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

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Liposomal Amphotericin B (L-AMB) Dosing Regimen (typical duration 2-12 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>General: 3-6 mg/kg/day IV + hydration + premeds</td>
</tr>
<tr>
<td></td>
<td>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 &amp; associated with high rate (up to 40%) of kidney injury.</td>
</tr>
<tr>
<td></td>
<td>Long term use: less frequent dosing, e.g. 3x a week, may be an option for some patients (usually in outpatient setting)</td>
</tr>
<tr>
<td></td>
<td>- Use total body weight (TBW); option to use adjusted BW in obese</td>
</tr>
<tr>
<td>ESRD on IHD, CRRT</td>
<td>Poorly dialyzed; no dosage adjustment or supplemental doses necessary</td>
</tr>
</tbody>
</table>

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

Pharmacokinetics/Pharmacodynamics

<table>
<thead>
<tr>
<th>Liposomal Amphotericin B (L-AMB) Pharmacokinetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability</td>
</tr>
<tr>
<td>Kinetics</td>
</tr>
<tr>
<td>Distribution</td>
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<tr>
<td>Metabolism</td>
</tr>
<tr>
<td>Half-life elimination</td>
</tr>
<tr>
<td>Terminal half-life: 100 – 153 hours (following multiple dosing up to 49 days)</td>
</tr>
<tr>
<td>Time to steady state</td>
</tr>
<tr>
<td>Excretion</td>
</tr>
</tbody>
</table>
Infusion reactions
- fever, chills, rigors
- chest pain
- dyspnea
- severe pain in abdomen, back, flank, leg
- flushing
- urticaria
- N/V
- tachycardia

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

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

Comparison to other formulations

<table>
<thead>
<tr>
<th>Conventional Amphotericin B Deoxycholate (AMB-D)</th>
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</thead>
<tbody>
<tr>
<td><strong>Clinical Use</strong></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td><strong>Penetration</strong></td>
</tr>
<tr>
<td>Brain/CSF</td>
</tr>
<tr>
<td>Kidney/Urine</td>
</tr>
<tr>
<td>Eye</td>
</tr>
<tr>
<td>Lung</td>
</tr>
<tr>
<td>Heart</td>
</tr>
<tr>
<td>Liver</td>
</tr>
<tr>
<td>Bone</td>
</tr>
</tbody>
</table>

*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
References:
8. Lexi-comp

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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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   Lina Meng, PharmD, BCPS, BCCCP 9/7/2017
E. Approvals
   1. Antimicrobial Subcommittee: 11/2017
   2. P&T: 12/2017 (pending)

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