Amphotericin B Injection : Uses, Indications, Side Effects

Amphotericin B is a broad-spectrum antifungal antibiotic derived from *Streptomyces nodosus* . It appears as a crystalline powder that is water-soluble and is formulated for parenteral use by adding sodium desoxycholate to form a colloidal dispersion suitable for intravenous infusion.

Pharmacodynamics and Mechanism of Action

- Amphotericin B binds to **ergosterol** , a key sterol in fungal cell membranes.
- This binding disrupts membrane integrity, increasing permeability and causing leakage of intracellular components, leading to fungal cell death.
- At clinically relevant concentrations, Amphotericin B is **fungistatic** , but fungicidal effects can be achieved at higher doses.
- Mammalian cell membranes contain cholesterol (similar to ergosterol), which partly explains Amphotericin B's toxicity.

Spectrum of Activity

Amphotericin B is highly active in vitro against many fungi including:

- *Histoplasma capsulatum*
- *Cryptococcus neoformans*
- *Candida* species
- *Blastomyces dermatitidis*
- *Rhodotorula* species
- *Sporothrix schenckii*

Additionally, Amphotericin B is used in **leishmaniasis** , particularly when first-line therapies fail.

Pharmacokinetics

- Initial dosing: 1–5 mg/day IV infusion.
- Gradual increase to 0.3–0.65 mg/kg/day based on tolerance.
- Peak plasma levels: 1.8–3.5 mcg/mL.
- Detectable levels (0.5–1.5 mcg/mL) persist for ~20 hours post-infusion.
- Excreted slowly via kidneys; about 40% of the drug is recovered in urine over 7 days.
- Treatment for leishmaniasis involves incremental dosing starting at 5–10 mg IV, increasing by 5–10 mg daily to 0.5–1.0 mg/kg, with total doses of 1–3 g.

Indications

Reserved for **serious, progressive, potentially fatal fungal infections** , including:

- Cryptococcosis (meningitis, tolurosis)
- North American blastomycosis

- Disseminated candidiasis and coccidioidomycosis
- Histoplasmosis
- American mucocutaneous leishmaniasis and Kala-azar (post conventional therapy failure)

Contraindications

- Known hypersensitivity to Amphotericin B.
- Use in pregnancy only if benefits outweigh risks (safety not well established).

Precautions

- Administer under close medical supervision, ideally in a hospital setting.
- Avoid concomitant use of nephrotoxic drugs (e.g., nitrogen mustards).
- Corticosteroids should only be used if necessary to manage drug reactions.
- Regular laboratory monitoring:
    - Renal function (BUN, serum creatinine or creatinine clearance) weekly.
    - If BUN > 40 mg/dL or serum creatinine > 3.0 mg/dL, reduce dose or discontinue.
    - Weekly complete blood count (CBC) and serum potassium levels.
- If therapy is interrupted for over 7 days, restart at low dose (0.25 mg/kg) and increase gradually.

Adverse Effects

Common side effects include:

- Infusion-related: fever, chills, headache, malaise, anorexia, nausea, vomiting, phlebitis, thrombophlebitis
- Musculoskeletal: muscle and joint pains
- Gastrointestinal: dyspepsia, cramping, diarrhea, epigastric pain
- Hematologic: normochromic normocytic anemia
- Electrolyte disturbances: hypokalemia
- Hepatic: transient liver function abnormalities (reversible upon drug discontinuation)

Management of side effects:

- Aspirin or antihistamines may reduce intolerance.
- Alternate-day dosing may lessen phlebitis and anorexia.
- Small doses of IV corticosteroids can decrease febrile reactions.
- Low-dose heparin added to infusion reduces thrombophlebitis.

Dosage and Administration

- Administer as a **slow intravenous infusion over 4–6 hours** .
- Recommended concentration: 0.1 mg/mL (1 mg/10 mL).
- Initial dose: 0.25 mg/kg/day, increased as tolerated.
- Maximum daily dose: **1.0 mg/kg/day** , with alternate-day doses up to 1.5 mg/kg permitted.
- Total duration: several weeks, depending on infection severity.
- **Do not exceed 1.5 mg/kg/day** under any circumstances.

Preparation and Storage

- Reconstitute dry powder with 10 mL sterile water (no bacteriostatic agents) to yield 5 mg/mL solution.
- Further dilute in 5% dextrose injection (pH > 4.2) to 0.1 mg/mL for infusion.
- **Do not use normal saline or solutions with bacteriostatic agents** (e.g., benzyl alcohol) to avoid precipitation.
- Maintain strict aseptic technique due to absence of preservatives.
- Store powder refrigerated and protected from light.
- Reconstituted concentrate stable for 24 hours at room temperature in the dark, or up to one week refrigerated.
- Infusion solution should be used promptly and protected from light during administration.