VI.2. Elements for a Public Summary

VI.2.1. Overview of disease epidemiology

Invasive candidiasis and aspergillosis are infections caused by certain yeasts and molds (funghi). They occur mainly in hospitalized patients with a compromised immune system, for example patients with AIDS or cancer patients receiving chemotherapy

A yeast called Candida can cause invasive candidiasis, a serious infection that can affect the blood, heart, brain, eyes, bones, and other parts of the body. The most common symptoms are fever and chills that don't improve after antibiotic treatment for suspected bacterial infections. Diagnosis is confirmed by verification of Candida yeasts in a blood sample.

Aspergillosis is caused by a type of mold which most commonly affects airways and lungs but may also spread within the body to organs such as the heart and kidneys. Typical symptoms are cough, fever, chest pain, and difficulty breathing. Diagnosis is made by chest X-ray and a blood test.

Invasive candidiasis and aspergillosis need treatment with antifungal medicines which are usually administered by intravenous infusion.

VI.2.2. Summary of treatment benefits

Caspofungin makes fungal cells fragile and stops the fungus from growing properly. This stops the infection from spreading and gives the body's natural defences a chance to completely get rid of the infection.

The efficacy and safety in patients with invasive candidiasis was compared to the reference drug amphotericin B in a clinical study with 239 patients. The mean duration of intravenous therapy was 11.9 days, with a range of 1 to 28 days. Response was defined as resolution of clinical symptoms and clearing of funghi from blood. While 72% of patients responded favourably to caspofungin 63% responded to amphotericin B, respectively.

In a second study in patients with invasive Candida infections the efficacy of daily doses of 50 mg or 150 mg caspofungin was tested. The favourable overall response rates at the end of caspofungin therapy were similar in the two treatment groups: 72 % and 78 % in the caspofungin 50-mg and 150-mg treatment groups, respectively.

Sixty-nine (69) adult patients with invasive aspergillosis were enrolled in an open-label, non-comparative study to evaluate the safety, tolerability, and efficacy of caspofungin therapy. An independent expert panel determined that 41 % of patients receiving at least one dose of caspofungin had a favourable response.

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 3 months of age. There are no or limited data from use in pregnant or breast-feeding women.

VI.2.4. Summary of safety concerns

Important identified risks		
Risk	**What is known**	**Preventability**

Impairment of liver function	Increase of liver enzymes is a common reaction to caspofungin occurring in more than 1/100 but less of 1/10 people. Impaired liver function is uncommon occurring in more than 1/1000 but less of 1/100 people. Clinical signs may be disturbed bile flow, increased liver size or elevated levels of bilirubin (a decomposition product of blood cells) causing jaundice.	Careful observation of patients for early symptoms and stop of treatment if indicated. Patients with pre-existing moderate liver disease can be treated with a reduced dose of caspofungin. There is no clinical experience in patients with severe liver disease (see also missing information). If such patents need treatment with caspofungin high caution is advised.
Allergic reactions (hypersensitivity and anaphylaxis)	Allergic reactions can occur against the active substance and other ingredients. They may present as redness and flushing, skin rash, and raised areas of the skin that itch. Reactions can be serious including anaphylaxis (weakness, drop in blood pressure, difficulty breathing, and swelling of the face).	People with known hypersensitivity to this medicine must not take it. The treating physician should take a careful history of each patient's known allergies to identify patients at risk.
Lack of efficacy against less common fungi	Precise diagnosis of the infective agent may take several days. If treatment in critically ill patients is started immediately on suspicion there is a risk that the infection is caused by fungi not responding to caspofungin. Also fungi may get resistant to treatment over time.	Assurance of infection with a susceptible agent by specific microbiological tests before start of treatment.
Drug interaction with rifampicin or other medication which reduce inactivation of caspofungin	Rifampicin is an antibiotic for the treatment of some serious bacterial infections. When taken together with caspofungin the elimination of caspofungin from the body may be impaired and blood levels elevated. The result is an increased risk of side effects. Apart from rifampicin certain other drugs can increase the activity of liver enzymes which are involved in the inactivation of medicines such as	The dose of caspofungin may have to be increased when taken together with efavirenz, nevirapine, rifampicin, dexamethasone, phenytoin, or carbamazepine.
	caspofungin. When such enzyme-inducers are co-administered with caspofungin its therapeutic effect may be decreased.	

Drug interaction with cyclosporine	Cyclosporine is an immunosuppressant drug widely used in organ transplantation to prevent rejection. When taken together with caspfungin the liver function may be altered.	Careful monitoring of liver function is required
Drug interaction with tacrolismus	Tacrolismus is a medicine used to prevent the rejection of transplanted organs from the body. When taken together with caspofungin the elimination of tacrolismus from the body may be increased causing a reduction of efficacy.	Monitoring of tacrolismus blood levels and adjustment of dosing is mandatory.
Important potential risks		
Potential risk	**What is known**	
Use in patients with fructose intolerance or sucrose-isomaltase insufficiency	This medicine contains sugar (sucrose) as an ingredient. Patients with rare hereditary problems of fructose intolerance or sucrase–isomaltase insufficiency may react with acute gut or stomach problems. Patients with known fructose intolerance or sucrose-isomaltase insufficiency should not take this medicine.	
Important missing information		
Missing information	**What is known**	
Use in pregnant and breast feeding women	There are no or limited data from the use of caspofungin in pregnant or breast feeding women. Caspofungin should not be used during pregnancy unless clearly necessary. It is unknown whether caspofungin is excreted in human milk and could be a risk for suckling babies. Women receiving caspofungin should not breast-feed.	
Use in neonates and infants below 3 months of age	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 and special dosing schemes are recommended.	

VI.2.5. Summary of additional 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.
This medicine has no additional risk minimisation measures.

VI.2.6. Planned post authorisation development plan

No post-authorisation development is currently planned.

VI.2.7. Studies which are a condition of the marketing authorisation

Not applicable.

VI.2.8. Summary of changes to the Risk Management Plan over time

Not applicable, as this is the first EU-RMP for Caspofungin Regiomedica.