PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

Mycamine 50 mg powder for solution for infusion

Mycamine 100 mg powder for solution for infusion

COMPOSITION:

Mycamine 50 mg: Each vial contains 50 mg of micafungin (as sodium salt).

Mycamine 100 mg: Each vial contains 100 mg of micafungin (as sodium salt).

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

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

Excipients: lactose monohydrate, citric acid anhydrous, sodium hydroxide.

PHARMACOLOGICAL CLASSIFICATION:

A.20.2.2 Antimicrobial (chemotherapeutic agents): Fungicides

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties

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

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 gene coding for a major subunit of glucan synthase.

Inherently resistant organisms

Cryptococcus spp., *Pseudallescheria* spp., *Scedosporium* spp., *Fusarium* spp., *Trichosporon* spp., *Zygomycetes* spp.

Pharmacokinetic properties

Absorption

Pharmacokinetics is 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 bi-exponential 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 (Vss) was approximately 18-19 litres.

Metabolism

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 ^{14}C-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

Paediatric patients: In paediatric patients, micafungin exposure is dose proportional in the dose range of 0,5-4 mg/kg, and up to 10 mg/kg in infants less than 4 months of age. Clearance is influenced by weight with mean values of weight-adjusted clearance 1,35 times higher in the younger children (4 months to 5 years) and 1,14 times higher in children aged 6 to 11 years.

Older children (12-16 years) had mean clearance values similar to those determined in adult patients. Mean weight-adjusted clearance in infants less than 4 months of age is approximately 2,6-fold greater than older children (12-16 years) and 2,3-fold greater than in adults. Weight-adjusted clearance differences support weight-based dosing up to body weights within the range of 40 (treatment) to 50 kg (prophylaxis), above which adult dosing is recommended. Micafungin dosed at 4 mg/kg in infants less than 4 months approximates drug exposures achieved in adults receiving 100 mg/day for the treatment of invasive candidiasis. Higher doses (e.g., 10 mg/kg) may be required to treat CNS infection in infants less than 4 months of age as demonstrated by a PK-PD bridging study that showed dose-dependent penetration of micafungin into the CNS to achieve maximum eradication of fungal burden in the CNS tissues. Population PK modeling demonstrated that a dose of 10 mg/kg in infants less than 4 months of age would be sufficient to achieve the target exposure for the treatment of CNS *Candida* infections.
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. In a study performed in patients with severe hepatic impairment (Child-Pugh score 10-12) (n=8), lower plasma concentrations of micafungin and higher plasma concentrations of the hydroxide metabolite (M-5) were seen compared to healthy subjects (n=8). These data are insufficient to support a dosing recommendation in patients with severe hepatic impairment.

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.

INDICATIONS:

Mycamine 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.

Commonly susceptible species [MIC ranges in Europe, mg/L] in vitro

Candida albicans [0,007 – 0,25], *Candida glabrata* [0,007 – 0,12], *Candida tropicalis* [0,007 – 0,12], *Candida krusei* [0,015 – 0,12], *Candida kefyr* [0,03 – 0,06], *Candida parapsilosis* [0,12 – 2], *Candida guilliermondii* [0,5], *Candida lusitaniae* [0,12 – 0,25], *Candida* spp. [0,015 – 0,5] (incl. *C. famata, C. dubliniensis, C. lipolytica, C. pelliculosa, C. rugosa, C. stellatoidea* and *C. zeylanoides), Aspergillus fumigatus, Aspergillus flavus, Aspergillus niger, Aspergillus terreus, Aspergillus nidulans, Aspergillus versicolor*.

The mycelial form of dimorphic fungi (e.g. *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Coccidioides immitis*).

The decision to use Mycamine should take into account a potential risk for the development of liver tumours. Mycamine should therefore only be used if other antifungals are not appropriate (refer to WARNINGS).

CONTRA-INDICATIONS:

Hypersensitivity to the active substance, to other echinocandins or to any of the excipients.

Pregnancy and lactation (see HUMAN REPRODUCTION).

WARNINGS AND SPECIAL PRECAUTIONS:

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 relevance of this finding for the therapeutic use in patients cannot be excluded. Liver function should be carefully monitored during Mycamine 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. Mycamine 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.

Mycamine 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.

Anaphylactic reactions:

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

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 commonly reported during therapy with Mycamine and only in patients with serious underlying conditions (e.g. advanced AIDS, malignancies) requiring multiple co-medications.

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 Mycamine discontinued if lesions progress.

Haemolysis:

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

Renal effects:

Mycamine may cause kidney problems, renal failure, and abnormal renal function tests. Patients should be closely monitored for worsening of renal function.

Interactions with other medicines:

A total of 14 clinical interaction studies were conducted in healthy volunteers to evaluate the potential for interaction between micafungin and mycophenolate mofetil, ciclosporin, tacrolimus, prednisolone, sirolimus, nifedipine, fluconazole, ritonavir, rifampicin, amphotericin B, itraconazole and voriconazole. In these studies, no interaction that altered the pharmacokinetics of micafungin was observed. Exposure (AUC) of sirolimus was increased in the presence of micafungin (21 %). Patients receiving sirolimus in combination with micafungin should be monitored for sirolimus toxicity and the sirolimus dosage should be adjusted if necessary.

Paediatric population:

The incidence of some adverse reactions was higher in paediatric patients than in adult patients (refer to SIDE EFFECTS).

Lactose:

This medicine for intravenous use contains lactose. Patients with rare hereditary problems of galactose intolerance (e.g. galactosaemia), the Lapp lactase deficiency or glucose-galactose malabsorption should not take Mycamine.

HUMAN REPRODUCTION:

Mycamine must not be used during pregnancy and lactation. Mothers receiving Mycamine must not breastfeed their infants.

Effects on ability to drive and use machines:

Adverse reactions may occur, which may influence the ability to drive and use machines (see SIDE EFFECTS).

INTERACTIONS:

Interaction with other medicines

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

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 Mycamine was observed. No Mycamine dose adjustments are necessary when these medicines are administered concomitantly.

Exposure (AUC) of itraconazole, sirolimus and nifedipine was slightly increased in the presence of Mycamine (22 %, 21 % and 18 % respectively). Patients receiving sirolimus, nifedipine or itraconazole in combination with Mycamine should be monitored for sirolimus, nifedipine or itraconazole toxicity and the sirolimus, nifedipine or itraconazole dosage should be reduced if necessary (see Warnings and Special Precautions).

HUMAN REPRODUCTION:

Pregnancy

Mycamine is contraindicated in pregnancy and lactation (see CONTRAINDICATIONS).

In animal studies micafungin crossed the placental barrier and reproductive toxicity was seen.

Lactation

Mothers receiving Mycamine must not breastfeed their infants.

Fertility

Testicular toxicity was observed in animal studies. Mycamine may have the potential to affect male fertility in humans.

DOSAGE AND DIRECTIONS FOR USE:

Treatment with Mycamine 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 Mycamine depends on the body weight of the patient as given in the following tables:

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

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.

Use in children ≥ 4 months of age up to adolescents < 16 years of age

Indication		
	Body weight >40 kg	Body weight ≤40 kg
Treatment of invasive candidiasis	100 mg/day*	2 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 weighing ≤40 kg.

Use in children (including neonates) < 4 months

Indication	
Treatment of invasive candidiasis	4-10 mg/kg/day*
Prophylaxis of *Candida* infection	2 mg/kg/day

*Micafungin dosed at 4 mg/kg in children less than 4 months approximates drug exposures achieved in adults receiving 100 mg/day for the treatment of invasive candidiasis. If central nervous system (CNS) infection is suspected, a higher dosage (e.g. 10 mg/kg) should be used due to the dose-dependent penetration of micafungin into the CNS. The safety and efficacy in children (including neonates) less than 4 months of age of doses of 4 and 10 mg/kg for the treatment of invasive candidiasis with CNS involvement has not been adequately established in controlled clinical studies.

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, Mycamine should be administered for at least one week after resolution of clinical signs and symptoms.

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

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

Use in patients with hepatic impairment:
No dose adjustment is necessary in patients with mild or moderate hepatic impairment. There are currently insufficient data available for the use of Mycamine in patients with severe hepatic impairment and its use is not recommended in these patients (refer to WARNINGS AND SPECIAL PRECAUTIONS and SIDE EFFECTS).

Use in patients with renal impairment:
No dose adjustment is necessary in patients with renal impairment.

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.

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

1. The plastic cap must be removed from the vial and the stopper disinfected with alcohol.
2. 5 ml of sodium chloride 9 mg/ml (0,9 %) solution for infusion or glucose 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 Mycamine 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, please discard unused reconstituted concentrate 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 96 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. Do not use if the solution 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)	**Mycamine 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 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.

SIDE EFFECTS:

Overall 32,2 % of the patients experienced adverse drug reactions. The most frequently reported adverse reactions were nausea (2,8 %), blood alkaline phosphatase increased (2,7 %), phlebitis (2,5 %, primarily in HIV infected patients with peripheral lines), vomiting (2,5 %), and aspartate aminotransferase increased (2,3 %). No clinically significant differences were seen when the safety data were analysed by gender or race.

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	**Common** ≥1/100 to <1/10	**Uncommon** ≥1/1,000 to <1/100	**Rare** ≥1/10,000 to <1/1,000	**Not known** (frequency cannot be estimated from available data)
Blood and lymphatic system disorders	leukopenia, neutropenia, anaemia	pancytopenia, thrombocytopenia, eosinophilia, hypoalbuminaemia	haemolytic anaemia, haemolysis	disseminated intravascular coagulation
Immune system disorders		anaphylactic/anaphylactoid reaction, hypersensitivity		
Endocrine disorders		hyperhidrosis		
Metabolism and nutritional disorders	hypokalaemia, hypomagnesaemia hypocalcaemia	hyponatraemia, hyperkalaemia, hypophosphataemia, anorexia		
Psychiatric disorders		insomnia, anxiety, confusion		
Nervous system disorders	headache	somnolence, tremor, dizziness, dysgeusia		

System Organ Class	**Common** ≥1/100 to <1/10	**Uncommon** ≥1/1,000 to <1/100	**Rare** ≥1/10,000 to <1/1,000	**Not known** (frequency cannot be estimated from available data)
Cardiac disorders		tachycardia, palpitations, bradycardia		
Vascular disorders	phlebitis	hypotension, hypertension, flushing		shock
Respiratory, thoracic and mediastinal disorders		dyspnoea		
Gastrointesti-nal disorders	nausea, vomiting, diarrhoea, abdominal pain	dyspepsia, constipation		

System Organ Class	**Common** ≥1/100 to <1/10	**Uncommon** ≥1/1,000 to <1/100	**Rare** ≥1/10,000 to <1/1,000	**Not known** (frequency cannot be estimated from available data)
Hepatobiliary disorders	increased blood alkaline phosphatase, increased aspartate aminotransferase, increased alanine aminotransferase, increased blood bilirubin (including hyperbilirubinaemia), abnormal liver function test	hepatic failure, increased gammaglutamyl-transferase, jaundice, cholestasis, hepatomegaly, hepatitis		hepatocellular damage including fatal cases
Skin and subcutaneous tissue disorders	rash	urticaria, pruritus, erythema		toxic skin eruption, erythema multiforme, Stevens-Johnson syndrome,

System Organ Class	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000	Not known (frequency cannot be estimated from available data)
				toxic epidermal necrolysis
Renal and urinary disorders		increased blood creatinine, increased blood urea, aggravated renal failure		renal impairment, acute renal failure
General disorders and administration site conditions	pyrexia, rigors	injection site thrombosis, infusion site inflammation, injection site pain, peripheral oedema		
Investigations		increased blood lactate dehydrogenase		

Hepatic adverse reactions

The overall incidence of hepatic adverse reactions in the patients treated with Mycamine 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.

Paediatric patients

The incidence of some adverse reactions (listed 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. 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

Common: thrombocytopenia

Cardiac disorders

Common: tachycardia

Vascular disorders

Common: hypertension, hypotension

Hepatobiliary disorders

Common: hyperbilirubinaemia, hepatomegaly

Renal and urinary disorders

Common: acute renal failure, blood urea increased

KNOWN SYMPTOMS OF OVER DOSAGE AND PARTICULARS OF ITS TREATMENT:

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

IDENTIFICATION:

White mass powder for solution for infusion.

PRESENTATION:

Mycamine 50 mg: 10 ml Type I glass vial with an isobutylene-isoprene (Fluoro resin film laminated) grey rubber stopper and a blue flip-off cap. The vial is wrapped with a UV-protective film. Supplied in packs of 1 vial.

Mycamine 100 mg: 10 ml Type I glass vial with an isobutylene-isoprene (Fluoro resin film laminated) grey rubber stopper and a red flip-off cap. The vial is wrapped with a UV-protective film. Supplied in packs of 1 vial.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from light.

Store in original package.

KEEP OUT OF REACH OF CHILDREN.

Reconstituted concentrate in vial:

Chemical and physical in-use stability has been demonstrated for up to 48 hours at 25 °C when reconstituted with sodium chloride 9 mg/ml (0,9 %) solution for infusion or glucose 50 mg/ml (5 %) solution for infusion.

Diluted infusion solution:

Chemical and physical in-use stability has been demonstrated for 96 hours at 25 °C when protected from light when diluted with sodium chloride 9 mg/ml (0,9 %) solution for infusion or glucose 50 mg/ml (5 %) solution for infusion.

Mycamine contains no preservatives. From a microbiological point of view, 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 to 8 °C, unless the reconstitution and dilution have taken place in controlled and validated aseptic conditions.

REGISTRATION NUMBERS:

Mycamine 50 mg: 44/20.2.2/0639

Mycamine 100 mg: 44/20.2.2/0640

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Sandoz SA (Pty) Ltd

Magwa Crescent West

Waterfall City

Jukskei View

Midrand

2090

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