BRIEF ADMINISTRATION GUIDE

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

Indications: Systemic fungal infection

Route: Intravenous

Dose: Initially 1 mg/kg once daily, increased to 3 - 5 mg/kg once daily

Supplied as: Amphotericin B Liposomal injection 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 0570 for conventional amphotericin B.

Preparation and administration:

Intravenous Infusion[1,4]

- Reconstitute each vial with 12 ml water for injection (concentration 4 mg/ml).
- Shake vigorously for at least 30 seconds to disperse contents completely.
- Withdraw the prescribed dose from the vial and add to glucose 5%, using the 5 micron filter provided, to make a final concentration of 0.25 mg/ml - 2 mg/ml.
- **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.
- Administer by intravenous infusion, over 30 to 60 minutes. The infusion time may be increased to 120 minutes if non-anaphylactic infusion related reactions occur.
- Any remaining solution should be discarded.

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

Monitoring:

- Ensure adequate hydration to reduce the risk of nephrotoxicity.[4,5]
- Monitor renal function, liver function, full blood count, potassium, magnesium at baseline and periodically during treatment.[1,4-7]
- Assess for signs of anaphylaxis or infusion related reactions.[4,5]
- Monitor blood pressure, heart rate, and respiratory rate every 30 minutes during treatment, for up to 4 hours after infusion complete.[4,5]

1. Purpose and scope

To facilitate the safe and effective use of amphotericin (liposomal) 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 0570 for conventional amphotericin B.

2. Drug

Drug	Amphotericin, Amphotericin B Liposomal, AmBisome®
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.[5,7] Amphotericin B liposomal concentrates in the liver and spleen and has poorer penetration into the central nervous system, kidneys, urinary tract and eyes than conventional amphotericin B.[2,7] It is less nephrotoxic than conventional amphotericin B.[7]
Indications	Treatment of systemic fungal infection caused by susceptible organisms, or in patients who are intolerant of conventional amphotericin B. [5,6] Amphotericin is active against Aspergillus, Candida, and Cryptococcus species.[3,6]
Presentation	• Amphotericin B Liposomal, 50 mg vial, powder for reconstitution[1,6] • Reconstituted solution yellow and translucent.[4]
Route	IV: Intermittent infusion[3]
Dose	**IV Infusion** Initially 1 mg/kg once daily, increased to 3 to 5 mg/kg once daily.[1,3,7,8]
Contraindications	Known hypersensitivity to amphotericin, or any components of the formulation.[3,5,6]
Precautions	• Renal or hepatic impairment[8] • Concurrent use with nephrotoxic medication[5,6,8] • Concurrent use with medications which enhance the hypokalaemic effects of amphotericin e.g. corticosteroids or diuretics, or potentiate potassium related toxicity e.g. digoxin.[1,8] • Avoid rapid infusion (risk of arrhythmias).[1]
Incompatibilities	• Compatible with dextrose 5%[3,4,7] • **Incompatible with sodium chloride 0.9%**[3,4,6,7] and most other medications and electrolytes[6,8]
Adverse effects	• Acute infusion reactions including fever, chills, dyspnoea and hypotension. Reactions generally lessen with continued treatment and subsequent doses can be administered at a slower rate. [5-7] • Nephrotoxicity[1,5,6] • Abnormal liver function[1,5]

	• Electrolyte disturbances including hypokalaemia, hypomagnesaemia[1] • Cardiovascular effects including arrhythmias, hypertension, hypotension, chest pain[1,5] • Anaemia, thrombocytopenia[1,5,7] • Nausea, vomiting**,** diarrhoea, abdominal pain[1,5] • Injection site inflammation or phlebitis[5] • Neurological disorders, bronchospasm, anaphylaxis (rare)[1,5]

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**[1,4] • Reconstitute each vial with 12 ml water for injection (concentration 4 mg/ml). • Shake vigorously for at least 30 seconds to disperse contents completely. • Withdraw the prescribed dose from the vial and add to glucose 5%, using the 5 micron filter provided, to make a final concentration of 0.25 mg/ml - 2 mg/ml. • 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. • Administer by intravenous infusion, over 30 to 60 minutes. The infusion time may be increased to 120 minutes if non-anaphylactic infusion related reactions occur. • Use glucose 5% for flushing line before and after infusing drug. • Any remaining solution should be discarded. <u>Note:</u> A new filter must be used for each vial.[4]
Observations and management	• Ensure adequate hydration to reduce the risk of nephrotoxicity[4,5] • Monitor renal function, liver function, full blood count, potassium, magnesium at baseline and periodically during treatment[1,4-7] • Assess for signs of anaphylaxis[4] • Infusion related reactions (refer to adverse reactions), which may occur 1 to 2 hours after starting the infusion. If this occurs, stop the infusion and consider restarting at a slower infusion rate[4,5] • Blood pressure, heart rate, and respiratory rate every 30 minutes during treatment, for up to 4 hours after infusion complete[4,5]
Special considerations (audit, funding, storage)	• Reconstituted solution has a pH of 5 to 6.[4] • Prepare immediately before use.[4,6] • Vials should be stored at room temperature (below 25 °C).[4,6] • Reconstituted solution may be refrigerated between 2 to 8 °C and used within 24 hours. Discard any unused solution.[4,6]
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[9]

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

Guardrails Drug Name	Amphotericin Liposm*			
Pump	CC			
	0.4 - 1 kg	**1 - 2 kg**	**2 - 3 kg**	**3 - 5 kg**
Concentration (mg/mL)				
Minimum	0.25	0.62	1.25	1.87
Maximum	2	2	2	2
Dose rate (mg/kg/h)				
Default	5	5	5	5
Soft minimum	1	1	1	1
Soft maximum	6	6	6	6
Hard max	10	10	10	10

5. Associated Documents

Waikato DHB. Amphotericin B deoxycholate (conventional) Drug Guideline. Document 2901.

6. References

1. New Zealand Formulary for Children (NZFC). 2018. Amphotericin B. Accessed 6th April 2018. Available from: http://www.nzfchildren.org.nz/nzf_3325.
2. Lexicomp. Liposomal amphotericin B: Pediatric drug information monograph. Uptodate. Accessed 6th April 2018. Available from: https://www.uptodate.com.
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. New Zealand Hospital Pharmacists Assoc. Inc. Notes on Injectable Drugs 7th ed, 2015.
5. American Pharmacists Association. Pediatric & Neonatal Dosage Handbook. 20th edition. 2013.
6. Gilead Sciences (NZ). Liposomal Amphotericin B 50 mg for Injection Data Sheet. 21 December 2017. Available from: http://www.medsafe.govt.nz/profs/datasheet/a/AmBisomeinj.pdf.
7. Truven Health Analytics Inc. Pediatrics and Neofax®. 2018. Amphotericin B Liposome monograph. Accessed 6th April 2018. Available from: http://www.micromedexsolutions.com.
8. Christchurch DHB Neonatal Services. Amphotericin B – Ambisome Drug Information Sheet. March 2016.Available from: http://www.cdhb.health.nz/Hospitals-Services/Health-Professionals/Neonatal-Clinical-Resources/Neonatal-Drug-Information-Sheets.
9. Waikato DHB. Guardrails Database. November 2016.