VI.2 Elements for a public summary

<Product name> 50 mg powder for concentrate for solution for infusion.

<Product name> 70 mg powder for concentrate for solution for infusion

VI.2.1 Overview of disease epidemiology

Due to the increasing number of patients with solid organ and bone marrow transplants, with HIV infections and critical illnesses, which often require invasive procedures, the incidence and the clinical importance of serious fungal infections have risen dramatically in the last 2 decades.

Epidemiological changes in the patterns of invasive fungal infections reflect not only the increasing population at risk but the emergence of antifungal-resistant fungal species. The most well-known causes of opportunistic fungal infections (mycoses) include *Candida albicans*, *Cryptococcus neoformans*, and *Aspergillus fumigatus*. The estimated annual incidence of invasive mycoses due to these pathogens is 72–228 infections per million population for *Candida* species, 30–66 infections per million population for *C. neoformans*, and 12–34 infections per million population for *Aspergillus* species. In addition to these agents, the growing list of "other" opportunistic fungi is of increasing importance.

VI.2.2 Summary of the treatment benefits

For many years, amphotericin B was the only systemic antifungal agent for the treatment of invasive fungal infections. The advent of other antifungal medicines as the triazoles and lipid amphotericin B formulations in the 1990s provided alternative therapeutic options. However, renal toxicity remains a major drawback of amphotericin B formulations, whilst drug interactions, hepatotoxicity and limitations to use in renal failure are primary concerns with newer-generation azoles.

The development of inhibitors of the synthesis of fungal cell wall glucan represents an important advancement in antifungal chemotherapy. Caspofungin was the first of a new class of antifungal agents, the echinocandins. The early promise of the echinocandins as effective anti-Candida and anti-Aspergillus agents has been supported by large clinical efficacy trials; these agents have had a significant impact on the prevention and management of selected fungal infections. Caspofungin is indicated in the treatment of invasive candidiasis (fungal infection due to Candida) and invasive aspergillosis (fungal infection due to Aspergillus). It is also indicated when patients is febrile and have an abnormally low number of white blood cells (neutropenic). Intravenous caspofungin was approved in 2001 for the treatment of fungal infections in adults, and in 2008 for use in paediatrics patients.

VI.2.3 Unknowns relating to treatment benefits

There is little or no data about the treatment of pregnant women with Caspofungin. Animal studies have shown that causes toxicity during development and that can pass through the placental barrier. Caspofungin should not be used in this groups of patients unless clearly necessary. The effect on children below 3 months of age has not been shown. Also, there is limited treatment experience in patients 65 years of age and older.

VI.2.4 Summary of safety concerns

Table 6 Important identified risks

Important Identified Risk	What is known	Preventability
Allergic reactions (Hypersensitivity reactions - anaphylaxis and possibly	Hypersensitivity reactions such as rash, itching, feeling warm, swelling of face, lips	By monitoring for early symptoms.

Important Identified Risk	What is known	Preventability
histamine-mediated adverse reactions-)	or throat, difficulty breathing with or without wheezing (whistling sound produce during breathing) have been reported during administration of caspofungin.	
Liver injury (Hepatotoxicity)	Side effects affecting the liver such as changes in some laboratory blood tests (including increased values of some liver tests) have been commonly reported (may affect up to 1 in 10 people) in adults and children. Other side effects such as a decreased flow of bile, enlarged liver, liver disorder and liver injury have also been reported (affecting up to 1 in 100 people).	By monitoring for early symptoms.
Development of drug resistance (when the virus becomes resistant to treatment with the medicine)	Caspofungin resistance has been rarely observed in patients with fungal infections that occurred in nose, nasal sinuses or lungs (called 'invasive aspergillosis').	By monitoring of treatment efficacy.
Drug interaction with rifampin and other medicines that could decrease the amount of caspofungin in the body (Drug interaction with rifampicin and other inducers of drug clearance)	Certain medicines (such as the anti-infective rifampicin) can affect the way caspofungin works by decreasing the amount of caspofungin in the body.	By consideration of an increase in the daily dose of caspofungin in paediatrics and adults patients
Drug interaction with cyclosporin	Ciclosporin may increase the amount of caspofungin in the body and may cause liver problems.	By monitoring of liver enzymes.
Drug interaction with tacrolimus	Caspofungin can affect the way tacrolimus (a medicine used to help prevent organ transplant rejection or to suppress the immune	By standard monitoring of tacrolimus blood concentrations and appropriate tacrolimus dosage adjustments

Important Identified Risk	What is known	Preventability
	system) works. Studies in healthy adult volunteers have shown that caspofungin reduces the blood levels of tacrolimus (through levels) by 26%.	

There are no important potential risks for this product.

Table 7 Missing information

Risk	What is known
Exposure during pregnancy and lactation	All echinocandins have embryo toxic potential and all three have been found in the breast milk of rats. There are no data on the excretion of caspofungin into human milk. Therefore, they should only be used during pregnancy or in nursing women if benefits outweigh the risks
Exposure in neonates and infants < 3 months of age	The safety and efficacy of caspofungin have not been sufficiently studied in clinical trials involving neonates and infants below 3 months of age. Caution is advised when treating this age group.
Exposure in patients ≥ 65 years old	There is limited treatment experience in patients 65 years of age and older. In elderly patients (65 years of age or more), the area under the curve (AUC) is increased by approximately 30 %. However, no dose adjustment is required.

VI.2.5 Summary of risk minimization measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post-authorisation development plan (if applicable)

Not applicable

VI.2.7 Summary of changes to risk management plan over time

Not applicable for the initial RMP.