PUBLIC SUMMARY OF RISK MANAGEMENT PLAN (RMP)

CASPOFUNGIN ORION

ORION CORPORATION

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VI.2 Elements for a Public Summary

Caspofungin Orion is an antifungal medicine. It is used to treat adults, adolescents and children with:

- invasive candidiasis (a type of fungal infection due to Candida);
- invasive aspergillosis (another type of fungal infection due to Aspergillus) when the patient does not respond to or does not tolerate amphotericin B or itraconazole (other antifungal medicines);
- suspected fungal infections (such as due to Candida or Aspergillus) when the patient is febrile (feverish) and neutropenic (lacking white blood cells). This is known as 'empirical treatment', which means that the treatment is started based on an observation of the patient before the doctor has a confirmation of the infection.

VI.2.1 Overview of disease epidemiology

Invasive candidiasis

Invasive candidiasis is an infection caused by a yeast (a type of fungus) called Candida.

Unlike Candida infections in the mouth and throat (also called "thrush") or vaginal "yeast infections," invasive candidiasis is a serious infection that can affect the blood, heart, brain, eyes, bones, and other parts of the body. Candidemia, a bloodstream infection with Candida, is a common infection in hospitalized patients.

The incidence of candidemia is approximately 10-14 per 100,000, but the incidence and the distribution of Candida species causing infection vary substantially by geographic location and patient population.

Known risk factors for invasive candidiasis include: HIV, diabetes, immunosuppressant medication – a type of medication used to stop the body rejecting newly-donated organs, high-dose chemotherapy or radiotherapy, central venous catheter (CVC) or dialysis.

Invasive aspergillosis

Aspergillosis is an infection caused by a type of mold. The illnesses resulting from aspergillosis infection usually affect the respiratory system, but their signs and severity vary greatly. The mold that triggers the illnesses, aspergillus, is everywhere, indoors and outdoors. Most strains of this mold are harmless, but a few can cause serious illnesses when people with weakened immune systems, underlying lung disease or asthma inhale their spores.

The most serious form of aspergillosis — invasive aspergillosis — occurs when the infection spreads to blood vessels and beyond.

Invasive aspergillosis is uncommon and occurs primarily in immunocompromised people.

Prospective surveillance among transplant recipients performed during 2001-2006 in found that invasive aspergillosis was the most common type of fungal infection among stem cell transplant recipients and was the second-most common type of fungal infection among solid organ transplant recipients, with a 12-month cumulative incidence of 19%.

VI.2.2 Summary of treatment benefits

The active substance in this medicinal product, caspofungin, belongs to a group of antifungal medicines known as 'echinocandins'. It works by interfering with the production of a component of the fungal cell wall called 'glucan polysaccharide', which is necessary for the fungus to continue living and growing. Fungal cells treated with caspofungin have incomplete or defective cell walls, making them fragile and unable to grow. This stops the infection from spreading and gives the body's natural defences a chance to completely get rid of the infection.

The following information is based on studies made with caspofungin originator product Candicas.

In invasive candidiasis, 73% of the adults treated with caspofungin who could be assessed had a favourable response (80 out of 109), compared with 62% of the adults treated with amphotericin B (71 out of 115).

In invasive aspergillosis, 41% of the adults had a favourable response at the end of the study (26 out of 63). Of the adults who did not respond to other treatments, 36% responded to caspofungin (19 out of 53). Of those who did not tolerate other treatments, 70% responded to caspofungin (7 out of 10).

Similar responses were seen in children and adolescents: 50% of those with invasive candidiasis (5 out of 10) and 81% of those with invasive aspergillosis (30 out of 37) responded to caspofungin.

In the empirical treatment of febrile neutropenic patients, caspofungin was as effective as amphotericin B. In the adult study, 34% of both groups of adults had a favourable response. Similar results were seen in the study of children and adolescents.

VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy of caspofungin have not been sufficiently studied in clinical trials involving neonates and infants below 12 months of age. Caution is advised when treating this age group.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Serious hypersensitivity reactions	Serious and sudden allergic reactions (anaphylaxis) have been reported in association with caspofungin administration. In addition rash, facial swelling, rapid swelling of e.g. mouth and throat (angioedema), itching, sensation of warmth, or bronchospasm have been reported.	Caspofungin must not be used if the patient is allergic/hypersensitive to caspofungin or to any of the other ingredients of this medicinal product. Doctor and nurse should be informed before onset of therapy if the patient has any allergies and/or any history of hypersensitivity

		reactions.
Increase in caspofungin levels in blood in adult patients with moderate liver impairment (increased caspofungin AUC in adult patients with moderate hepatic impairment)	In patients with moderately impaired liver function, liver eliminates caspofungin slower than normally thus concentration of caspofungin in blood may increase to too high levels causing adverse effects.	Lower dose should be administered in patients with moderately impaired liver function.
Increased liver enzymes when used concomitantly with cyclosporine (medicine used to help to prevent organ transplant rejection or to suppress immune system)	Concomitant administration of caspofungin and cyclosporine may affect liver which causes increase liver enzyme levels in blood.	Close monitoring of liver enzymes with blood tests may be necessary if caspofungin and cyclosporine are used concomitantly.

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Harmful effects on liver (hepatotoxicity)	Laboratory abnormalities in liver function tests have been seen in healthy volunteers and adult and child patients treated with caspofungin. In some adult and child patients with serious underlying conditions who were receiving multiple concomitant medications with caspofungin, cases of clinically significant liver dysfunction, inflammation of the liver and liver failure have been reported; however a causal relationship to caspofungin has not been established. Patients who develop abnormal liver function tests during caspofungin therapy should be monitored for evidence of worsening liver function and the risk/benefit of continuing caspofungin therapy should be re-evaluated.

Missing information

Risk	**What is known**
Administration in children with any degree liver impairment or adult patients with severe liver impairment	There is no clinical experience in adult patients with severe liver impairment and in children with any degree of liver impairment.
Administration during pregnancy or breast-feeding	There are no or limited data from the use of caspofungin in pregnant women. Caspofungin should not be used during

	pregnancy unless clearly necessary. Animal studies have shown harmful effects on development of the fetus. It is unknown whether caspofungin is excreted in human milk. Animal studies have shown that caspofungin is excreted in milk. Women receiving caspofungin should not breast-feed.

VI.2.5 Summary of risk minimisation 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. The Summary of Product Characteristics and the Package leaflet for this medicinal product can be found in the national authority's web page.

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 the Risk Management Plan over time

Not applicable.