Amphotericin B - Clinical Pharmacology

**Microbiology**

Amphotericin B shows a high order of *in vitro* activity against many species of fungi. *Histoplasma capsulatum*, *Coccidioides immitis*, *Candida* species, *Blastomyces dermatitidis*, *Rhodotorula, Cryptococcus neoformans*, *Sporothrix schenckii*, *Mucor mucedo,* and *Aspergillus fumigatus* are all inhibited by concentrations of Amphotericin B ranging from 0.03 to 1.0 mcg/mL *in vitro*. While*Candida albicans* is generally quite susceptible to Amphotericin B, non-*albicans* species may be less susceptible. *Pseudallescheria boydii* and *Fusarium* sp. are often resistant to Amphotericin B. The antibiotic is without effect on bacteria, rickettsiae, and viruses.

**Susceptibility Testing**

Standardized techniques for susceptibility testing for antifungal agents have not been established and results of susceptibility studies have not been correlated with clinical outcomes.

**PHARMACOKINETICS**

Amphotericin B is fungistatic or fungicidal depending on the concentration obtained in body fluids and the susceptibility of the fungus. The drug acts by binding to sterols in the cell membrane of susceptible fungi with a resultant change in membrane permeability allowing leakage of intracellular components. Mammalian cell membranes also contain sterols and it has been suggested that the damage to human cells and fungal cells may share common mechanisms.

An initial intravenous infusion of 1 to 5 mg of Amphotericin B per day, gradually increased to 0.4 to 0.6 mg/kg daily, produces peak plasma concentrations ranging from approximately 0.5 to 2 mcg/mL. Following a rapid initial fall, plasma concentrations plateau at about 0.5 mcg/mL. An elimination half-life of approximately 15 days follows an initial plasma half-life of about 24 hours. Amphotericin B circulating in plasma is highly bound (>90%) to plasma proteins and is poorly dialyzable. Approximately two thirds of concurrent plasma concentrations have been detected in fluids from inflamed pleura, peritoneum, synovium, and aqueous humor. Concentrations in the cerebrospinal fluid seldom exceed 2.5% of those in the plasma. Little Amphotericin B penetrates into vitreous humor or normal amniotic fluid. Complete details of tissue distribution are not known.

Amphotericin B is excreted very slowly (over weeks to months) by the kidneys with 2 to 5% of a given dose being excreted in the biologically active form. Details of possible metabolic pathways are not known. After treatment is discontinued, the drug can be detected in the urine for at least 7 weeks due to the slow disappearance of the drug. The cumulative urinary output over a 7 day period amounts to approximately 40% of the amount of drug infused.

SOURCE: <http://www.drugs.com/pro/amphotericin-b.html>