82.00 mm

175.00 mm

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

℞ Amphotericin B Injection IP 50 mg

AMPHOLIZED B

Injection

DESCRIPTION :

Amphotericin B Injection IP 50mg contains amphotericin B, an antifungal polyene antibiotic obtained from a strain of Streptomyces nodosus. The molecular formula is $C_{47}H_{73}NO_{17}$ and the molecular weight is 924.09.

Each vial contains a sterile, nonpyrogenic, lyophilized powder providing 50 mg amphotericin B and sodium deoxycholate q.s. with sodium phosphate as buffer. Crystalline amphotericin B is insoluble in water, therefore, the antibiotic is solubilised by the addition of sodium deoxycholate to form a mixture which provides a colloidal dispersion for intravenous infusion following reconstitution.

Composition:

Each vial contains:

Amphotericin B IP..... 50 mg

Excipients.....Q.S.

CLINICAL PHARMACOLOGY:

Microbiology: Amphotericin B shows a high order of invitro 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 invitro.

Pharmacokinetics - Amphotericin B is fungistatic and fungicidal depending on the concentration obtained in body fluids and the susceptibility of the fungus. The drug acts by binding to steroids in the cell membrane of susceptible fungi with a resultant change in membrane permeability allowing leakage of intracellular components. 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. Concentrations in the cerebrospinal fluid seldom exceed 2.5 percent of those in the plasma. Little amphotericin B penetrates into vitreous humor or normal amniotic fluid. Amphotericin B is excreted very slowly (over weeks to months) by the kidneys with two to five percent of a given dose being excreted in the biologically active form. The cumulative urinary output over a seven day period amounts to approximately 40 percent of the amount of drug infused.

INDICATIONS AND USAGE:

Amphotericin-B For Injection IP should be administered primarily to patients with progressive, potentially life threatening systemic fungal infections. This drug should not be used to treat noninvasive fungal infections, such as oral thrush, vaginal candidiasis and oesophageal candidiasis in patients with normal neutrophil counts.

Amphotericin-B is specifically intended to treat potentially life-threatening systemic fungal infections: leishmaniasis, aspergillosis, cryptococcosis (torulosis), North American blastomycosis, systemic candidiasis, coccidioidomycosis, histoplasmosis, zygomycosis including mucormycosis due to susceptible species of the genera Absidia, Mucor and Rhizopus, and infections due to related susceptible species of Conidiobolus, Basidiobolus and Sporotrichosis.

CONTRAINDICATIONS :

Amphotericin-B is contraindicated in those patients Who have shown hypersensitivity to amphotericin B or any other component in the formulation unless, in the opinion of the physician, the condition requiring treatment is life-threatening and amenable only to amphotericin B therapy.

WARNINGS:

Amphotericin B is frequently the only effective treatment available for potentially life-threatening fungal disease. In each case, its possible life-saving benefits must be weighed against its untoward and dangerous side effects.

PRECAUTIONS:

Amphotericin B should be administered intravenously under close clinical observation by medically trained personnel. It should be reserved for treatment of patients with progressive, potentially life-threatening systemic fungal infections due to susceptible organisms. 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 therefore, should 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 administered with amphotericin B during or shortly after leukocyte transfusion, it is advisable to temporarily separate these infusions as far as possible and to monitor pulmonary function.

Whenever medication is interrupted for a period longer than seven days, therapy should be resumed by starting with the lowest dosage level, e.g., 0.25 mg/kg body weight and increased gradually as outlined under Dosage and Administration.

Nursing mothers - It is not known whether amphotericin B is excreted in human milk; since many drugs are excreted in human milk and considering the potential toxicity of amphotericin B, it is prudent to advise a nursing mother to discontinue nursing.

Pediatric use - Safety and effectiveness in pediatric patients have not been established through adequate and well controlled studies. Systemic fungal infections have been successfully treated in pediatric patients without reports of unusual side effects. Amphotericin B for Injection when administered to pediatric patients should be limited to the smallest dose compatible with an effective therapeutic regimen.

ADVERSE REACTIONS:

Although some patients may tolerate full intravenous doses of amphotericin B without difficulty, most will exhibit some intolerance, often at less than the full therapeutic dose. Tolerance may be improved by treatment with aspirin, antihistamines or antiemetics. Meperidine (25 to 50 mg IV) has been shown in some patients to decrease the duration of shaking chills and fever that may accompany the infusion of amphotericin B.

The adverse reactions most commonly observed are:

General (body as a whole)	:	Fever, malaise, weight loss
Cardiopulmonary	:	Hypotension, tachypnea
Gastrointestinal	:	Anorexia, nausea, vomiting, diarrhoea, dyspepsia, cramping, epigastric pain
Haematologic	:	Normochromic, normocytic anemia
Musculoskeletal	:	Generalized pain, including muscle and joint pains
Neurologic	:	Headache
Renal	:	Decreased renal function and renal function abnormalities including azotemia, hypokalemia, hyposthenuria, renal tubular acidosis and nephrocalcinosis

OVERDOSAGE:

Amphotericin B overdoses can result in cardio-respiratory arrest. If an overdose is suspected discontinue therapy and monitor the patient's clinical status (e.g. cardio-respiratory, renal and liver function, haematologic status & serum electrolytes) and administer supportive therapy as required. Amphotericin B is not haemodialyzable.

DOSAGE AND ADMINISTRATION:

CAUTION: Under no circumstances should a total daily dose of 1.5 mg/kg be exceeded. Amphotericin B overdoses can result in cardio-respiratory arrest.

AMFOCARE™ should be administered by slow intravenous infusion. Intravenous infusion should be given over a period of approximately 2 to 6 hours (depending on the dose). The recommended concentration for intravenous infusion is 0.1 mg/ml (1 mg/10 ml). A single intravenous **test dose** of 1 mg is prepared by diluting 10 ml of the final reconstituted solution to 20 ml with 5% Dextrose Injection I.P. which may be administered over 20-30 minutes. The patient's temperature, pulse, respiration and blood pressure should be recorded every 30 minutes for 2 to 4 hours. In patients with **good cardio-renal function** and a **well tolerated test dose,** therapy is usually initiated with a daily dose of 0.25 mg/kg of body weight. However, in those patients having **severe and rapidly progressive fungal infection,** therapy may be initiated with a daily dose of 0.3 mg/kg of body weight. In patients with **impaired cardio-renal function** or a **severe reaction to the test dose,** therapy should be initiated with smaller daily doses (i.e. 5 to 10 mg).

RECONSTITUTION:

An initial concentrate of 5 mg amphotericin B per ml is first prepared by rapidly expressing 10 ml of Sterile Water for Injection I.P. without a bacteriostatic agent directly into the vial using a sterile needle (minimum diameter: 20 gauge) and syringe. Shake the vial immediately until the colloidal solution is clear. The infusion solution, providing 0.1 mg amphotericin B per ml, is obtained by further dilution (1:50) with 5% Dextrose Injection I.P. of pH above 4.2. The pH of each container of Dextrose Injection I.P. should be ascertained before use. Commercial Dextrose injection usually has a pH above 4.2; however, if it is below 4.2, then 1 or 2 ml of buffer should be added to the Dextrose Injection I.P. before it is used to dilute the concentrated solution of amphotericin B. The recommended buffer has the following composition:

Dibasic sodium phosphate (anhydrous)	1.59 g
Monobasic sodium phosphate (anhydrous)	1.96 g
Water for Injection I.P.	q.s. 100 ml

The buffer solution should be sterilized before it is added to the Dextrose Injection, either by filtration through a bacterial retentive stone, mat or membrane, or by autoclaving for 30 minutes at 15 lb pressure (121°C).

CAUTION:

Aseptic technique must be strictly observed in all handling, since no preservative or bacteriostatic agent is present in the antibiotic or in the materials used to prepare it for administration. **All entries into the vial or into the diluents must be made with a sterile needle. Do not reconstitute with saline solutions. The use of any diluent other than the ones recommended or the presence of a bacteriostatic agent** (e.g. benzyl alcohol) **in the diluent may cause precipitation of the antibiotic. Do not use the initial concentrate or the infusion solution if there is any evidence of precipitation or foreign matter in either one.**

An in-line membrane filter may be used for intravenous infusion of amphotericin B, **however, the mean pore diameter of the filter should not be less than 1.0 micron in order to assure passage of the antibiotic dispersion.**

STORAGE:

Store in tightly closed containers at 2° to 8°C. Protect from light.

PRESENTATION:

Amphotericin B Injection IP 50mg is supplied as sterile lyophilized powder providing 50 mg amphotericin B.

Manufactured for:

AMERICAN REMEDIES ©

Care & Cure with Research

American Remedies Healthcare Pvt. Ltd.
(An ISO 9001-2015 Certified Company)
ICO: American Remedies LLC, DE, USA
Gala No. T-18, Groud Floor,
Jai Matadi Compound, Kalher,
Bhiwandi, Mumbai-421302
E-mail: info@americanremedies.in

Scan for Batch Certificate