Amphotericin B

**Antibiotic Class:**
Antifungal agent

**Antimicrobial Spectrum:**
Fungi: *Candida albicans*, *C. tropicalis*, *C. parapsilosis*, *C. krusei*, *C. guilliermondii*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *A. flavus*, *A. niger*, *Absidia corymbifera*, *Rhizopus oryzae*, *R. rhizopodiformis*, *Blastomyces dermatitidis*, *Coccidioides immitis*, *Histoplasma capsulatum*, *Paracoccidioides brasiliensis*, *Sporothrix schenckii*, *Malassezia furfur*

**Mechanism of Action:**
Induces membrane permeability by forming complexes with ergosterol located in fungal membranes, leading to intracellular leakage and cell death.

**Pharmacodynamics:**
Peak serum level in relation to MIC is the pharmacodynamic parameter of best predictive outcome, while the AUC:MIC ratio and T > MIC are only slightly less predictive.

**Pharmacokinetics:**
Absorption: generally classified as a non-absorbable drug, however, oral administration may result in low but detectable blood concentrations
Distribution: minimal amounts enter the aqueous humor, bile, CSF (inflamed or noninflamed meninges), amniotic fluid, pericardial fluid, pleural fluid, and synovial fluid
Metabolism: elimination half life is approximately 24 hours; only 3% of the total administered dose of amphotericin B is excreted as unchanged drug
Elimination: urine; ~ 40% eliminated over 7 day period
Plasma protein binding: ~90 to 95%
Volume of distribution: 4 L/kg

**Adverse Effects:**
CNS – headache, chills, fever
Renal – nephrotoxicity
Gastrointestinal – dyspepsia, epigastric pain, anorexia, cramping, weight loss
Cardiovascular – hypotension
Respiratory – tachypnea
Hematologic – normochromic normocytic anemia
Other – muscle and joint pain, anaphylaxis (rare), hypomagnesemia, hypokalemia

**Dosage:**
Table 3

Disease state based dosing:
Renal Failure: In case of deterioration of renal function (defined as a doubling of serum creatinine from baseline), a brief cessation of drug administration for one or several days has been advocated.

Hepatic failures: No dosage adjustment required.

**Dosing during Continuous Renal Replacement Therapy**

Abbreviations:
- CVVH (Continuous venovenous hemofiltration)
- CVVHD (Continuous venovenous hemodialysis)
- CVVHDF (Continuous venovenous hemodiafiltration)

Amphotericin B deoxycholate:
- CVVH: 0.4-1mg/kg q24h
- CVVHD or CVVHDF: 0.4-1mg/kg q24h

Amphotericin B lipid complex
- CVVH: 3-5mg/kg q24h
- CVVHD or CVVHDF: 3-5mg/kg q24h

Amphotericin B liposomal
- CVVH: 3-5mg/kg q24h
- CVVHD or CVVHDF: 3-5mg/kg q24h

Note: CVVH is mainly for fluid removal alone. Many institutions will employ more CVVHD or CVVHDF which combine dialysis with fluid removal.

**Contraindications/Warnings/Precautions:**
Contraindications: Hypersensitivity to amphotericin B
Precautions: Anaphylaxis has been reported. During initial dosing, the drug should be administered under close observation.

**Drug Interactions:**
Aminoglycosides, cyclosporine, antineoplastic agents (cisplatin, nitrogen mustard compounds) – nephrotoxic effects
Skeletal muscle relaxants and digitalis glycosides – hypokalemia may be exaggerated
Flucytosine – amphotericin B may increase the toxicity of flucytosine

**Pregnancy:**
Category B: No evidence of risk in humans but studies inadequate.

**Monitoring Requirements:**
Renal function (monitor Scr), Electrolytes (especially potassium and magnesium)

**Generic names/Brand names/Manufacturer:**
- ABELCET – Amphotericin B Lipid Complex (Enzon - UNITED KINGDOM, SPAIN, IRELAND, SWEDEN, DENMARK, USA, AUSTRALIA, FRANCE, AUSTRIA,
NORWAY, ITALY, SINGAPORE, FINLAND, SWITZERLAND, CANADA, BRAZIL, GREECE, HUNGARY, CZECH REPUBLIC, BELGIUM, PORTUGAL, HONG KONG)

- AMBISOME – Amphotericin B Liposomal (Astellas - UNITED KINGDOM, SWEDEN, NETHERLANDS, BELGIUM, AUSTRIA, SPAIN, ITALY, USA, DENMARK, AUSTRALIA, HONG KONG, FRANCE, ISRAEL, THAILAND, FINLAND, SWITZERLAND, GERMANY, NEW ZEALAND, IRELAND, CANADA, GREECE, HUNGARY, NORWAY)

- FUNGIZONE – Amphotericin B deoxycholate (Bristol-Myers Squibb – NETHERLANDS, CANADA, SOUTH AFRICA, SWEDEN, SWITZERLAND, BELGIUM, NORWAY, SOUTH AFRICA, SWEDEN, SWITZERLAND, BELGIUM, NORWAY, IRELAND, HONG KONG, AUSTRALIA, ISREAL, THAILAND, SINGAPORE, FINLAND, NEW ZEALAND, MALAYSIA, GREECE, DENMARK, FRANCE, USA, ITALY, UNITED KINGDOM, )

- AMPHOTEC – Amphotericin B Cholesteryl Sulfate Complex (Sequus – USA, Oryx – Canada, )

- AMPHOCIL - Amphotericin B Cholesteryl Sulfate Complex (Cambridge – UK, IRELAND, AUSTRIA, NETHERLANDS, MEXICO, ISREAL, SINGAPORE, SPAIN, BRAZIL, AUSTRALIA, GREECE, HUNGARY, CZECH REPUBLIC, HONG KONG, MALAYSIA, SWEDEN, ITALY, DENMARK, PORTUGAL)