### 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). Confusion between these products has led to fatal overdose as well as subtherapeutic dosing. Clinicians should liaise with local ID specialists when treating systemic fungal infections.

### Indication

Treatment of invasive fungal infections by susceptible fungi including **Candida spp.**, **Aspergillus spp.** and **Cryptococcus species.** \(^1\,2\,3\)**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.\(^4\)

### Drug Type

Polyene antifungal

### Trade Name

AmBisome

### Presentation

Vial contains amphotericin BP equivalent to 50 mg of amphotericin B.\(^5\)

### Dosage/Interval

3 mg/kg/dose daily.\(^6\)

### Route

Intravenous (IV)

### Maximum Daily Dose

7 mg/kg/day.\(^7\)

### Preparation/Dilution

Add 12 mL of water for injection to the 50 mg vial for reconstitution to make a concentration of 4 mg/mL. Shake the vial vigorously for at least 30 seconds to disperse completely. Use the 5 micrometre filter supplied to add 4 mL of this solution (= 16 mg) to 4 mL of 5% glucose to make a final volume of 8 mL with a concentration of 2 mg/mL solution.\(^3,5\)

### Administration

IV infusion over 60 minutes.\(^3 IV line must be flushed with 5% glucose before and after the dose.** 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 (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

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%.
- 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.** |
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<tr>
<td>Stability</td>
<td>Reconstituted and diluted solution: Stable for up to 24 hours at 2–8 degrees Celsius.</td>
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| Storage         | Vial: Store below 25 degrees Celsius. 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. |
| Special Comments| If infusion-related immediate reactions occur (e.g. fever, hypotension), duration of infusion may be increased to 3–4 hours.  
Liposomal amphotericin B 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.  
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\(^9\) 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 summary
- Refer to full version.

References
- Refer to full version.

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