ABELCET (Amphotericin B Lipid Complex)

BASIC CHARACTERISTICS

Class: Polyene.
Mechanism of Action: Amphotericin B inserts into the cytoplasmic membrane through ergosterol, leading to increased permeability of the fungal membrane and loss of intracellular ions. Amphotericin B also affects oxidation and may cause fungal death in this manner.
Mechanism of Resistance: Resistance is rare, but is due to changes in the cell membrane that prevent amphotericin from inserting into the membrane.
Metabolic Route: Amphotericin B is excreted very slowly by the kidneys, with 2 to 5% of a given dose being excreted in the biologically active form. After discontinuation of treatment, amphotericin is detectable in urine for at least seven weeks. Details of possible metabolic pathways are not known.

FDA-APPROVED INDICATIONS

Invasive fungal infections in patients who are refractory to or intolerant of conventional amphotericin B therapy.

SIDE EFFECTS/TOXICITY

Side effects are similar to those seen with amphotericin B deoxycholate but tend to be less frequent or less severe. Contraindicated in patients who have shown hypersensitivity to amphotericin B or any other component in the formulation. Acute reactions including fever, shaking chills, hypotension, anorexia, nausea, vomiting, headache, and tachypnea are common 1 to 3 hours after starting an intravenous infusion. Rapid intravenous infusion has been associated with hypotension, hypokalemia, arrhythmias, and shock and should, therefore, be avoided.
Amphotericin B should be used with care in patients with reduced renal function; frequent monitoring of renal function is recommended.
Since acute pulmonary reactions have been reported in patients given amphotericin B during or shortly after leukocyte transfusions, it is advisable to temporarily separate these infusions as far as possible and to monitor pulmonary function. Leukoencephalopathy has been reported following use of amphotericin B.

DRUG INTERACTIONS

Antineoplastic agents may enhance the potential for renal toxicity, bronchospasm and hypotension and should be given concomitantly only with great caution.
Corticosteroids and corticotropin (ACTH): closely monitor serum electrolytes and cardiac function.
Digitalis glycosides: amphotericin B-induced hypokalemia may potentiate digitalis toxicity.
Flucytosine: concomitant use may increase the toxicity of flucytosine.
Imidazoles (e.g., fluconazole): imidazoles may induce fungal resistance to amphotericin B. Combination therapy should be administered with caution.

Other nephrotoxic medications: may enhance the potential for drug-induced renal toxicity and should be used concomitantly only with great caution.

Skeletal muscle relaxants: amphotericin B-induced hypokalemia may enhance the curariform effect of skeletal muscle relaxants.

Leukocyte transfusions: acute pulmonary toxicity has been reported in patients receiving intravenous amphotericin B and leukocyte transfusions.

**DOSING**

5 mg/kg/day given as a single infusion.

**SPECIAL POPULATIONS**

RENAL IMPAIRMENT: Monitor renal function closely. No dosage adjustment recommended for renal impairment or for dialysis.

HEPATIC IMPAIRMENT: Liver tests should be monitored routinely.

PEDIATRICS: As for adults.

**THE ART OF ANTIMICROBIAL THERAPY**

Clinical Pearls

1. There are various forms of amphotericin with many important differences: amphotericin B deoxycholate, amphotericin B lipid dispersion, amphotericin B lipid complex or liposomal amphotericin B. This section pertains only to amphotericin B lipid complex. Side effects of amphotericin B lipid complex are similar to those seen with amphotericin B deoxycholate but tend to be less frequent or less severe.

2. Premedication with acetaminophen, diphenhydramine, meperidine, and even hydrocortisone can decrease infusion-related toxicity.

3. Hydration and sodium repletion prior to amphotericin B administration may reduce the risk of developing nephrotoxicity.

4. *Candida lusitaniae*, *Pseudallescheria boydii*, and *Fusarium* spp. are often resistant to amphotericin B. Voriconazole is frequently used for these infections.

5. It is advisable to monitor on a regular basis liver function, serum electrolytes (particularly magnesium and potassium), blood counts, and hemoglobin concentrations.