BRIEF ADMINISTRATION GUIDE

(For more detailed guideline information please see the following pages)

Indications: Severe systemic and central nervous system fungal infection

Route: Intravenous

Dose: Initially 0.25 - 0.5 mg/kg once daily, increased to 0.5 - 1 mg/kg once daily

Maximum dose must not exceed 1.5 mg/kg daily

Supplied as: Amphotericin B, 50 mg vial, powder for reconstitution.

Amphotericin is available in two forms in New Zealand, amphotericin B liposomal and conventional amphotericin B[1]. Lipid based and conventional amphotericin formulations are not interchangeable and have different dosing recommendations[2,3]. Medication errors have occurred with incorrect selection of amphotericin products and have resulted in fatal overdoses, and sub-therapeutic dosing[2,3]. Please ensure you have selected the correct product and are using the correct guideline.

Refer to drug guideline 2901 for amphotericin B liposomal.

Preparation and administration:

Intravenous Infusion[4-7]

- 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 0.1 mg/ml solution.
- **Do not administer medication though the NICU clear fluid filter** – at 0.2 micron this filter is very fine and will filter out the active drug.
- Visually inspect for particulate matter, do not administer if present.
- Draw up prescriber dose and administer by intravenous infusion over 2 to 6 hours.
- Any remaining solution should be discarded.

Note: Amphotericin B is **incompatible with sodium chloride 0.9%**

Monitoring:

- Ensure adequate hydration and consider sodium repletion to prevent or reduce the risk of nephrotoxicity.[3,5]
- Monitor renal function, liver function, full blood count, potassium, magnesium at baseline and at least every other day during treatment.[2,5]
- Monitor fluid balance.[2]
- Blood pressure, heart rate, respiratory rate and temperature periodically during treatment.[2,3]
- Monitor IV site for irritation, or phlebitis.[2,5]
- Assess for signs of anaphylaxis or adverse reactions.[2,6]

1. Purpose and scope

To facilitate the safe and effective use of amphotericin (conventional) in the Neonatal Intensive Care Unit (NICU).

Note:
Amphotericin is available in two forms in New Zealand, amphotericin B liposomal and conventional amphotericin B.[1] Lipid based and conventional amphotericin formulations are not interchangeable and have different dosing recommendations.[2,3] Medication errors have occurred with incorrect selection of amphotericin products and have resulted in fatal overdoses, and sub-therapeutic dosing.[2,3] Please ensure you have selected the correct product and are using the correct guideline.

Refer to drug guideline 2901 for amphotericin B liposomal.

2. Drug

Drug	Amphotericin, Amphotericin B deoxycholate (conventional)
Drug action	Polyene antifungal. Acts by binding to the sterol component of a cell membrane in susceptible fungi, leading to leakage of cell components with subsequent cell death.[2,5] Amphotericin B conventional is active against many species of fungi and may be fungicidal or fungistatic, depending on the drug concentration obtained and the sensitivity of the fungus.[4,5,8] It is highly protein bound (greater than 90%) and may accumulate in tissues to a significant concentration and be excreted renally for months.[5]
Indications	Treatment of severe systemic and central nervous system fungal infection caused by susceptible organisms.[2,4] Amphotericin is active against Candida, Aspergillus, Cryptococcus neoformans, Histoplasma capsulatum, Blastomyces dermatitidis, Coccidioides immitis, Rhodotorula, Sporothrix schenckii, and Mucor mucedo species.[2,4]
Presentation	• Amphotericin B, 50 mg vial[4] • Yellow to orange powder for reconstitution[4]
Route	IV: Intermittent Infusion[4]
Dose	**IV Infusion** Initially 0.25 - 0.5 mg/kg once daily, increased daily in 0.25 - 0.5 mg/kg increments as tolerated to a maintenance dose 0.5 - 1 mg/kg once daily.[2-5] For patients with severe infections, the dose should be initiated at the target dose.[5] Maximum dose must not exceed 1.5 mg/kg daily. If the prescribed dose exceeds this, the product name and dosage need to be verified.[2-4]
Contraindications	Known hypersensitivity to amphotericin, or any components of the formulation.[2-4]
Precautions	• Avoid use in minor or non-invasive fungal infections.[2,3,8] • Renal impairment.[2,9] • Concurrent use with nephrotoxic medication.[2,9] • Concurrent use with medications which enhance the hypokalaemic effects of amphotericin e.g. corticosteroids or diuretics, or potentiate

	potassium related toxicity e.g. digoxin, or skeletal muscle relaxants.[4] • Avoid concurrent leukocyte infusions (acute pulmonary reactions).[2,4,9] • Avoid rapid infusion (risk of hypotension, hypokalaemia, arrhythmias, shock).[2] • Avoid extravasation, may cause chemical irritation.[2]
Incompatibilities	• Compatible with glucose 5%[3,5,6] • **Incompatible with sodium chloride 0.9%[5]**
Adverse effects	• Infusion reactions due to rapid administration including hypokalaemia, arrhythmias, and shock[5] • Flushing, hypertension, hypotension, tachypnoea[2,4,9] • Reduced renal function, renal tubular acidosis[2-5] • Electrolyte disturbances including hypokalaemia, hypomagnesaemia[2,4,5,9] • Anaemia[2,5,7], leucocytosis[2,7], thrombocytopenia[4,5] • Nausea, vomiting**,** diarrhoea, abdominal pain[4,9] • Fever, chills, headache[5,9] • Venous irritation, pain and thrombophlebitis at injection site[4,5,8,9] • Convulsions, haemorrhagic gastroenteritis, acute liver failure, anaphylaxis (rare)[2,4]

3. Administration

Competency for administration	This procedure is carried out by, or under, the direct supervision of a registered nurse/registered midwife who holds current Waikato DHB Generic Medicine Management competency certification and Neonatal specific competency NCV/NAC as well as Guardrails competency.
Preparation & Administration	**Intravenous Infusion**[4,5,8,9] • 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 0.1 mg/ml solution. • Do not administer medication though the NICU clear fluid filter – at 0.2 micron this filter is very fine and will filter out the active drug. • Visually inspect for particulate matter, do not administer if present. • Draw up the prescribed dose and administer by intravenous infusion over 2 to 6 hours. • Any remaining solution should be discarded.
Observations and management	• Ensure adequate hydration and consider sodium repletion to prevent or reduce the risk of nephrotoxicity[3,5] • Monitor renal function, liver function, full blood count, potassium, magnesium at baseline and at least every other day during treatment[2,5] • Monitor fluid balance[2] • Blood pressure, heart rate, respiratory rate and temperature periodically during treatment[2,3] • Monitor IV site for irritation, or phlebitis[2,5] • Assess for signs of anaphylaxis or adverse reactions[2,6]

Special considerations (audit, funding, storage)	• Amphotericin B deoxycholate (conventional) is an unregistered medicine available under section 29. Names of the patient and prescriber must be sent to Pharmacy when ordering • Amphotericin B deoxycholate (conventional) has a pH of 5.7[9] • Sodium content: contains less than 0.5 mmol of sodium per vial[9] • Protect form light[2,4,5] • Vials should be refrigerated between 2 to 8 °C.[4] • Reconstituted vials are stable at room temperature (below 25 °C) for 24 hours, or refrigerated (2 to 8 °C) for 1 week[2,4] • Diluted solution may be stored at room temperature (below 25 °C) and used within 24 hours[2] • Discard any unused solution
Rescue medication	Discontinue immediately and seek urgent medical assistance if anaphylaxis or severe adverse reactions occur. Administer adrenaline and maintain airway as appropriate.

4. Guardrails[10]

Amphotericin is Guardrail profiled on the CC pump for NICU. Following are the guardrail limits:

Guardrails Drug Name		Amphotericin*
Pump		CC
Concentration (microgram/mL)		
	Minimum	100
	Maximum	100
Dose rate (mg/kg/h)		
	Default	0.17
	Soft minimum	0.16
	Soft maximum	0.25
	Hard max	0.25

5. Associated Documents

Waikato DHB. Amphotericin B Liposomal (AmBisome®) for neonates Drug Guideline. Document 2901.

6. References

1. New Zealand Formulary for Children (NZFC). 2018. Amphotericin B. Accessed 24th April 2018. Available from: http://www.nzfchildren.org.nz/nzf_3325.
2. American Pharmacists Association. Pediatric & Neonatal Dosage Handbook. 20th edition. 2013.
3. Phelps SJ, Hagemann TM, Lee KR, Thompson AJ. The Teddy Bear Book: Pediatric Injectable Drugs. 10th edition. Amphotericin B Liposomal. American Society of Health-System Pharmacists; 2013.
4. X-GEN Pharmaceuticals. Amphotericin B for injection USP Data Sheet. April 2010. Available from: http://www.x-gen.us/wp-content/uploads/sites/21/2014/03/XGSS_TSM_AM.0118.pdf
5. Truven Health Analytics Inc. Pediatrics and Neofax®. 2018. Amphotericin B monograph. Accessed 24th April 2018. Available from: http://www.micromedexsolutions.com.
6. The Royal Children's Hospital Melbourne. Paediatric Injectable Guidelines. Accessed 24th April 2018. Available from: https://pig.rch.org.au.
7. Gray A, Wright J, Goodey V, Bruce L. Injectable drugs guide. London: Pharmaceutical Press. 2011.
8. Auckland DHB Newborn Services. Amphotericin B Deoxycholate (conventional amphotericin) Drug Protocol. June 2015. Available from: http://www.adhb.govt.nz/newborn/DrugProtocols
9. Lexicomp. Amphotericin B deoxycholate (conventional): Pediatric drug information monograph. Uptodate. Accessed 24th April 2018. Available from: https://www.uptodate.com.
10. Waikato DHB. Guardrails Database. November 2016.