PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VFEND® (VORICONAZOLE)

Marketing Authorization Number 55945, 55946 and 56819

Powder for concentrate for solution for infusion 200 mg, film-coated tablets 50 mg and 200 mg, powder for oral suspension 40 mg/ml

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LIST OF ABBREVIATIONS

CD4	Cluster of Differentiation 4
EMA	European Medicines Agency
EPAR	European Public Assessment Report
HSCT	Haematopoietic Stem Cell Transplant
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
SCC	Squamous Cell Carcinoma
SmPC	Summary Of Product Characteristics

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 Vfend 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 Vfend in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic. Pfizer is fully responsible for the accuracy and correctness of the content of the published RMP summary of Vfend.

SUMMARY OF RISK MANAGEMENT PLAN FOR VFEND (VORICONAZOLE)

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

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

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

I. The Medicine and What It Is Used For

Vfend is authorised for:

- Treatment of invasive aspergillosis.
- Treatment of candidaemia in non-neutropenic patients.
- Treatment of fluconazole-resistant serious invasive Candida infections (including *C. krusei*).
- Treatment of serious fungal infections caused by *Scedosporium spp.* and *Fusarium spp.*

Voriconazole should be administered primarily to patients with progressive, possibly life-threatening infections.

- Prophylaxis of invasive fungal infections in high-risk allogeneic haematopoietic stem cell transplant (HSCT) recipients.

It contains voriconazole as the active substance and it is given by intravenous and oral route of administration.

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

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

Important risks of Vfend, together with measures to minimise such risks and the proposed studies for learning more about Vfend'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 the case of Vfend, these measures are supplemented with *additional risk minimisation* measures mentioned under relevant important risks, below.

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 Vfend is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Vfend are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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 Vfend. 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).

Table 1. List of Important Risks and Missing Information

Important Identified Risks	Phototoxicity Squamous cell carcinoma (SCC)
Important Potential Risks	None
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 Identified Risk: Phototoxicity

Evidence for linking the risk to the medicine	Clinical studies, post-marketing safety database.
Risk factors and risk groups	Phototoxicity reactions are frequent in patients with immunocompromised status and with exposure to direct sunlight. A higher reporting proportion of phototoxicity reactions in the paediatric population compared to that of adult population was observed in the post-marketing experience.
Risk minimisation measures	Routine: SmPC section 4.4 and 4.8 Additional: None.

Table 3. Important Identified Risk: Squamous cell carcinoma (SCC)

Evidence for linking the risk to the medicine	Clinical studies, post-marketing safety database and literature.
Risk factors and risk groups	In general, skin type, advanced age, sun exposure, genetic predisposition as well as exposure to ionizing radiation, arsenic, or industrial chemicals; pre- existing burns and scars; and immunosuppression[1] are the risk factors for SCC of the skin. Immunocompromised patients, including patients who have received organ transplant, are at a greater risk of SCC of the skin compared to the immuno-competent population. The risk of SCC in organ transplant recipients has been associated with the following risk factors in epidemiologic investigations: older age, prolonged occupational sunlight exposure, long duration of immunosuppressive therapy, intense immunosuppressive therapy, significant prior exposure to ultraviolet radiation; infection with human papillomavirus, lower CD4 cell counts, and certain hosts factors (eye or hair colour, complexion, White race, patients with Fitzpatrick skin types I, II, or III).[2 3 4] Squamous cell carcinoma of the skin has been reported with long-term exposure to voriconazole in patients with immunosuppressed status.
Risk minimisation measures	Routine: SmPC section 4.2, 4.4 and 4.8 Additional: 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 Vfend.

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

None.

REFERENCES

1 Hacker SM, Flowers FP. Squamous cell carcinoma of the skin. Will heightened awareness of risk factors slow its increase? Postgrad Med 1993; 93(8):115-21, 125-6.[Available upon request]

2 Berg D, Otley CC. Skin cancer in organ transplant recipients: epidemiology, pathogenesis, and management. J Am Acad Dermatol 2002; 47(1 Jul):1-17.

3 Euvrard S. [Skin cancers after organ transplants]. Presse Med 2008; 37(10):1475-9.

4 Jashin IF. Squamous cell carcinoma in solid-organ transplantation. Dermatology Online Journal 2009; 8(2):4.