigh the possible risks to the foetus as specified in Section 4.6 of the SmPC and PL section 2. Additional risk minimisation measures: None.

VI.II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There is no study that is a condition of the marketing authorisation.

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

None.