SANDOZ A Novartis Division

Anidulafungin

100 mg

Powder for concentrate for solution for infusion

1.8.2 Safety Risk Management Plan

Active substance(s) (INN or common name):	Anidulafungin
Pharmacotherapeutic group (ATC Code):	Pharmacotherapeutic group: Antimycotics for systemic use, other antimycotics for systemic use ATC code: JO2AX06
Name of Marketing Authorization Holder or Applicant:	Sandoz
Number of medicinal products to which this RMP refers:	1
Product(s) concerned (brand name(s)):	[Nationally completed name] 100 mg Powder for concentrate for solution for infusion
Version number	1.1
Data lock point for this RMP	09 Jun 2017
Date of final sign off	09 Jun 2017

4.2 Part VI.2 Elements for a Public Summary

4.2.1 Part VI.2.1 Overview of disease epidemiology

Invasive candidiasis/ candidemia (presence of candida (type of fungus) in the blood) is the most frequently occurring invasive fungal infection worldwide. *Candida albicans* remains the most common Candida type responsible for candidemia. A survey performed by the European Confederation of Medical Mycology in several European countries reported an occurrence of 2.0-3.8 cases of candidemia per 10,000 surveys. The majority of the cases were diagnosed on surgical and intensive care units (ICU) (48.2% and 40.2%, respectively), 22.5% of the patients had tumours, 17.4% received steroids (such as cholesterol and sex hormones) and 12.3% had haematological malignancies (types of cancer that affect blood, bone marrow, and lymph nodes) [Gloeckner, 2001].

4.2.2 Part VI.2.2 Summary of treatment benefits

The main treatment of invasive Candida infections remains fluconazole (another antifungal medicine) for most healthcare professionals. However, the types of *Candida* which are resistant to the treatment with fluconazole have made treatment decisions more critical [Kuti and Kuti 2010]. According to the Infectious Diseases Society of America (IDSA) and European Society for Clinical Microbiology and Infectious Diseases (ESCMID), anidulafungin as well as other echinocandins (antifungal drugs) could manage this condition, because resistance against echinocandins still remains rare. 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) being compared with fluconazole. Anidulafungin was more effective than fluconazole in treating invasive candidiasis. At the end of the treatment course, 76% of the patients receiving anidulafungin had responded to treatment (96 out of 127), compared with 60% of the patients receiving fluconazole [Ecalta Pfizer SmPC, 2007].

4.2.3 Part VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy of anidulafungin in children and adolescents below 18 years have not been established. There are no data regarding the use of anidulafungin in pregnant women, elderly and resistance.

4.2.4 Part VI.2.4 Summary of safety concerns

Table 4-5 Important identified risks

Risk	What is known	Preventability
Serious, life-threatening allergic reaction and reactions due to introduction of foreign substance into body (Anaphylaxis and Infusion-associated reactions)	Anidulafungin or any other ingredients of this medicine may induce allergic reactions. This medicine may also trigger allergies when prescribed with other medicinal products of the echinocandin (antifungal drugs) class. Rash and pruritus may affect upto 1 in 10 people, hot flush and hives may affect up to 1 in 100 people. Infusion-related adverse events have been reported when the rate of anidulafungin infusion does not exceed 1.1 mg/min.	Patients should inform the doctor or any other healthcare professional immediately if they experience rash, pruritus (itching), urticaria (a kind of skin rash with red, raised, itchy bumps), hot flush, hives, breathlessness or shortness of breath, bronchial spasm and low blood pressure.
Liver and biliary disorders (hepatobiliary events)	Increased levels of hepatic enzymes have been seen in healthy people and patients treated with anidulafungin. Changes in blood test of liver function are a common side effect which may affect up to 1 in 10 people.	Patients with increased liver enzymes during anidulafungin therapy should be monitored for evidence of worsening liver function and evaluated if anidulafungin therapy is appropriate for them.

Table 4-6 Important potential risks

Risk	What is known
Abnormal activity in the brain that lead to fits(Convulsions)	Convulsions have been seen as a common (1 in 10 people) side effect in patients treated with anidulafungin.
Worsening of infusion related reactions during use of anidulafungin and agents that cause numbness at the same time (Anesthetic exacerbation of infusion associated reactions)	Care should be taken when administering anidulafungin and anesthetic agents at the same time as the patients experience side effects like rashes, flush, breathlessness and low blood pressure.
Type of abnormal heart rate that can lead to sudden death of heart (QT Prolongation / torsade de pointes)	Patient should talk to the doctor or pharmacist before using anidulafungin if they have QT Prolongation / torsade de pointes.

Table 4-7 Missing information

Risk	What is known
Children/adolescents	Anidulafungin should be place out of the range of the children as it is not used for patients under 18 years of age.
Pregnant women	The effect of anidulafungin in pregnant women is not known. Therefore anidulafungin is not recommended during pregnancy. Effective contraception should be used in women of childbearing age. Patients should tell the doctor immediately if they become pregnant while taking anidulafungin.

Risk	What is known
Elderly	Dosing adjustments are not required in elder patients during anidulafungin therapy
Lack of sensitivity to a medicine (Resistance)	Animal experiments have shown resistance to all three strains of fungi when treated with anidulafungin.

4.2.5 Part VI.2.5 Summary of additional 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 minimizing 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 minimization measures.

This medicine has no additional risk minimization measures.

4.2.6 Part VI.2.6 Planned post authorization development plan

None

4.2.7 Part VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable (first submission)