### 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. *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.

### Drug Type
Polyene antifungal

### Trade Name
AmBisome

### Presentation
Vial contains amphotericin BP equivalent to 50 mg of amphotericin B.

### Dosage/Interval
3 mg/kg/dose daily.

### Route
Intravenous (IV)

### Maximum Daily Dose
7 mg/kg/day.

### 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, take 4 mL (=16 mg) of the diluted drug and make up to a final volume of 8 mL using glucose 5% with a final concentration of 2 mg/mL solution.

### Administration
IV infusion over 60 minutes. 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. Corticosteroids and diuretics: May enhance the hypokalaemic effect of amphotericin B.

### Adverse Reactions

### 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

Reconstituted and diluted solution: Stable for up to 24 hours at 2–8 degrees Celsius.

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\(^8\) 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 summary

Refer to full version.

References

Refer to full version.