# PROFESSIONAL INFORMATION

**SCHEDULING STATUS:** S4

## 1. NAME OF THE MEDICINE

Micafungin 50 Sandoz (powder for concentrate for solution for infusion)

Micafungin 100 Sandoz (powder for concentrate for solution for infusion)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**MICAFUNGIN 50 SANDOZ**

Each vial contains micafungin sodium equivalent to 50 mg micafungin.

After reconstitution, each ml contains 10 mg micafungin.

MICAFUNGIN 50 SANDOZ contains sugar (200 mg lactose monohydrate per vial).

**MICAFUNGIN 100 SANDOZ**

Each vial contains micafungin sodium equivalent to 100 mg micafungin.

After reconstitution, each ml contains 20 mg micafungin.

MICAFUNGIN 100 SANDOZ contains sugar (200 mg lactose monohydrate per vial).

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder for concentrate for solution for infusion.

Lyophilised white to off white powder.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

MICAFUNGIN SANDOZ is indicated for:

Adults, adolescents ≥ 16 years of age and elderly:

- Treatment of invasive candidiasis.

- Treatment of oesophageal candidiasis in patients for whom intravenous therapy is appropriate.
- Prophylaxis of Candida infection in patients undergoing allogeneic haematopoietic stem cell transplantation or patients who are expected to have neutropenia (absolute neutrophil count < 500 cells/µl) for 10 or more days.

Children (including neonates) and adolescents < 16 years of age:

- Treatment of invasive candidiasis.
- Prophylaxis of Candida infection in patients undergoing allogeneic haematopoietic stem cell transplantation or patients who are expected to have neutropenia (absolute neutrophil count < 500 cells/µl) for 10 or more days.

The decision to use MICAFUNGIN SANDOZ should take into account a potential risk for the development of liver tumours. MICAFUNGIN SANDOZ should therefore only be used if other antifungals are not appropriate (see section 4.4).

**4.2. Posology and method of administration**

**Posology:**

Treatment with MICAFUNGIN SANDOZ should be initiated by a medical practitioner experienced in the management of fungal infections.

Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies are known. However, once these results become available, antifungal therapy should be adjusted accordingly.

The dose regimen of MICAFUNGIN SANDOZ depends on the body weight of the patient as given in the following table:

| Indication | Body weight >40 kg | Body weight ≤40 kg |
|---|---|---|
| Treatment of invasive candidiasis | 100 mg/day* | 2 mg/kg/day* |
| Treatment of oesophageal candidiasis | 150 mg/day | 3 mg/kg/day |

| | | |
|---|---|---|
| Prophylaxis of *Candida* infection | 50 mg/day | 1 mg/kg/day |

*If the patient's response is inadequate, e.g. persistence of cultures or if clinical condition does not improve, the dose may be increased to 200 mg/day in patients weighing >40 kg or 4 mg/kg/day in patients ≤ 40 kg.

***Treatment duration:***

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: For the treatment of oesophageal candidiasis, MICAFUNGIN SANDOZ should be administered for at least one week after resolution of clinical signs and symptoms.

Prophylaxis of *Candida* infections: For prophylaxis of *Candida* infection, MICAFUNGIN SANDOZ should be administered for at least one week after neutrophil recovery.

Experience with MICAFUNGIN SANDOZ in patients less than 2 years of age is limited.

***Special populations:***

*Use in patients with hepatic impairment:*

No dose adjustment is necessary in patients with mild or moderate hepatic impairment. There are currently no data available for the use of MICAFUNGIN SANDOZ in patients with severe hepatic impairment and its use is not recommended in these patients (see section 4.4 and 4.8).

*Use in patients with renal impairment:*

No dose adjustment is necessary in patients with renal impairment.

**Method of administration:**

For intravenous use.

**4.3 Contraindications**

- Hypersensitivity to the active substance micafungin, or to any of the excipients (listed in section 6.1).

**4.4 Special warnings and precautions for use**

**Hepatic effects:**

**The development of foci of altered hepatocytes (FAH) and hepatocellular tumours after a treatment period of 3 months or longer were observed in rats. The assumed threshold for tumour development in rats is approximately in the range of clinical exposure. The clinical relevance of this finding is not known. Liver function should be carefully monitored during micafungin treatment. To minimise the risk of adaptive regeneration and potentially subsequent liver tumour formation, early discontinuation in the presence of significant and persistent elevation of ALT/AST is recommended. MICAFUNGIN SANDOZ treatment should be conducted on a careful risk/benefit basis, particularly in patients having severe liver function impairment or chronic liver diseases known to represent preneoplastic conditions, such as advanced liver fibrosis, cirrhosis, viral hepatitis, neonatal liver disease or congenital enzyme defects, or receiving a concomitant therapy including hepatotoxic and/or genotoxic properties.**

Micafungin treatment was associated with significant impairment of liver function (increase of ALT, AST or total bilirubin > 3 times ULN) in both healthy volunteers and patients. In some patients more severe hepatic dysfunction, hepatitis, or hepatic failure including fatal cases have been reported. Paediatric patients < 1 year of age might be more prone to liver injury (see section 4.8).

**Anaphylactic reactions:**

During administration of micafungin, anaphylactic/anaphylactoid reactions, including shock, may occur. If these reactions occur, MICAFUNGIN SANDOZ infusion should be discontinued, and appropriate treatment administered.

**Skin reactions:**

Exfoliative cutaneous reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported. If patients develop a rash, they should be monitored closely, and MICAFUNGIN SANDOZ discontinued if lesions progress.

**Haemolysis:**

Cases of haemolysis, including acute intravascular haemolysis or haemolytic anaemia, have been reported in patients treated with micafungin. Patients who develop clinical or laboratory evidence of haemolysis during MICAFUNGIN SANDOZ therapy should be monitored closely for evidence of worsening of these conditions and evaluated for the risk/benefit of continuing MICAFUNGIN SANDOZ therapy.

**Renal effects:**

Micafungin as in MICAFUNGIN SANDOZ may cause kidney problems, renal failure, and abnormal renal function test. Patients should be closely monitored for worsening of renal function.

**Interactions with other medicines:**

Co-administration of micafungin as in MICAFUNGIN SANDOZ and amphotericin B desoxycholate should only be used when the benefits clearly outweigh the risks, with close monitoring of amphotericin B desoxycholate toxicities (see section 4.5).

Patients receiving sirolimus, nifedipine or itraconazole in combination with micafungin as in MICAFUNGIN SANDOZ should be monitored for sirolimus, nifedipine or itraconazole toxicity and the sirolimus, nifedipine or itraconazole dosage should be reduced if necessary (see section 4.5).

**Paediatric population:**

The incidence of some adverse reactions was higher in paediatric patients than in adult patients (see section 4.8).

**Lactose content:**

MICAFUNGIN SANDOZ contains lactose. Patients with the rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take MICAFUNGIN SANDOZ.

**4.5. Interaction with other medicines and other forms of interaction**

Micafungin has a low potential for interactions with medicines metabolised via CYP3A mediated pathways.

Drug interaction studies in healthy human subjects were conducted to evaluate the potential for interaction between micafungin and mycophenolate mofetil, ciclosporin, tacrolimus, prednisolone, sirolimus, nifedipine, fluconazole, ritonavir, rifampicin, itraconazole, voriconazole and amphotericin B. In these studies, no evidence of altered pharmacokinetics of micafungin was observed. No micafungin dose adjustments are necessary when these medicines are administered concomitantly. Exposure (AUC) of itraconazole, sirolimus and nifedipine was slightly increased in the presence of micafungin (22 %, 21 % and 18 % respectively).

Co-administration of micafungin and amphotericin B desoxycholate was associated with a 30 % increase in amphotericin B desoxycholate exposure. Since this may be of clinical significance this co-administration should only be used when the benefits clearly outweigh the risks, with close monitoring of amphotericin B desoxycholate toxicities (see section 4.4).

Patients receiving sirolimus, nifedipine or itraconazole in combination with micafungin should be monitored for sirolimus, nifedipine or itraconazole toxicity and the sirolimus, nifedipine or itraconazole dosage should be reduced if necessary (see section 4.4).

**4.6 Fertility, pregnancy and lactation**

**Pregnancy:**

There are no data from the use of micafungin in pregnant women. In animal studies, micafungin crossed the placental barrier and reproductive toxicity was seen. The potential risk for humans is unknown.

MICAFUNGIN SANDOZ should not be used during pregnancy.

**Breastfeeding:**

It is not known whether micafungin is excreted in human breast milk. Animal studies have shown excretion of micafungin in breast milk.

MICAFUNGIN SANDOZ should not be used whilst breastfeeding.

**Fertility:**

Testicular toxicity was observed in animal studies. Micafungin as in MICAFUNGIN SANDOZ may have the potential to affect male fertility in humans.

**4.7. Effects on ability to drive and use machines**

Micafungin has no or negligible influence on the ability to drive or use machines. However, patients should be informed that dizziness has been reported during treatment with micafungin as in MICAFUNGIN SANDOZ (see section 4.8).

**4.8. Undesirable effects**

**Summary of the safety profile:**

Based on clinical trial experience, overall 32,2 % of the patients experienced adverse drug reactions. The most frequently reported adverse reactions were nausea, blood alkaline phosphatase increased, phlebitis (primarily in HIV infected patients with peripheral lines), vomiting, and aspartate aminotransferase increased.

In the following table adverse reactions are listed by system organ class and MedDRA preferred term. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

| **System Organ Class** | **Frequent** | **Less frequent** | **Frequency unknown** |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Blood and Lymphatic System Disorders | Leukopenia, neutropenia, anaemia | Pancytopenia, thrombocytopenia, eosinophilia, hypoalbuminaemia, haemolytic anaemia, haemolysis (see section 4.4) | Disseminated intravascular coagulation |
| Immune System Disorders | | Anaphylactic / anaphylactoid reaction (see section 4.4), Hypersensitivity | Anaphylactic and anaphylactoid shock (see section 4.4) |
| Endocrine disorders | | Hyperhidrosis | |
| Metabolism and Nutrition Disorders | Hypokalaemia, hypomagnesaemia, hypocalcaemia | Hyponatraemia, hyperkalaemia, hypophosphataemia, anorexia | |
| Psychiatric disorders | | Insomnia, anxiety, confusion | |
| Nervous System Disorders | Headache | Somnolence, tremor, dizziness, dysgeusia | |
| Cardiac disorders | | tachycardia, palpitations, bradycardia | |
| Vascular Disorders | Phlebitis | Hypotension, hypertension, flushing | Shock |
| Respiratory, Thoracic and | | Dyspnoea | |

| | | | |
|---|---|---|---|
| Mediastinal Disorders | | | |
| Gastrointestinal Disorders | Nausea, vomiting, diarrhoea, abdominal pain | Dyspepsia, constipation | |
| Hepatobiliary Disorders | Blood alkaline phosphatase increased, aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased (including hyperbilirubinaemia), liver function test abnormal | Hepatic failure (see section 4.4), gammaglutamyltransferase increased, jaundice, cholestasis, hepatomegaly, hepatitis | Hepatocellular damage including fatal cases (see section 4.4) |
| Skin and Subcutaneous Tissue Disorders | Rash | Urticaria, pruritus, erythema | Toxic skin eruption, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (see section 4.4) |
| Renal and Urinary Disorders | | Blood creatinine increased, blood urea increased, renal failure aggravated | Renal impairment (see section 4.4), acute renal failure |
| General Disorders | Pyrexia, rigors | Injection site thrombosis, infusion site inflammation, | |

| | | | |
|---|---|---|---|
| and Administration Site Conditions | | injection site pain, peripheral oedema | |
| Investigations | | Blood lactate dehydrogenase increased | |

**Description of selected adverse reactions:**

***Possible allergic-like symptoms:***

Symptoms such as rash and rigors have been reported in clinical studies. The majority were of mild to moderate intensity and not treatment limiting. Serious reactions (e.g. anaphylactoid reaction 0,2 %, 6/3028) were uncommonly reported during therapy with micafungin and only in patients with serious underlying conditions (e.g. advanced AIDS, malignancies) requiring multiple co-medications.

***Hepatic adverse reactions:***

The overall incidence of hepatic adverse reactions in the patients treated with micafungin in clinical studies was 8,6 % (260/3028). The majority of hepatic adverse reactions were mild and moderate. Most frequent reactions were increase in AP (2,7 %), AST (2,3 %), ALT (2,0 %), blood bilirubin (1,6 %) and liver function test abnormal (1,5 %). Few patients (1,1 %; 0,4 % serious) discontinued treatment due to a hepatic event. Cases of serious hepatic dysfunction occurred uncommonly (see section 4.4).

***Injection-site reactions:***

None of the injection-site adverse reactions were treatment limiting.

**Paediatric population:**

The incidence of some adverse reactions (listed in the table below) was higher in paediatric patients than in adult patients. Additionally, paediatric patients < 1 year of age experienced about two times more often an increase in ALT, AST and AP than older paediatric patients (see section 4.4). The most likely reason for these differences were different underlying conditions compared with adults or older paediatric patients observed in clinical studies. At the time of entering the study, the proportion of paediatric patients with

neutropenia was several-fold higher than in adult patients (40,2 % and 7,3 % of children and adults, respectively), as well as allogeneic HSCT (29,4 % and 13,4 %, respectively) and haematological malignancy (29,1 % and 8,7 %, respectively).

***Blood and lymphatic system disorders:***

*Frequent:* Thrombocytopenia

***Cardiac disorders:***

*Frequent:* Tachycardia

***Vascular disorders:***

*Frequent:* Hypertension, hypotension

***Hepatobiliary disorders:***

*Frequent:* Hyperbilirubinaemia, hepatomegaly

***Renal and urinary disorders:***

*Frequent:* Acute renal failure, blood urea increased

**Reporting of suspected adverse reactions:**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.
Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

## 4.9 Overdose

Repeated daily doses up to 8 mg/kg (maximum total dose 896 mg) in adult patients have been administered in clinical trials with no reported dose-limiting toxicity. One case of misdosage of 7,8 mg/kg/day for 7 days was reported in a newborn patient. No adverse reactions associated with this high dose were noted.

There is no experience with overdoses of micafungin as in MICAFUNGIN SANDOZ. In case of overdose, general supportive measures and symptomatic treatment should be administered. Micafungin is highly protein-bound and not dialysable.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

Category and class: A.20.2.2 Antimicrobial (chemotherapeutic agents): Fungicides

Pharmacotherapeutic group: Antimycotics for systemic use, other antimycotics for systemic use, ATC code: J02AX05

**Mode of action:**

Micafungin non-competitively inhibits the synthesis of 1,3-β-D-glucan, an essential component of the fungal cell wall. 1,3-β-D-glucan is not present in mammalian cells.

Micafungin exhibits fungicidal activity against most *Candida* species and prominently inhibits actively growing hyphae of *Aspergillus* species.

**PK/PD relationship:**

An additive or synergistic pharmacodynamic interaction of micafungin and amphotericin B was found in a mouse model of pulmonary aspergillosis (immunosuppression with hydrocortisone, intranasal infection with *Aspergillus fumigatus*).

**Mechanism(s) of resistance:**

As for all antimicrobial medicines, cases of reduced susceptibility and resistance have been reported and cross-resistance with other echinocandins cannot be excluded. Reduced susceptibility to echinocandins has been associated with mutations in the Fks1 and Fks2 genes coding for a major subunit of glucan synthase.

### 5.2. Pharmacokinetic properties

**Absorption:**

Pharmacokinetics are linear over the daily dose range of 12,5 mg to 200 mg and 3 mg/kg to 8 mg/kg. There is no evidence of systemic accumulation with repeated administration and steady-state is generally reached within 4 to 5 days.

**Distribution:**

Following intravenous administration concentrations of micafungin show a biexponential decline. Micafungin is rapidly distributed into tissues.

In systemic circulation, micafungin is highly bound to plasma protein (> 99 %), primarily to albumin. Binding to albumin is independent of micafungin concentration (10-100 µg/ml). The volume of distribution at steady state ($V_{ss}$) was approximately 18-19 litres.

**Biotransformation:**

Unchanged micafungin is the principal circulating compound in systemic circulation. Micafungin has been shown to be metabolised to several compounds; of these M-1 (catechol form), M-2 (methoxy form of M-1) and M-5 (hydroxylation at the side chain) of micafungin have been detected in systemic circulation. Exposure to these metabolites is low and metabolites do not contribute to the overall efficacy of micafungin.

Even though micafungin is a substrate for CYP3A *in vitro*, hydroxylation by CYP3A is not a major pathway for micafungin metabolism *in vivo*.

**Elimination and excretion:**

The mean terminal half-life is approximately 10 - 17 hours and stays consistent across doses up to 8 mg/kg and after single and repeated administration. Total clearance was 0,15 - 0,3 ml/min/kg in healthy subjects and adult patients and is independent of dose after single and repeated administration.

Following a single intravenous dose of 14C-micafungin (25 mg) to healthy volunteers, 11,6 % of the radioactivity was recovered in the urine and 71,0 % in the faeces over 28 days. These data indicate that

elimination of micafungin is primarily non-renal. In plasma, metabolites M-1 and M-2 were detected only at trace concentrations and metabolite M-5, the more abundant metabolite, accounted for a total of 6,5 % relative to parent compound.

**Special populations:**

***Elderly:***

When administered as a single 1-hour infusion of 50 mg the pharmacokinetics of micafungin in the elderly (aged 66-78 years) were similar to those in young (20-24 years) subjects. No dose adjustment is necessary for the elderly.

***Patients with hepatic impairment:***

In a study performed in patients with moderate hepatic impairment (Child-Pugh score 7-9), (n=8), the pharmacokinetics of micafungin did not significantly differ from those in healthy subjects (n=8). Therefore, no dose adjustment is necessary for patients with mild to moderate hepatic impairment. The pharmacokinetics of micafungin has not been studied in patients with severe hepatic insufficiency.

***Patients with renal impairment:***

Severe renal impairment (Glomerular Filtration Rate [GFR] < 30 ml/min) did not significantly affect the pharmacokinetics of micafungin. No dose adjustment is necessary for patients with renal impairment.

***Paediatric patients:***

In paediatric patients AUC values were dose proportional over the dose range of 0,5 - 4 mg/kg. Clearance was influenced by age, with mean values of clearance in younger children (2 - 11 years) being approximately 1,3-fold greater than those in older children (12 - 17 years). Older children had mean clearance values similar to those determined in adult patients. Mean clearance in premature infants (gestational age approximately 26 weeks) is approximately 5-fold greater than in adults.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Lactose monohydrate

Citric acid (to adjust the pH)

Sodium hydroxide (to adjust the pH)

**6.2. Incompatibilities**

This medicine must not be mixed or co-infused with other medicines or electrolytes except those mentioned in section 6.6.

**6.3. Shelf life**

**Unopened vial:**

50 mg – 36 months

100 mg – 30 months

**Reconstituted concentrate in vial:**

Chemical and physical in-use stability has been demonstrated for up to **24 hours** at 25 °C when reconstituted with sodium chloride 9 mg/ml (0,9 %) solution for infusion or dextrose 50 mg/ml (5 %) solution for infusion.

**Diluted infusion solution:**

Chemical and physical in-use stability has been demonstrated for **24 hours** at 25 °C when protected from light when diluted with sodium chloride 9 mg/ml (0,9 %) solution for infusion or dextrose 50 mg/ml (5 %) solution for infusion.

From a microbial point of view, **Micafungin 50mg & 100 mg Powder for concentrate for solution for infusion** contains no preservatives; the reconstituted and diluted solutions should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 ºC to 8 ºC.

**6.4. Special precautions for storage**

**Unopened vial:**

Store in the original package in order to protect from light. Product can withstand direct light exposure for up to 60 days (2 months).

For storage conditions after reconstitution and dilution of the medicine, see section 6.3.

### 6.5. Nature and contents of container

MICAFUNGIN 50 SANDOZ, Powder for concentrate for solution for infusion is packed in a 10 ml Type I glass vial wrapped with acrylate transparent UV-resistant protection film, closed with a grey isobutylene isoprene rubber stopper and sealed with an aluminium seal and blue plastic flip-off cap.

MICAFUNGIN 100 SANDOZ, Powder for concentrate for solution for infusion is packed in a 10 ml Type I glass vial wrapped with acrylate transparent UV-resistant protection film, closed with a grey isobutylene isoprene rubber stopper and sealed with an aluminium seal and red plastic flip-off cap.

Pack size of 1 vial.

### 6.6. Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

**Instructions for reconstitution and dilution:**

After reconstitution and dilution, the solution should be administered by intravenous infusion over approximately 1 hour. More rapid infusions may result in more frequent histamine mediated reactions.

MICAFUNGIN SANDOZ must not be mixed or co-infused with other medicines except those mentioned below. Using aseptic techniques at room temperature, MICAFUNGIN SANDOZ is reconstituted and diluted as follows:

1. The plastic cap must be removed from the vial and the stopper disinfected with alcohol.
2. Five ml of sodium chloride 9 mg/ml (0,9 %) solution for infusion or dextrose 50 mg/ml (5 %) solution for infusion (taken from a 100 ml bottle/bag) should be aseptically and slowly injected into each vial along the side of the inner wall. Although the concentrate will foam, every effort should be made to minimise

the amount of foam generated. A sufficient number of vials of MICAFUNGIN SANDOZ must be reconstituted to obtain the required dose in mg (see table below).

3. The vial should be rotated gently. DO NOT SHAKE. The powder will dissolve completely. The concentrate should be used immediately. The vial is for single use only. Therefore, unused reconstituted concentrate must be discarded immediately.
4. All of the reconstituted concentrate should be withdrawn from each vial and returned into the infusion bottle/bag from which it was originally taken. The diluted infusion solution should be used immediately. Chemical and physical in-use stability has been demonstrated for 24 hours at 25 °C when protected from light and diluted as described above.
5. The infusion bottle/bag should be gently inverted to disperse the diluted solution but NOT agitated in order to avoid foaming. The solution must not be used if it is cloudy or has precipitated.
6. The infusion bottle/bag containing the diluted infusion solution should be inserted into a closable opaque bag for protection from light.

Preparation of the solution for infusion

| **Dose (mg)** | **MICAFUNGIN SANDOZ vial to be used (mg/vial)** | **Volume of sodium chloride (0,9 %) or dextrose (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 100 + 1 x 50 | 5 ml | approx. 10 ml | 1,5 mg/ml |
| 200 | 2 x 100 | 5 ml | approx. 10 ml | 2,0 mg/ml |

After reconstitution and dilution, the solution should be administered by intravenous infusion over approximately 1 hour.

**7. HOLDER OF CERTIFICATE OF REGISTRATION**

Sandoz SA (Pty) Ltd[1]

Magwa Crescent West

Waterfall City, Jukskei View

Midrand

Gauteng

2090

## 8. REGISTRATION NUMBERS

MICAFUNGIN 50 SANDOZ: 55/20.2.2/0495

MICAFUNGIN 100 SANDOZ: 55/20.2.2/0496

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 June 2023

## 10. DATE OF REVISION OF THE TEXT

Not applicable.

[1]Company Reg. No.: 1990/001979/07