# Micafungin
## Newborn use only

2023

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| **Alert** | Use in consultation with a paediatric infectious disease physician<br>Not recommended routinely as the first line therapy in neonates with disseminated candidiasis |
| **Indication** | Invasive neonatal candidiasis |
| **Action** | Selectively inhibits enzymes essential for fungal cell wall synthesis |
| **Drug type** | Echinocandin antifungal |
| **Trade name** | Mycamine |
| **Presentation** | Micafungin Sodium 50mg and 100mg vials |
| **Dose** | Invasive candidiasis where central nervous system and/or ocular infection is present or not excluded[1,2,3]<br>10mg/kg/day once a day<br><br>Invasive candidiasis without meningoencephalitis and/or ocular dissemination[1]<br>4mg/kg/day once a day |
| **Dose adjustment** | Therapeutic hypothermia: Limited data<br>ECMO: Supplemental dose not required[1,4,5]<br>Renal impairment: No dosage adjustment necessary[1,6]<br>Hepatic impairment: No dosage adjustment necessary in mild to moderate impairment.[1,7] |
| **Maximum dose** | 15mg/kg/day |
| **Total cumulative dose** | |
| **Route** | Intravenous |
| **Preparation** | Add 5 mL of 5% glucose or 0.9% sodium chloride to 50mg vial to make a concentration of 10 mg/mL.<br>Gently dissolve micafungin powder by swirling the vial to avoid shaking and excessive foaming.<br>**Further dilution**<br>**Peripheral intravenous venous cannula**<br>Draw up 5 mL (50mg of micafungin) of the above solution and add to 28 mL of 5% glucose or 0.9% sodium chloride to make a final concentration of 1.5mg/mL.<br>**Central venous catheter**<br>Draw up 5 mL (50mg of micafungin) of the above solution and add to 7.5 mL of 5% glucose or 0.9% sodium chloride to make a final concentration of 4mg/mL. |
| **Administration** | **IV infusion**: over 1 hour. Cover infusion bag/bottle with an opaque bag to protect from light.<br>More rapid infusions may result in a higher incidence of histamine-mediated reactions.<br>For final concentration greater than 1.5 mg/mL, a central catheter is preferred. |
| **Monitoring** | Serum electrolytes, liver and renal function.<br>Monitor IV site for signs of irritation/extravasation. |
| **Contraindications** | Hypersensitivity to micafungin, any components of the product or other echinocandins |
| **Precautions** | Haemolytic anaemia, thrombocytopenia, moderate to severe hepatopathy, and renal impairment |
| **Drug interactions** | Concurrent use may increase plasma levels of itraconazole, nifedipine, methotrexate, and sirolimus. |
| **Adverse reactions** | Hyponatremia, hypochloremia, hypokalemia, monocytosis, infusion site phlebitis, fever, rash and transient elevation of hepatic enzymes, diarrhoea, vomiting, elevated creatinine levels, anaemia, and thrombocytopenia.<br>Infusion reactions and anaphylaxis have been reported. |
| **Compatibility** | **Fluids**<br>Sodium chloride 0.9%, 5% glucose, Ringer lactate, and lipid emulsion. Refer to Micromedex for amino acid compatibility.<br>**Y-site**<br>Aminophylline, calcium chloride, calcium gluconate, dopamine hydrochloride, esmolol, furosemide, heparin, lidocaine, lorazepam, magnesium sulfate, milrinone lactate, glyceryl trinitrate, noradrenaline bitartrate, potassium chloride, sodium nitroprusside, sodium phosphate, tacrolimus, and vasopressin |
| **Incompatibility** | **Fluids**: no information<br>Adrenaline, albumin, amiodarone, dobutamine, insulin, labetalol, midazolam hydrochloride, morphine sulfate, octreotide acetate, phenytoin sodium, rocuronium bromide, and vecuronium bromide |
| **Stability** | Infusion solution is stable for 24 hours below 25°C or at 2 to 8°C. Protect from light.[24] |
| **Storage** | Unopened vial: store below 25°C.[25]<br>Reconstituted solution in vial: can be stored for up to 24hours below 25°C, protected from light.[25] |

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| | Protect from light. |
| **Excipients** | Lactose, citric acid, and sodium hydroxide. |
| **Special comments** | May cause fever, and injection-site pain and inflammation. Anaphylactic reactions have been reported. |
| **Evidence** | **Efficacy**<br>Invasive candidiasis is reported in 1.5% to 9% very low birth weight neonates.[8,9] It is associated with high mortality (20-40%) and neurodevelopmental disability (50-60%) in survivors.[10]<br>**Treatment of candida infection**<br>In one RCT of 98 children which included 7 neonates, micafungin was administered for a median duration of 14 days to treat acute candidaemia. The treatment was commenced at a daily dose of 2mg/kg/day and increased to 4mg/kg/day if clinical signs of candidaemia or positive blood culture persisted for 5 days or more. In this trial the rate of overall treatment success for micafungin (73%) was comparable with liposomal amphotericin-B (76%). During the entire study including the 12-week follow-up, the mortality rates were 25% and 24% for the micafungin and amphotericin-B group respectively. 4% of participants from the micafungin group and 16% from the liposomal amphotericin-B group had treatment discontinued due to adverse events.[11] In another RCT, 20 infants aged < 4 months received 10mg/kg/day micafungin for a mean duration of 18 days for proven invasive candida infection.[12] Candida albicans (41%) and Candida parapsilosis (34%) were the most commonly isolated organisms. A complete clinical response and fungal free survival at 1 week after completion of the treatment was achieved in 60% participants. 25% of participants were alive after 1 week of treatment but were not free of fungal infection. Authors reported recurrence of infection in about 10-15% patient receiving micafungin.[11,12] Auriti et al used micafungin at a dose of 8-15mg/kg/day in a cohort of 18 infants with invasive candida infection including meningitis. The mean gestational age of the infants at birth was 35 weeks and the mean postnatal age was 9 weeks at treatment. Candida was isolated from blood in 10, urine in 6, and CSF in 2 participants. The mean duration of treatment for C. Albicans (n=9) and C. Parapsilosis (n=7) was 19 days. The overall survival with clinical resolution of infection was 78%. In this study 20% of the surviving infants developed neurological impairment.[13]<br>**Prophylaxis for fungal infection**<br>When co-administered with enteral miconazole, micafungin at a dose of 3mg/kg/day intravenously was more effective than fluconazole in prevention of fungal infection (71 vs 39% success) in extremely preterm infants.[14,15] In a cohort study primarily designed to study the pharmacokinetics of prophylactic dose, 25 very low birthweight who received intravenous micafungin at a dose of 1mg/kg/day for a mean duration of 13 days did not develop fungal infection.[18]<br>**ANMF consensus:** Prophylaxis with micafungin should only be given in consultation with a paediatric ID specialist, in situations where prophylaxis is indicated and neither nystatin nor fluconazole are feasible/appropriate.<br>**Safety**<br>Although results from several trials of micafungin in infants have shown the drug to be generally well tolerated, these trials are small. Studies have reported reversible haemolytic anaemia in as high as 30-40% of the recipients. Moderate elevation of serum creatinine, 2-3 times higher levels of hepatic transaminases and disturbances in serum electrolytes have also been reported in up to 20-40% participants. Thrombocytopenia has been described in about 10% patients receiving micafungin. [12,16]<br>**Pharmacokinetics**<br>Several studies have assessed the pharmacokinetics of micafungin in neonates.[1,12,17-22] Micafungin displays linear pharmacokinetics with minimal systemic accumulation after repeated administration. A steady state is reached within 4 days with once daily dosing regimen. Its volume of distribution (0.39–0.76L/kg) in premature neonates is comparable to adults. In neonates, 96.7% micafungin is bound to albumin and its elimination half-life is (5.5–11 hours) shorter than adults. Total body clearance of micafungin is faster in neonates compared to children and adults. Micafungin concentrates the highest in the lungs, liver, spleen, and kidneys. It is metabolized primarily by the liver into various metabolites and excreted in bile. Faecal excretion is the major route of elimination and < 1% of micafungin is excreted unchanged in the urine. Micafungin has poor oral bioavailability.<br>Hope et al pooled the pharmacokinetic data on micafungin for suspected or proven invasive candida infection on 47 infants aged < 4 months across three trials.[2,12,17,19] In these trials micafungin was administered at a dose ranging from 0.75 to 15mg/kg/day. The proportion of the patients receiving 8, 10, and 12mg/kg/day with an AUC less than the target (166.5mg x h/L) was 29.3%, 17.4%, and 10.5%, |

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| | respectively. A dosage of 10mg/kg/day resulted in 82.6% of patients with AUCs that are associated with near-maximal decline in fungal burden within the central nervous system. The AUCs also suggested that at 15mg/kg/day micafungin in preterm neonates provided a similar systemic exposure to a dose of approximately 5mg/kg in adults. Based on Monte Carlo simulations of 81 concentrations, Leroux et al showed attainment of the $AUC_{0-24}$ target of 166.5mg x h/L in 100% neonates when micafungin was administered at a dose of 10mg/kg/day with or without a 15mg/kg loading dose.[23] |
| **Practice points** | |
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