

## 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 schencki*, *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 (Astelas - 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)