VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Invasive candidiasis/candidaemia is the most frequently occurring invasive fungal infection worldwide. *Candida albicans* remains the most common *Candida* spp. responsible for candidaemia, whereas non-albicans spp. composes 40%. A multi-institutional survey performed by the European Confederation of Medical Mycology in several European countries reported incidences of 2.0-3.8 cases of candidaemia per 10,000 admissions. The majority of cases were diagnosed on surgical and intensive care units (48.2% and 40.2%, respectively), 22.5% of patients had solid tumours, 17.4% received steroids and 12.3% had blood related cancer. Candida fungal infection has been observed to be the fourth leading cause of bloodstream infections in paediatric patients (<18 years of age), cancer patients, and hospitalised patients with mortality rates from 20% in paediatric patients to 47% in intensive care unit patients. Premature birth is a major predisposing factor in neonates. For intensive care patients, the rate of invasive fungal infections increases with the duration of stay, particularly >7 days.

VI.2.2 Summary of treatment benefits

The main treatment of invasive *Candida* infections remains fluconazole for most clinicians. However, triazole-resistant species including *Candida glabrata* and *Candida krusei*, along with the emergence of azole-resistant *C. albicans*, which previously were uniformly susceptible to fluconazole, have made treatment decisions more critical. According to the Infectious Diseases Society of America (IDSA) and European Society for Clinical

Microbiology and Infectious Diseases (ESCMID) guidelines, anidulafungin as well as other Echinocandins could manage this condition, because resistance against Echinocandins still remains rare. Anidulafungin is approved for treatment of invasive candidiasis and candidaemia in Europe. Anidulafungin has been studied in one main study involving 261 patients with invasive candidiasis and who did not have neutropenia (low white blood cell counts). Anidulafungin was compared with fluconazole (another antifungal medicine). Both medicines were given by infusion, for between 14 and 42 days. An analysis of other studies evaluated the effects of anidulafungin in 46 patients with neutropenia. The main measure of effectiveness was the number of patients who had responded to treatment at the end of treatment course. A response was defined as significant or complete improvement of symptoms, with no need for further antifungal treatment and no *Candida* found in the specimens taken from patient.

VI.2.3 Unknowns relating to treatment benefits

Data on safety and efficacy of anidulafungin in children below 18 years and its use during pregnancy and breast feeding have not yet been established.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Infusion associated reactions (allergic reaction)	Adverse events related to infusion with anidulafungin have been reported, such as rash, pruritis (itching), hot flush, and hives. These side effects are common (may affect up to 1 in 10 people). Infusion-related adverse events are infrequent when the rate of anidulafungin infusion does not exceed 1.1	Tell doctor or another healthcare professional immediately should any of the following occur: flushing, rash, pruritis (itching), hot flush, hives, sudden contraction of the muscles around the airways resulting in wheezing or coughing, difficulty of breathing. It is recommended that

	mg/min. Life-threatening allergic reactions that might include difficulty breathing with wheezing or worsening of an existing rash have been rarely reported with anidulafungin (may affect up to 1 in 100 people).	anidulafungin should be administered at a rate of infusion that does not exceed 1.1 mg/min. Patient should not be treated with anidulafungin if allergic to anidulafungin, other echinocandins (eg, CANCIDAS), or any of the other ingredients of this medicine.
Liver-related (Hepatobiliary) events	Liver problems, such as changes in blood tests of liver function, are common in patients treated with anidulafungin (may affect up to 1 in 10 people). In some patients with other serious medical conditions who were receiving additional medicines along with anidulafungin, significant liver problems have occurred like abnormal flow of bile from the gallbladder into the intestine (cholestasis), which is uncommon (may affect up to 1 in 100 people).	Doctor may decide to monitor liver function more closely if patient develop liver problems during treatment.
Convulsions (fits)	Although there is no clear evidence that the risk of convulsions is caused by anidulafungin, convulsions have been observed in patients treated with other drugs in this class (i.e., Echinocandins). The frequency of this event is common (may affect up to 1 in 10 people).	Talk with doctor or another healthcare professional immediately if this reaction occurs.

	Tell doctor or another healthcare professional immediately if patient have fits/convulsions.	

Important potential risks

Risk	**What is known**
Worsening of infusion associated allergic reactions because of anaesthesia (anesthesia exacerbated infusion associated reactions)	Rats given high doses of anidulafungin experienced a worsening of allergic reactions related to infusion with anidulafungin and anesthesia. The cause of the worsening of these reactions in rats is unknown. Although the relevance of this finding to humans is unknown, any patient experiencing allergic reaction related to infusion and receiving concurrent anesthesia might be at risk. Doctor may decide to monitor if patient is given anaesthetics during treatment with anidulafungin. No instances of anesthesia-exacerbated infusion-associated reactions have been observed in humans.
QT Prolongation/*Torsade de Pointes* (abnormal ecocardiogram)	None proposed

Missing Information

Risk	**What is known**
Use in children/adolescents	The safety and the benefits of anidulafungin in children below 18 years have not yet been established. To date, experience with anidulafungin in the pediatric population is limited.
Use during pregnancy and	Pregnant women were not allowed in anidulafungin studies. There are insufficient safety data in pregnancy/breast-feeding

breast-feeding (lactation)	to recommend the use of anidulafungin during pregnancy without clear potential benefit.
Use in elderly	A limited number of elderly patients were studied in clinical trials. However, no dosing adjustments are required for elderly patients.
Resistance to anidulafungin	Anidulafungin is fungicidal for *Candida* species. Resistance to anidulafungin was not observed in laboratory experiments designed to detect it, including in vitro (in culture dish, outside a living organism) passage experiments and animal infection experiments.

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.

This medicine has no additional risk minimisation measures.

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

No studies planned.

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

Version	Date	Safety Concern	Comment
2.0	26-Oct-2017	Following safety concerns have been updated in RMP. • Important potential risk	RMP has been updated as per Day 70 assessment report of anidulafungin

		"Convulsions" has been updated as an important identified risk. • Missing information "Use in neutropenic patients" has been removed.	(UK/H/6626/01/DC).