Amphotericin B – Conventional

Newborn Use Only

2017

Alert	The Antimicrobial Stewardship Team has listed this drug under the following category: Restricted. Amphotericin B is available in 4 forms: **Amphotericin B-conventional, Amphotericin B-liposomal,** Amphotericin B (phospho)lipid complex and Amphotericin B colloidal dispersion (also known as Amphotericin B Cholesteryl Sulfate Complex). Amphotericin B – Conventional is also called Amphotericin B deoxycholate. The current TGA approved name is amphotericin B (amphotericin). Confusion among these products has led to fatal overdose as well as sub-therapeutic dosing.[1] Clinicians should liaise with local ID specialists when treating systemic fungal infections. Amphotericin B – Conventional is only available via Special Access Scheme (SAS) in Australia.
Indication	Treatment of invasive fungal infections by susceptible fungi including *Candida spp.*, *Aspergillus spp.* and *Cryptococcus* species.[2,17] *Candida lusitaniae* and *A. terreus* are resistant.
Action	Fungicidal agent which works by binding with a cytoplasmic membrane ergosterol on the organism's surface, causing cell death by increasing cell membrane permeability.[3]
Drug Type	Polyene antifungal.
Trade Name	Fungizone.
Presentation	Vial contains 50 mg of amphotericin B.[4] It also contains sodium deoxycholate and sodium phosphate.
Dosage/Interval	0.5–1 mg/kg/dose **daily**.[5] 0.5–0.7 mg/kg/dose daily is recommended for *Candida* urinary tract infections including renal tract fungal balls.[5] 1 mg/kg/dose daily is recommended for *Aspergillus* systemic infection.[9] Liaise with ID specialists for further dose adjustments.
Route	Intravenous
Maximum Daily Dose	1 mg/kg/day.[5]
Preparation/Dilution	1. Reconstitute the 50 mg vial with 10 mL water for injection to make a concentration of 5 mg/mL. Shake the vial immediately until the solution is clear. Dilute 1 mL of the reconstituted solution with 49 mL of 5% glucose to make a concentration of 0.1 mg/mL.[4] 2. For fluid restricted patients: Reconstitute the 50 mg vial with 10 mL water for injection to make a concentration of 5 mg/mL. Shake the vial immediately until the solution is clear. Dilute 1 mL of the reconstituted solution with 11.5 mL of 5% glucose to make a concentration of 0.4 mg/mL.
Administration	IV infusion over 2–6 hours.[4] **IV line must be flushed with 5% glucose before and after the dose.** Do not infuse concentrations greater than 0.1 mg/mL through a peripheral line. Use a central venous catheter for 0.4 mg/mL concentration.[4]
Monitoring	Urine output. Full blood count (FBC) for anaemia and thrombocytopenia. Renal function (for elevated creatinine), electrolytes (for hypokalaemia) and liver function (for derangements of liver enzymes). Monitor serum concentrations of concomitant nephrotoxic drugs.
Contraindications	Hypersensitivity to amphotericin B.
Precautions	Amphotericin B (conventional) has variable pharmacokinetics in neonates and this may lead to unexpected treatment failure or toxicity. Administer under close clinical supervision during the initial dosing. Anaphylaxis and respiratory distress have been reported in adults (though not in neonates). Renal impairment: Risk of nephrotoxicity. Concomitant use of corticosteroids and corticotropin (ACTH) should be avoided.[16]
Drug Interactions	Increased risk of nephrotoxicity if used concurrently with other nephrotoxic drugs e.g. aminoglycosides, vancomycin. Monitor renal function and relevant drug concentrations closely. Amphotericin B may enhance the toxicity of flucytosine by increasing its cellular uptake and impeding its renal excretion.[17] Corticosteroids and diuretics: May enhance the hypokalaemic effect of amphotericin B.
Adverse Reactions	Electrolyte derangements: Hypokalaemia, hypomagnesaemia, hyperkalaemia, hypocalcaemia. Renal: Elevated urea and creatinine, nephrogenic diabetes insipidus.

	Haematological: Anaemia**,** leucopenia, thrombocytopenia. Thrombophlebitis at the injection site. Gastrointestinal: Diarrhoea, vomiting, elevated liver enzymes. Infusion-related reactions: Fever, hypotension (rare in neonates). Skin rashes. Tachyarrhythmias, hypotension, hypertension and respiratory distress have been reported in adults.
Compatibility	Fluids: Glucose 5%. Y site: Zidovudine.
Incompatibility	**Fluids:** Sodium chloride 0.9%, Amino acid/glucose solution, lipid emulsion. **Y Site:** Not compatible with any medications commonly used in newborns. **Do not mix with any medications.**
Stability	Vial: Store at 2–8°C. Protect from light. Reconstituted solution: Stable for 24 hours below 25°C and for 1 week at 2–8°C. Do not use the reconstituted solution or infusion if cloudy or a precipitate is present. **Protect from light.** Diluted solution: Stable for 24 hours at 25°C. **Protect from light.** There is no need to protect from light during the infusion.
Storage	As above
Special Comments	The minimum infusion duration is 2 hours.[4] The osmolality of amphotericin B – conventional at a concentration of 0.1 mg/mL has been reported as 265–314.8 mOsm/kg.[18,19] If infusion-related, immediate reactions occur (e.g. fever, hypotension), duration of infusion may be increased to 6 hours. If total parenteral nutrition (TPN) or IV fluids are turned off during the infusion, consider monitoring of blood glucose. **If amphotericin B – conventional is used for *Candida* urinary tract infection including instances of renal tract fungal balls, a dose of 0.5–0.7 mg/kg/dose daily is suggested.[5] However, fluconazole may be a preferred agent in susceptible *Candida* urinary tract infections due to favourable pharmacokinetics and fewer side effects.[8]** Although amphotericin B formulations are known to cause nephrotoxicity and may cause hepatotoxicity, reducing the dose in these disease states is not currently recommended.[21] If nephrotoxicity or hepatotoxicity is a significant concern, consider other antifungals.
Evidence summary	Refer to full version.
References	Refer to full version.

Original version Date: 17/07/2017	**Author: NMF Consensus Group**
Current Version number: 1.0	**Version Date:** 17/07/2017
Risk Rating: Medium	**Due for Review:** 17/07/2020
Approval by: As per Local policy	**Approval Date:**