Amphotericin B:

Class: Antifungal Agent, Parenteral

Indications: Treatment of severe systemic and central nervous system infections caused by susceptible fungi such as *Candida* species, *Histoplasma capsulatum*, *Cryptococcus neoformans*, *Aspergillus* species,*Blastomyces dermatitidis*, *Torulopsis glabrata*, and *Coccidioides immitis*; fungal peritonitis; irrigant for bladder fungal infections; used in fungal infection in patients with bone marrow transplantation, amebic meningoencephalitis, ocular aspergillosis (intraocular injection), candidal cystitis (bladder irrigation), chemoprophylaxis (low-dose I.V.), immunocompromised patients at risk of aspergillosis (intranasal/nebulized), refractory meningitis (intrathecal), coccidioidal arthritis (intra-articular/I.M.)

Available dosage form in the hospital: 50MG VIAL

Trade Names:

Dosage:

Note: Premedication: For patients who experience infusion-related immediate reactions, premedicate with the following drugs 30-60 minutes prior to drug administration: NSAID and/or diphenhydramine **or** acetaminophen with diphenhydramine **or** hydrocortisone. If the patient experiences rigors during the infusion, meperidine may be administered.

Test dose: I.V.: 1 mg infused over 20-30 minutes. Many clinicians believe a test dose is unnecessary.

-Susceptible fungal infections: I.V.: Adults: 0.3-1.5 mg/kg/day; 1-1.5 mg/kg over 4-6 hours every other day may be given once therapy is established; aspergillosis, rhinocerebral mucormycosis, often require 1-1.5 mg/kg/day; do not exceed 1.5 mg/kg/day

-Aspergillosis, disseminated: I.V.: 0.6-0.7 mg/kg/day for 3-6 months

-Bone marrow transplantation (prophylaxis): I.V.: Low-dose amphotericin B 0.1-0.25 mg/kg/day has been administered after bone marrow transplantation to reduce the risk of invasive fungal disease.

-Candidemia (neutropenic or non-neutropenic): I.V.: 0.5-1 mg/kg/day until 14 days after first negative blood culture and resolution of signs and symptoms (Pappas, 2009).

-Candidiasis, chronic, disseminated: I.V.: 0.5-0.7 mg/kg/day for 3-6 months and resolution of radiologic lesions (Pappas, 2009).

-Dematiaceous fungi: I.V.: 0.7 mg/kg/day in combination with an azole

-Endocarditis: I.V.: 0.6-1 mg/kg/day (with or without flucytosine) for 6 weeks after valve replacement; **Note:** If isolates susceptible and/or clearance demonstrated, guidelines recommend step-down to fluconazole; also for long-term suppression therapy if valve replacement is not possible (Pappas, 2009)

- Endophthalmitis, fungal (unlabeled use):

-Intravitreal (unlabeled use): 10 mcg in 0.1 mL (in conjunction with systemic therapy)

-I.V.: 0.7-1 mg/kg/day (with flucytosine) for at least 4-6 weeks .

-Esophageal candidiasis: I.V.: 0.3-0.7 mg/kg/day for 14-21 days after clinical improvement (Pappas, 2009)

-Histoplasmosis**:** Chronic, severe pulmonary or disseminated: I.V.: 0.5-1 mg/kg/day for 7 days, then 0.8 mg/kg every other day (or 3 times/week) until total dose of 10-15 mg/kg; may continue itraconazole as suppressive therapy (lifelong for immunocompromised patients)

-Meningitis:

-*Candidal:* I.V.: 0.7-1 mg/kg/day (with or without flucytosine) for at least 4 weeks; **Note:** Liposomal amphotericin favored by IDSA guidelines based on decreased risk of nephrotoxicity and potentially better CNS penetration (Pappas, 2009)

-*Cryptococcal or Coccidioides:* I.T.: Initial: 0.01-0.05 mg as single daily dose; may increase daily in increments of 0.025-0.1 mg as tolerated (maximum: 1.5 mg/day; most patients will tolerate a maximum dose of ~0.5 mg/treatment). Once titration to a maximum tolerated dose is achieved, that dose is administered daily. Once CSF improvement noted, may decrease frequency on a weekly basis (eg, 5 times/week, then 3 times/week, then 2 times/week, then once weekly, then once every other week, then once every 2 weeks, etc) until administration occurs once every 6 weeks. Typically, concurrent oral azole therapy is maintained (Stevens, 2001). **Note:** IDSA notes that the use of I.T. amphotericin for cryptococcal meningitis is generally discouraged and rarely necessary (Perfect, 2010).

-*Histoplasma:* I.V.: 0.5-1 mg/kg/day for 7 days, then 0.8 mg/kg every other day (or 3 times/week) for 3 months total duration; follow with fluconazole suppressive therapy for up to 12 months

-Meningoencephalitis, cryptococcal (Perfect, 2010): I.V.:

-*HIV positive:* Induction: 0.7-1 mg/kg/day (plus flucytosine 100 mg/kg/day) for 2 weeks, then change to oral fluconazole for at least 8 weeks; alternatively, amphotericin (0.7-1 mg/kg/day) may be continued uninterrupted for 4-6 weeks; maintenance: amphotericin 1 mg/kg/week for ≥1 year may be considered, but inferior to use of azoles

-*HIV negative:* Induction: 0.7-1 mg/kg/day (plus flucytosine 100 mg/kg/day) for 2 weeks (low-risk patients), ≥4 weeks (non-low-risk, but without neurologic complication, immunosuppression, underlying disease, and negative CSF culture at 2 weeks), >6 weeks (neurologic complication or patients intolerant of flucytosine) Follow with azole consolidation/maintenance treatment.

-Oropharyngeal candidiasis: I.V.: 0.3 mg/kg/day for 7-14 days (Pappas, 2009)

-Osteoarticular candidiasis: I.V.: 0.5-1 mg/kg/day for several weeks, followed by fluconazole for 6-12 months (osteomyelitis) or 6 weeks (septic arthritis) (Pappas, 2009)

-*Penicillium marneffei:* I.V.: 0.6 mg/kg/day for 2 weeks

-Pneumonia: Cryptococcal (mild-to-moderate): I.V.:

HIV positive: 0.5-1 mg/kg/day

HIV negative: 0.5-0.7 mg/kg/day (plus flucytosine) for 2 weeks

-Sporotrichosis**:** Pulmonary, meningeal, osteoarticular or disseminated: I.V.: Total dose of 1-2 g, then change to oral itraconazole or fluconazole for suppressive therapy

-Urinary tract candidiasis (Pappas, 2009):

-*Fungus balls:* I.V.: 0.5-0.7 mg/kg/day with or without flucytosine 25 mg/kg 4 times daily

-*Pyelonephritis:* I.V.: 0.5-0.7 mg/kg/day with or without flucytosine 25 mg/kg 4 times daily for 2 weeks

-*Symptomatic cystitis:* I.V.: 0.3-0.6 mg/kg/day for 1-7 days

-*Bladder irrigation:* Irrigate with 50 mcg/mL solution instilled periodically or continuously for 5-10 days or until cultures are clear for fluconazole-resistant *Candida*

Renal Impairment:

If renal dysfunction is due to the drug, the daily total can be decreased by 50% or the dose can be given every other day. I.V. therapy may take several months.

Renal replacement therapy: Poorly dialyzed; no supplemental dose or dosage adjustment necessary, including patients on intermittent hemodialysis or CRRT.

Peritoneal dialysis (PD): Administration in dialysate: 1-2 mg/L of peritoneal dialysis fluid either with or without low-dose I.V. amphotericin B (a total dose of 2-10 mg/kg given over 7-14 days). Precipitate may form in ionic dialysate solutions.

Common side effect: Hypotension, tachypnea, Fever, chills, headache, ,Hypokalemia,

Hypomagnesemia, anorexia, nausea ,vomiting ,diarrhea, heartburn.

Pregnancy Risk Factor:B