Stanford Medication Usage Guide
Amphotericin B - Liposomal (AmBisome)

Usage

- Liposomal amphotericin B is FDA approved for the treatment of cryptococcal meningitis in HIV-infected patients, empiric antifungal therapy for febrile neutropenia, invasive or pulmonary aspergillosis, candidiasis, cryptococcosis, and visceral leishmaniasis.
- Off-label uses
  - Coccidioidomycosis, histoplasmosis, and mucormucosis.
  - Amphotericin B may be given via other routes.
    - For intrathecal, inhalation, bladder irrigations, use conventional formulation.
- Note: intrinsic resistance common for *Aspergillus terreus, Fusarium* spp., *Scedosporium* spp., *Trichosporon asahii*. *Candida lusitaniae*: phenotypic switching to amphotericin-resistant isolates when exposed to drug.

Dosing

CrCl	Liposomal Amphotericin B (L-AMB) Dosing Regimen (typical duration 2-12 weeks)
All	General: 3-6 mg/kg/day IV + hydration + premeds Mucor: 5mg/kg q24h is standard. High doses (7.5-10mg/kg q24h) have been proposed, but studies show that these are no more effective & associated with high rate (up to 40%) of kidney injury.[2] Long term use: less frequent dosing, e.g. 3x a week, may be an option for some patients (usually in outpatient setting) • Use total body weight (TBW); option to use adjusted BW in obese
ESRD on IHD, CRRT	Poorly dialyzed; no dosage adjustment or supplemental doses necessary

ESRD=end stage renal disease; IHD=intermittent hemodialysis; CRRT=continuous renal replacement therapy

Pharmacokinetics/Pharmacodynamics

Liposomal Amphotericin B (L-AMB) Pharmacokinetics	
Bioavailability	100% (IV route)
Kinetics	Exhibits nonlinear kinetics; greater than proportional increase in serum concentration with an increase in dose.
Distribution	Vd 0.1 – 0.16 L/kg, > 90% protein binding
Metabolism	Not metabolized
Half-life elimination	7-10 hours (following a single 24-hour dosing interval) Terminal half-life: 100 – 153 hours (following multiple dosing up to 49 days)
Time to steady state	Steady state generally achieved within 4 days of dosing.
Excretion	Mean clearance at steady state was shown to be independent of dose. ~43% in feces, ~33% in urine (unchanged)

Administration

- Administer 1st dose over 2 hours
  - 1 hour in patients who tolerate treatment well
  - 4 hours if patient experiences discomfort
- Only compatible in D5W, **not** in NS
- Hydration: 500 mL NS IV given pre- and post-infusion
  - If fluid overloaded, use 250 mL pre/post or skip post-hydration
  - If hyperchloremic, may use normosol instead of NS
- Pre-medication (for patients that experience non-anaphylactic infusion reaction):
  - Give 30-60 min prior to L-AMB dose
  - APAP 650–1000 mg + diphenhydramine 25–50 mg
  - Misc supportive meds:
    - Meperidine 25 mg IV q15min PRN x 4 doses for rigors
    - Hydrocortisone 25 mg PO/IV PRN (usually for deoxycholate formulation)
- Do not filter for intrathecal route. In-line filters may be used for amphotericin deoxycholate and Ambisome (not Abelcet): pore size must be > 1 µm
- Continuous infusions has been associated with less nephrotoxicity, however the efficacy is unknown, as it exhibits concentration-dependent killing.

Monitoring Parameters

- Acute infusion reactions
  - May occur 1 – 3h after starting infusion, though usually within first 5 min.
  - More common in the first few doses, generally diminish with subsequent doses.
- Frequently monitor renal function, electrolytes (especially potassium and magnesium), signs of hypokalemia, LFTs, temperature, CBC, and cardiac function (if on steroids) during therapy.
- Limit use of concomitant nephrotoxic drugs

Infusion reactions
fever,chills, rigors
chest pain
dyspnea
severe pain in abdomen, back, flank, leg
flushing
urticaria
N/V
tachycardia

Special Circumstances

- Amphotericin B formulations are **not** interchangeable and have different dosing recommendations.
- Pregnancy FDA risk category B.

Comparison to other formulations

Conventional Amphotericin B Deoxycholate (AMB-D)	
Clinical Use	Topical (inhalation, bladder irrigation, etc.), intraperitoneal, intrathecal, intravitreal
Dose	0.1 – 1.5 mg/kg/day IV + hydration + pre-medication
Penetration	Brain/CSF: **AMB-D ≈ L-AMB** Kidney/Urine: **AMB-D > L-AMB**; consistent with reduced nephrotoxicity with L-AMB Eye: **AMB-D ≈ L-AMB**; higher in inflamed eyes Lung: **AMB-D < L-AMB** Heart: **AMB-D ≈ L-AMB** Liver: **AMB-D ≈ L-AMB** Bone: **AMB-D < L-AMB**; both still have high penetration *AMB-D=amphotericin B deoxycholate; L-AMB=liposomal amphotericin B
Adverse Effects	More nephrotoxicity and higher incidence of infusion-related reactions compared to AmBisome and other lipid-based formulations

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B. Gatekeeper: Antimicrobial Stewardship Program

C. Review and Renewal Requirement

This document will be reviewed every three years and as required by change of law or practice

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E. Approvals

1. Antimicrobial Subcommittee: 11/2017
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