Ezokamine®
(micafungin)

Administration and Monitoring Guide
Information for prescribers and nurses.
Revision Date: December 2020

Introduction

This booklet for prescribers and nurses provides practical guidance on the safe use and administration of micafungin, an echinocandin antifungal drug. This booklet also highlights ways to minimize the potential risks associated with micafungin use.

This Document has been approved by SFDA

About micafungin

Micafungin is an echinocandin antifungal drug. It is active against many fungal species, including most clinically relevant species of Candida and Aspergillus spp. In vitro data show that micafungin is also active against fluconazole-resistant Candida strains.
EZOKAMINE® is indicated for the treatment of the following infections caused by Aspergillus sp. and Candida sp.: Fungemia, respiratory mycosis, gastrointestinal mycosis.
The decision to use micafungin should take into account the potential risk for the development of liver tumours. Micafungin should therefore only be used if other antifungals are not appropriate. Treatment with micafungin should only be initiated by a physician experienced in the management of systemic fungal infections.

Side effects

The most frequently reported adverse reactions in clinical studies were nausea (%2.8), increased blood alkaline phosphatase (%2.7), phlebitis(%2.5, primarily in HIV infected patients with peripheral lines), vomiting (%2.5) and increased aspartate aminotransferase (%2.3). No clinically significant differences were seen when the safety data were analysed by gender or race.
Micafungin is associated with the potential risk of liver tumour formation. For details of the main risks (anaphylactic/anaphylactoid reactions, exfoliative cutaneous reactions, hepatotoxicity, haemolysis and renal toxicity) and specific monitoring recommendations during micafungin treatment, refer to the patient information leaflet (PIL)

Initiating treatment

Micafungin should be used if other antifungals are not appropriate in accordance with the SPC, the key features of which are summarised in the Prescriber Checklist. The Prescriber Checklist should be used before administering micafungin to a new patient. The completed checklist should be kept in the patient's notes.

Use in adults, adolescents ≥ 16 years of age and elderly

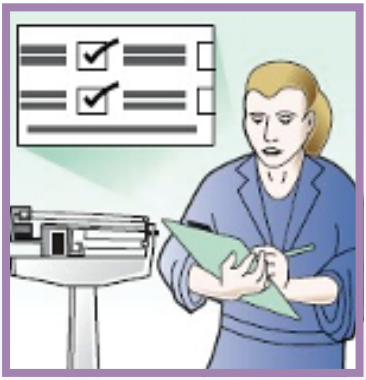
Aspergillosis: the usual single daily dose is 150 - 50 mg of micafungin sodium infused intravenously once daily. The dosage can be increased according to the patient's condition for severe or refractory aspergillosis up to 300 mg/day.
Candidiasis: the usual single daily dose is 50 mg of micafungin sodium infused intravenously once daily. The dosage can be increased according to the patient's condition for severe or refractory candidiasis up to 300 mg/day.
No dose adjustment necessary for renal or mild or moderate hepatic impairment, in elderly patients, or based on gender or race. There are currently insufficient data available for the use of micafungin in patients with severe hepatic impairment and its use is not recommended in these patients.

Preparation of the solution for infusion

Dose (mg)	Micafungin vial to be used (mg/vial)	Volume of sodium chloride (0.9%) or glucose (5%) to be added per vial	Volume (concentration) of reconstituted powder	Standard infusion (added up to 100 ml) Final concentration
50	1 x 50	5 ml	approx. 5 ml (10 mg/ml)	0.5 mg/ml
100	1 x 100	5 ml	approx. 5 ml (20 mg/ml)	1.0 mg/ml
150	1 x 50 + 1 x 100	5 ml	approx. 10 ml	1.5 mg/ml
200	2 x 100	5 ml	approx. 10 ml	2.0 mg/ml

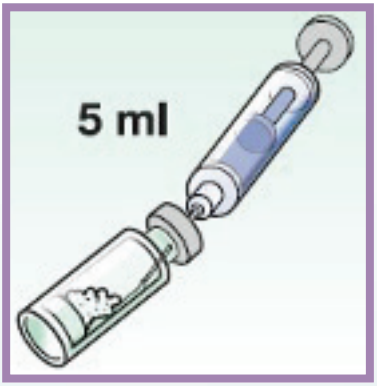
Administration

1.



Check the patient's weight and calculate appropriate dose, referring to dose table. Take the appropriate number of micafungin vials and, using aseptic techniques, remove the plastic cap from the vial and disinfect the stopper with alcohol.

2.



Withdraw 5 ml of sodium chloride 9mg/ml (%0.9) solution for infusion or glucose 50 mg/ml (%5) solution for infusion (taken from a 100 ml bottle/bag) and inject aseptically and slowly into each vial along the side of the inner wall. Although the concentrate will foam, make every effort to minimise the amount of foam generated.

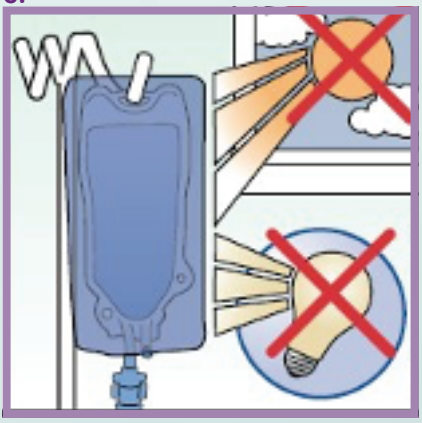
3.

Rotate the vial gently until the powder is completely dissolved.
DO NOT SHAKE.

4.

Withdraw all of the reconstituted concentrate from each vial and return into the infusion bottle/bag from which it was taken. Gently invert the infusion bottle/bag to disperse the diluted solution.
DO NOT SHAKE. Do not use if the solution is cloudy or has precipitated.

5.



PROTECT THE INFUSION BAG FROM LIGHT.

6.

Infuse the solution intravenously over approximately 1 hour. Monitor the patient for allergic reactions.

Use the reconstituted and diluted solutions as soon as they are made up. Dispose of any unused product or waste material in accordance with local requirements. Do not mix or co-infuse micafungin with other medicinal products except those mentioned above.

Recommended treatment duration

- **Candidaemia and invasive candidiasis:**
  The treatment duration of Candida infection should be a minimum of 14 days. The antifungal treatment should continue for at least one week after two sequential negative blood cultures have been obtained and after resolution of clinical signs and symptoms of infection.
- **Oesophageal candidiasis:**
  Micafungin should be administered for at least one week after resolution of clinical signs and symptoms.
- **Prophylaxis of Candida infections:**
  Micafungin should be administered for at least one week after neutrophil recovery. Experience with micafungin in patients less than 2 years of age is limited.

Patient monitoring

Patients undergoing micafungin treatment are likely to be critically ill, with a wide variety of complex underlying conditions requiring multiple drugs, including antineoplastic chemotherapy, potent systemic immuno-suppressants and broad spectrum antibiotics. They are therefore likely to be already undergoing intensive monitoring. Micafungin treatment should not be administered to patients with known hypersensitivity to micafungin, other echinocandins, or lactose monohydrate.

During micafungin therapy, monitor patients specifically for the following.

• **Anaphylactic/anaphylactoid reactions,** including shock – if such reactions occur, stop the drug infusion and administer appropriate treatment.

• **Exfoliative cutaneous reactions,** such as Stevens-Johnson syndrome and toxic epidermal necrolysis. If patients develop a rash they should be monitored closely and micafungin discontinued if lesions progress.

• **Worsening of liver function** – early discontinuation is recommended in the presence of significant and persistent elevation of ALT/AST levels, to minimize the risk of liver abnormalities and potentially subsequent liver tumour formation.

• **Clinical or laboratory evidence of haemolysis,** including acute intravascular haemolysis or haemolytic anaemia – if there is evidence of haemolysis, monitor closely for evidence of worsening and evaluate the benefit/risk of continuing micafungin therapy.

• **Worsening of renal function** – micafungin may cause kidney problems, renal failure, and abnormal renal function tests.

• **Other side effects** – the most frequently reported adverse reactions during micafungin clinical studies were nausea, increased blood alkaline phosphatase levels, phlebitis (primarily in HIV infected patients with peripheral lines), vomiting, and raised AST.

• **Clinical and microbiological resolution of infection.**

• **Concomitant drug therapy** – monitor for sirolimus, nifedipine or itraconazole toxicity and reduce dose if necessary. Close monitoring of amphotericin B desoxycholate toxicity required.

For further information about this product or to report any Adverse Event, please contact:

Pharmacovigilance department in SAJA Pharmaceuticals Co. Ltd.:
Tel: + 966 12 606 6667
Email: Drug.safety@sajapharma.com
Website: sajapharma.com

National Pharmacovigilance Center (NPC):
SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa