

Amphotericin B - Liposomal

Newborn use only

2020

Alert	Antimicrobial Stewardship Team has listed this drug as Restricted. Clinicians should liaise with local ID specialists when treating systemic fungal infections. 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. Confusion between these products has led to fatal overdose as well as subtherapeutic dosing.¹
Indication	Treatment of invasive fungal infections by susceptible fungi including <i>Candida spp.</i> , <i>Aspergillus spp.</i> and <i>Cryptococcus species</i> . ^{2,3} <i>Candida lusitanae</i> and <i>A. terreus</i> 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. ⁴
Drug type	Polyene antifungal
Trade name	<u>AmBisome (amphotericin B) liposome for injection</u>
Presentation	Amphotericin BP equivalent to 50 mg of amphotericin B vial. ⁵ Premade syringe by local pharmacy
Dose	3 mg/kg/dose daily. ⁶
Dose adjustment	To be updated.
Maximum dose	7 mg/kg/day. ⁷
Total cumulative dose	
Route	IV
Preparation	Add 12 mL of water for injection to 50 mg vial to make a 4 mg/mL solution. Shake vigorously for at least 30 seconds to disperse completely. FURTHER DILUTE Use the 5 micrometre filter supplied, draw up 4 mL (16 mg of amphotericin B liposomal) of the above solution and add 12 mL of glucose 5% to make a final volume of 16mL with a final concentration of 1mg/mL. ^{3,5}
Administration	IV line must be flushed with 5% glucose before and after the dose. IV infusion over 60 minutes. ³ In-line filters must have a port diameter of at least 1 micrometre. Do not mix with any medications.
Monitoring	Urine output. Full blood count for anaemia and thrombocytopenia Renal function electrolytes for hypokalaemia Liver function. Serum concentrations of concomitant nephrotoxic drugs.
Contraindications	Known hypersensitivity to amphotericin B.
Precautions	Administer under close clinical supervision during the initial dosing. Anaphylaxis and respiratory distress have been reported in adults (though not in neonates).
Drug interactions	Increased risk of nephrotoxicity if used concurrently with other nephrotoxic drugs (even though the liposomal preparation is safer than conventional amphotericin B in this regard) e.g. aminoglycosides, vancomycin. Monitor renal function and relevant drug concentrations closely. Adequate clinical studies of the use of the combination of flucytosine with AmBisome have not been conducted. Whilst synergy between flucytosine and amphotericin has been reported, amphotericin B may enhance the toxicity of flucytosine by increasing its cellular uptake and impeding its renal excretion. ³ 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%.

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	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	Reconstituted and diluted solution stable for up to 24 hours at 2–8 °C.
Storage	Vial: Store below 25 °C. Do not freeze. Reconstituted solution: Stable for 24 hours at 2–8°C. Discard unused portion after 24 hours. Do not use the reconstituted solution or infusion if cloudy or a precipitate is present. Protect from light.
Excipients	No information
Special comments	If infusion-related immediate reactions occur (e.g. fever, hypotension), duration of infusion may be increased to 3–4 hours. Amphotericin B Liposomal is considered to be at a lower risk of causing harm if extravasated (as compared to amphotericin B – conventional). ¹⁷ If total parenteral nutrition (TPN) or IV fluids are turned off during the infusion, consider monitoring of blood glucose level. Cerebrospinal fluid (CSF) penetration of lipid formulations of amphotericin B is poor. ^{8,9} Therefore, in cases of fungal meningitis, additional antifungal therapy is required. Even though a neonatal pharmacokinetic study ⁸ using amphotericin B - lipid complex showed substantial drug concentration in urine, a recent review ² suggests that the liposomal preparation of amphotericin B is a poor candidate for the treatment of neonatal candiduria as it has lesser renal tissue penetration. This reduced penetration is considered to be responsible for its reduced nephrotoxicity as compared to conventional amphotericin B. Although amphotericin B formulations are known to cause nephrotoxicity and may cause hepatotoxicity, reducing the dose in these disease states is not currently recommended. ¹⁹ If nephrotoxicity or hepatotoxicity is a significant concern, consider other antifungals.
Evidence	Refer to full version.
Practice points	Refer to full version.
References	Refer to full version.

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