PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1. NAME OF THE MEDICINE

MYGIN™ 50, powder for solution for infusion

MYGIN™ 100, powder for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

MYGIN 50: Each vial contains 50 mg micafungin (as sodium).

MYGIN 100: Each vial contains 100 mg micafungin (as sodium).

Contains sugar (lactose monohydrate 200 mg/vial).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for infusion.

White lyophilised solid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MYGIN 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 – 2,0], *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 MYGIN should take into account a potential risk for the development of liver tumours (see section 4.4). MYGIN should therefore only be used if other antifungals are not appropriate.

Principles of antibiotics stewardship should be adhered to.

4.2 Posology and method of administration

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

Posology

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 MYGIN depends on the body mass of the patient as given in the following tables:

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

Indication	**Dose regimen**	
	Body mass > 40 kg	**Body mass ≤ 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	**Dose regimen**	
	Body mass > 40 kg	**Body mass ≤ 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 ≤ 40 kg.

Use in children (including neonates) < 4 months

Indication	**Dose regimen**
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 medicine 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 (see 5.2).

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

Prophylaxis of Candida infections: For prophylaxis of *Candida* infection, MYGIN should be administered for at least one week after neutrophil recovery. Experience with MYGIN in patients less than 2 years of age is limited.

Special populations

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 MYGIN in patients with severe hepatic impairment and its use is not recommended in these patients (see sections 4.4 and 4.8).

Renal impairment

No dose adjustment is necessary in patients with renal impairment (see section 5.2).

Paediatric population

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.

Method of administration

For intravenous use.

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.

For reconstitution instructions see section 6.6.

4.3 Contraindications

MYGIN is contraindicated in:

- Patients with hypersensitivity to micafungin, to other echinocandins or to any of the excipients listed in section 6.1.
- Pregnancy and breastfeeding (see section 4.6).

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 for the therapeutic use in patients cannot be excluded. Liver function should be carefully monitored during MYGIN 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. MYGIN 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, as in MYGIN, 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, as in MYGIN, anaphylactic/anaphylactoid reactions, including shock, may occur. If these reactions occur, micafungin 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) were reported during therapy with micafungin 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 MYGIN discontinued if lesions progress.

Haemolysis

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

Renal effects

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

Paediatric population

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

Excipients

Sodium

MYGIN contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicines and other forms of interaction

MYGIN 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, as in MYGIN, 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 MYGIN 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 as in MYGIN.

Co-administration of micafungin, as in MYGIN, 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.

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.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females:

The use of MYGIN in women of childbearing potential should only be given when appropriate contraceptive measures is taken.

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

Pregnancy

MYGIN is contraindicated in pregnancy (see section 4.3).

Breastfeeding

Mothers receiving MYGIN should not breastfeed their infants (see section 4.3).

Fertility

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

4.7 Effects on ability to drive and use machines

MYGIN may cause side effects, such as dizziness, which may affect the ability to drive and use machinery (see section 4.8). Caution is advised before driving a vehicle or operating machinery until the effects of MYGIN are known.

4.8 Undesirable effects

Summary of the safety profile

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.

Tabulated list of adverse reactions

Blood and the lymphatic system disorders	
Frequent:	leukopenia, neutropenia, anaemia
Less frequent:	pancytopenia, thrombocytopenia, eosinophilia, hypoalbuminaemia, haemolytic anaemia, haemolysis (see section 4.4)
Frequency unknown:	disseminated intravascular coagulation
Immune system disorders	
Less frequent:	anaphylactic/anaphylactoid reaction (see section 4.4), hypersensitivity
Frequency unknown:	anaphylactic and anaphylactoid shock (see section 4.4)
Endocrine disorders	
Less frequent:	hyperhidrosis
Metabolism and nutrition disorders	
Frequent:	hypokalaemia, hypomagnesaemia, hypocalcaemia
Less frequent:	hyponatraemia, hyperkalaemia, hypophosphataemia, anorexia
Psychiatric disorders	
Less frequent:	insomnia, anxiety, confusion
Nervous system disorders	
Frequent:	headache

Less frequent:	somnolence, tremor, dizziness, dysgeusia
Cardiac disorders	
Less frequent:	tachycardia, palpitations, bradycardia
Vascular disorders	
Frequent:	phlebitis
Less frequent:	hypotension, hypertension, flushing
Frequency unknown:	shock
Respiratory, thoracic and mediastinal disorders	
Less frequent:	dyspnoea
Gastrointestinal disorders	
Frequent:	nausea, vomiting, diarrhoea, abdominal pain
Less frequent:	dyspepsia, constipation
Hepatobiliary disorders	
Frequent:	increased blood alkaline phosphatase, increased aspartate aminotransferase, increased alanine aminotransferase, increased blood bilirubin (including hyperbilirubinaemia), abnormal liver function test
Less frequent:	hepatic failure (see section 4.4), increased gamma-glutamyl transferase, jaundice, cholestasis, hepatomegaly, hepatitis
Frequency unknown:	hepatocellular damage including fatal cases (see section 4.4)
Skin and subcutaneous tissue disorders	
Frequent:	rash
Less frequent:	urticaria, pruritus, erythema
Frequency unknown:	toxic skin eruption, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (see section 4.4)

Renal and urinary disorders	
Less frequent:	increased blood creatinine, increased blood urea, aggravated renal failure
Frequency unknown:	renal impairment (see section 4.4), acute renal failure
General disorders and administration site conditions	
Frequent:	pyrexia, rigors
Less frequent:	injection site thrombosis, infusion site inflammation, injection site pain, peripheral oedema
Investigations	
Less frequent:	increased blood lactate dehydrogenase

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) were less frequently reported during therapy with micafungin, as in MYGIN, and only in patients with serious underlying conditions (e.g., advanced AIDS, malignancies) requiring concomitant treatment with multiple medicines.

Hepatic adverse reactions

Reports have shown that the overall incidence of hepatic adverse reactions in the patients treated with micafungin in clinical studies was 8,6 %. The majority of hepatic adverse reactions were mild and moderate. Most frequent reactions were increase in AP, AST, ALT, blood bilirubin and abnormal liver function test. Few patients discontinued treatment due to a hepatic event. Cases of serious hepatic dysfunction occurred less frequently (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 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. It has been reported at the time of entering the study, that the proportion of paediatric patients with neutropenia was several-fold higher than in adult patients, as well as allogeneic HSCT and haematological malignancy.

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 MYGIN is important. It allows continued monitoring of the benefit/risk balance of MYGIN. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA's website.

4.9 Overdose

There is no experience with overdoses of MYGIN. In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8). General supportive measures and symptomatic treatment should be administered. MYGIN is highly protein bound and not dialysable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 20.2.2 Antimicrobial (chemotherapeutic agents), other than antibiotics: Fungicides.

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

Mechanism 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

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.

Inherently resistant organisms

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

5.2 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.

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 ^{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 medicine 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 modelling 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

Anhydrous citric acid (for pH adjustment)

Sodium hydroxide (for pH adjustment).

6.2 Incompatibilities

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

6.3 Shelf life

Unopened vial: 36 months.

Reconstituted concentrate in vial:

Chemical and physical in-use stability has been demonstrated for 48 hours when stored at or below 25 °C and 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 24 hours when stored at or below 25 °C when protected from light and diluted with sodium chloride 9 mg/ml (0,9 %) solution for infusion or glucose 50 mg/ml (5 %) solution for infusion.

MYGIN 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.

6.4 Special precautions for storage

Unopened vial: Store at or below 25 °C. Keep in the original carton in order to protect from light.

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

6.5 Nature and contents of container

MYGIN 50: 10 ml Type I clear glass vial sealed with a grey chlorobutyl rubber stopper, laminated with ethylene tetrafluorethylene (ETFE) and a blue flip-off cap.

MYGIN 100: 10 ml Type I clear glass vial sealed with a grey chlorobutyl rubber stopper, laminated with ethylene tetrafluorethylene (ETFE) and a red flip-off cap.

Each vial is packed in a small carton.

6.6 Special precautions for disposal and other handling

MYGIN, once reconstituted or diluted is a clear, colourless solution. The reconstituted or diluted solution is sterile, pyrogen-free and free of visible particles.

MYGIN must not be mixed or co-infused with other medicines except those mentioned below.

Using aseptic techniques at room temperature, MYGIN is reconstituted and diluted as follows:

1. The flip-off cap must be removed from the vial and the stopper disinfected with alcohol.
2. Five (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 MYGIN 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 96 hours at 25 °C and 24 hours at 2 - 8 °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 if it 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)	**MYGIN 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.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Abex Pharmaceutica (Pty) Ltd

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Moreleta Park 0181

South Africa

8. REGISTRATION NUMBERS

MYGIN 50: 59/20.2.2/0082

MYGIN 100: 59/20.2.2/0083

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

MYGIN 50: 03 February 2026

MYGIN 100: 03 February 2026

10. DATE OF REVISION OF THE TEXT

Not applicable.

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