Amphotericin B – Conventional
Newborn Use Only

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. It also contains sodium deoxycholate and sodium phosphate.

Dosage/Interval
0.5–1 mg/kg/dose daily.3
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.3

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.
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<th>Adverse Reactions</th>
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<th>Compatibility</th>
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<td>Fluids: Glucose 5%. Y site: Zidovudine.</td>
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<td>Fluids: Sodium chloride 0.9%, Amino acid/glucose solution, lipid emulsion. Y Site: Not compatible with any medications commonly used in newborns. <strong>Do not mix with any medications.</strong></td>
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<td>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. <strong>Protect from light.</strong> Diluted solution: Stable for 24 hours at 25°C. <strong>Protect from light.</strong> There is no need to protect from light during the infusion.</td>
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<th>Storage</th>
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<th>Special Comments</th>
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<td>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. <strong>If amphotericin B – conventional is used for <em>Candida</em> urinary tract infection including instances of renal tract fungal balls, a dose of 0.5–0.7 mg/kg/dose daily is suggested.</strong>(^5) However, fluconazole may be a preferred agent in susceptible <em>Candida</em> 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.</td>
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**Approved by: JHCH CQ&PCC**

**Author: NMF Consensus Group**

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