Liposomal amphotericin B (AmBisome®) Monograph - Paediatric

Scope (Staff): Medical, Nursing, Pharmacy
Scope (Area): Perth Children’s Hospital (PCH)

This document should be read in conjunction with this DISCLAIMER

DESCRIPTION

- Liposomal amphotericin B (AmBisome®) is a polyene antifungal. It binds irreversibly to ergosterol in the fungal cell membrane resulting in fungal cell death by altering the permeability and allowing leakage of the intracellular contents.\(^{(1, 2)}\)
- Liposomal amphotericin B (AmBisome®) is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

- **AmBisome®** is indicated in the treatment of severe systemic or deep mycoses and suspected or proven infection in febrile neutropenic patients unresponsive to broad spectrum antibacterials.\(^{(2)}\)
- **AmBisome®** is also used for prophylaxis in patients at high risk of mould infections who are intolerant to micafungin prophylaxis.\(^{(2)}\)

**IV: Monitored (orange) antifungal**

- If the use is consistent with a standard approved indication, this must be communicated to ChAMP by documenting that indication on all prescriptions (inpatient and outpatient).
- The ChAMP team will review if ongoing therapy is required and/or if the order does not meet ChAMP Standard Indications.
- If use is not for a standard approved indication, phone approval must be obtained from ChAMP before prescribing.

**Inhalation: Restricted (red) antifungal**

- Refer to the **inhaled amphotericin B monograph**

CONTRAINdications

- Liposomal amphotericin B (AmBisome®) is contraindicated in patients with a history of hypersensitivity reactions with any formulation of amphotericin B.\(^{(3-5)}\)
- Liposomal amphotericin B (AmBisome®) is INCOMPATIBLE with sodium chloride 0.9% - IV lines should be flushed with glucose 5% prior to administration.\(^{(6)}\)
## PRECAUTIONS

Different preparations of intravenous amphotericin are available and vary in their pharmacodynamics, pharmacokinetics, dosage and administration. They are **NOT** considered interchangeable. To avoid confusion, they should be prescribed by trade name.\(^3\)

- Maintain adequate hydration throughout treatment to reduce the risk of nephrotoxicity.\(^3,7\)
- Electrolyte abnormalities may occur during treatment. Regular monitoring is required and supplements given as necessary.\(^1,3\)

## FORMULATIONS

**Available at PCH:**
- Liposomal amphotericin B 50mg powder for injection vial (AmBisome®)

**Other formulations available:**
- Nil

## DOSAGE

- The doses listed below fall within the standard range. Higher doses may be prescribed for certain situations in consultation with an infectious diseases or clinical microbiology consultant.

### Neonates (<1month):
- Please refer to neonatal clinical care drug protocols

### IV:

- **Treatment of Aspergillus infection (suspected or confirmed) including prolonged febrile neutropenia:**
  - 3mg/kg/dose given once daily.\(^1,8,9\)

- **Treatment of Mucormycosis:**
  - 5mg/kg/dose given once daily. May be increased to a maximum of 10mg/kg once daily only on advice from an infectious diseases or clinical microbiology consultant.\(^8\)

- **Mould prophylaxis:**
  - 1mg/kg/dose given either 3 times per week or once daily.\(^10\)

### Inhalation:
- Please refer to separate inhaled amphotericin B monograph

## DOSAGE ADJUSTMENT

- No dosage adjustments required for impaired hepatic function or impaired renal function. However use of AmBisome\(^®\) with other nephrotoxic agents may increase the risk of renal impairment.\(^1-3,9\)

## RECONSTITUTION

- Reconstitute each vial with 12mL of water for injection to obtain a concentration of 4mg/mL (assumes a 0.5mL displacement volume for the powder).\(^6\)
- Shake the vial for 30 seconds to ensure the powder has dissolved.\(^6\)
### ADMINISTRATION
**IV infusion:**
- Withdraw the required dose and using a 5 micrometre filter (supplied) add the solution to glucose 5% to produce a final concentration between 0.2 mg/mL and 2 mg/mL.\(^{[5, 6, 9]}\)
- Dilute with glucose 5% to a final concentration between 0.2 mg/mL and 2 mg/mL and infuse over 2 hours.
- If no adverse effects are seen, subsequent infusions may be administered over 1 hour, provided that there has not been more than 1 week since the last tolerated infusion.\(^{[5, 6, 9]}\)
- If doses infused over 1 hour are tolerated, then infusion may be given over 30 minutes if necessary provided there has not been more than 1 week since the last rapid infusion.\(^{[6]}\)

### MONITORING
- Renal, hepatic, haematological function and electrolyte (including magnesium, potassium and sodium) levels should be monitored at least weekly throughout therapy and until stable after treatment is ceased.\(^{[3, 7, 9]}\) Increased serum creatinine, hypokalaemia and hypomagnesaemia are frequent; anuria or oliguria may occur; correct electrolyte losses.\(^{[1]}\)
- Monitoring for infusion related reactions should occur especially during the first dose.
- Paracetamol and/or an antihistamine or a slowing of the infusion rate may be required.\(^{[1, 4]}\)

### ADVERSE EFFECTS
**Common:**
Infusion related reactions (including fever, chills, hypotension, anorexia, nausea, vomiting, headache, malaise, muscle and joint pain – usually lessen with continued treatment and with a slowing of the infusion rate), thrombophlebitis, anaemia, nephrotoxicity, hypoxia, hyperglycaemia, abdominal pain, altered liver function tests, tachycardia and electrolyte abnormalities (hypokalaemia, hyponatraemia, hypomagnesaemia).\(^{[1, 9]}\)

**Rare:**
anaphylactoid reactions, GI bleeding, hepatotoxicity, hyperkalaemia, hypertension, arrhythmias, blood dyscrasias, rash (including Stevens-Johnson syndrome and toxic epidermal necrolysis) and neurologic effects.\(^{[1, 9]}\)

### COMPATIBLE FLUIDS
- Glucose 5%\(^{[6]}\)
- AmBisome\(^\circledR\) is INCOMPATIBLE with sodium chloride 0.9% - IV lines should be flushed with glucose 5% prior to administration.\(^{[6, 7]}\)

### STORAGE
- 50 mg powder for injection vial should be stored below 25°C
- Products prepared by PCS should be stored between 2 and 8°C.\(^{[6]}\)
### INTERACTIONS

- Liposomal amphotericin B (AmBisome®) may interact with other medications; please consult PCH approved references (e.g. Clinical Pharmacology), your ward pharmacist or Pharmacy on extension 63546 for more information.

- There is an increased risk of nephrotoxicity when AmBisome® is used in conjunction with other nephrotoxic agents (e.g. aminoglycosides, loop diuretics, vancomycin, ciclosporin and tacrolimus).(1, 9, 11)

- The use of AmBisome® and azole antifungals may have an antagonistic effect. The combination should be avoided unless on the advice of infectious diseases or clinical microbiology.(1, 9)

- Any hypokalaemia caused by AmBisome® may increase the toxicity of cardiac glycosides (e.g. digoxin).(9)

- Corticosteroids may increase the risk of hypokalaemia when used in conjunction with AmBisome®.(9)

- AmBisome® given concurrently with leucocyte transfusions may result in acute pulmonary toxicity. Infusions should be separated for as long as possible and patients pulmonary function monitored.(11)

### COMMENTS

- Each 50mg vial of liposomal amphotericin B contains 900mg of sucrose(11)

### MANUFACTURER SAFETY DATA SHEET (SDS)

- To access to the Manufacturer SDS for this product, use the following link to ChemAlert.

**Please note: The information contained in this guideline is to assist with the preparation and administration of liposomal amphotericin B (AmBisome®). Any variations to the doses recommended should be clarified with the prescriber prior to administration**

### Related internal policies, procedures and guidelines

- Antimicrobial Stewardship Policy (Medication Management Manual)
- ChAMP Empiric Guidelines (ChAMP Manual)
References


This document can be made available in alternative formats on request for a person with a disability.