neoformans, Aspergillus spp., Mucor spp., Sporothrix schenckii, Blastomyces dermatitidis, Coccidioides immitis and Histoplasma capsulatum. Most strains are inhibited by Amphotericin B concentrations of 0.03-1.0 mg/ml. Amphotericin B has little or no activity against bacteria or viruses.

Pharmacokinetic Properties :
The pharmacokinetic properties of **Ampholip** and conventional formulation of Amphotericin B containing desoxycholate are different. Pharmacokinetic studies in animals showed that, after administration of **Ampholip**, Amphotericin B levels were higher in the liver and spleen. Amphotericin B in **Ampholip** was rapidly distributed to tissues. The ratio of drug concentrations in tissues to those in blood increased disproportionately with increasing dose, suggesting that elimination of the drug from the tissues was delayed. Peak blood levels of Amphotericin B were lower after administration of **Ampholip** than after administration of equivalent amounts of conventional drug. Administration of conventional Amphotericin B resulted in much lower tissue levels than did dosing with **Ampholip**.

The rapid clearance and large volume of distribution of **Ampholip** result in a relatively low AUC and are consistent with preclinical data showing high tissue concentrations. The kinetics of **Ampholip** is nonlinear.

PHARMACEUTICAL INFORMATIONS :
Storage Conditions :
Ampholip should be stored under refrigeration at 2°C to 8°C. Do not freeze. Protect from direct exposure to light.

Presentation :
Single dose vials containing 10ml (50mg Amphotericin B). Each vial is packed individually in a carton along with one 5µ filter needle and a pack insert.

Keep out of reach of children.

Incompatibilities :
The use of any solution other than those recommended or the presence of a bacteriostatic agent (eg. benzyl alcohol) in the solution may cause precipitation of **Ampholip**.

Date of revision :
May 2025.

Mode of administration :
Intravenous.

Manufactured by :
BHARAT SERUMS AND VACCINES LIMITED
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FOR THE USE ONLY OF A REGISTERED MEDICAL PRACTITIONER OR A HOSPITAL OR A LABORATORY

Amphotericin B Lipid Complex Injection I.V.

AMPHOLIP Injection 50 mg/10ml

For I.V. use only

DESCRIPTION :
Yellow coloured suspension, which settles on keeping and gets dispersed uniformly on mild shaking.

COMPOSITION :
Each ml of the suspension contains 5.0mg of Amphotericin B. Additionally it contains Dimyristoylphosphatidylcholine (DMPC), Dimyristoylphosphatidylglycerol (DMPG), Sodium Chloride and Water for Injection.

CLINICAL INFORMATION :
Clinical Indications :
Ampholip is indicated for the treatment of severe systemic and/or deep mycoses in cases where toxicity or renal failure precludes the use of conventional Amphotericin B in effective doses, and in cases where prior systemic antifungal therapy has failed. Fungal infections successfully treated with **Ampholip** include disseminated candidiasis and aspergillosis.
Ampholip has been used successfully in severely neutropenic patients.
Ampholip is not intended for use in common, clinically inapparent fungal diseases diagnosed only by skin tests or serological determinations.

Dosage and Administration :
The recommended daily dosage for adults and children is 5 mg/kg given as a single infusion. **Ampholip** should be administered by intravenous infusion at a rate of 2.5 mg/kg/h. If the infusion time exceeds 2 hours, mix the contents by shaking the infusion bag every 2 hours.
Renal toxicity of **Ampholip**, as measured by serum creatinine levels, has been shown to be dose dependent. Decisions about dose adjustments should be made only after taking into account the overall clinical condition of the patient.
Preparation of Admixture for Infusion : Shake the vial gently until there is no evidence of any yellow sediment at the bottom. Withdraw the appropriate dose of **Ampholip** from the required number of vials into one or more sterile syringes using an 18-gauge needle. Remove the needle from each syringe filled with **Ampholip** and replace with the 5µ filter needle supplied with each vial.
Each filter needle may be used to filter the contents of up to four 100 mg vials or eight 50 mg vials. Insert the filter needle of the syringe into an IV bag containing 5% Dextrose Injection USP, and empty the contents of the syringe into the bag. The final infusion concentration should be 1mg/mL.
For pediatric patients and patients with cardiovascular disease the drug may be diluted with 5% Dextrose Injection to a final infusion concentration of 2 mg/mL.
Before infusion, shake the bag until the contents are thoroughly mixed. Do not use the admixture after dilution with 5% Dextrose Injection if there is any evidence of foreign matter. Vials are for single use. Unused material should be discarded. Aseptic technique must be strictly observed throughout handling of **Ampholip**, since no bacteriostatic agent or preservative is present.
DO NOT DILUTE WITH SALINE SOLUTIONS OR MIX WITH OTHER DRUGS OR ELECTROLYTES as the compatibility of **Ampholip** with these materials has not been established: An existing intravenous line should be flushed with 5% Dextrose Injection before infusion of **Ampholip**, or a separate infusion line should be used.
DO NOT USE AN IN-LINE FILTER.

Contraindication :
Ampholip is contra-indicated in patients with known hypersensitivity to Amphotericin B or any of its components, unless in the opinion of the physician the advantages of using Ampholip outweigh the risks of hypersensitivity.

Special warnings and special precautions for use :
Systemic Fungal Infections :
Ampholip should not be used for treating common or superficial, clinically inapparent fungal infections that are detectable only by positive skin or serologic tests.

Renal Disease :
Since **Ampholip** is a potentially nephrotoxic drug, monitoring of renal function should be performed before initiating treatment and during the treatment. This is particularly important in patients with pre-existing renal disease, who have already experienced renal failure, or in patients receiving nephrotoxic medications. Laboratory evaluation of serum electrolytes, particularly potassium should be performed regularly before and during therapy. Cases of hyperkalaemia (some of them leading to cardiac arrhythmias and cardiac arrest) have been reported. Some of them occurred in patients with renal impairment, or after potassium supplementation in patients with previous hypokalaemia.

Liver Disease :
Patients with concurrent hepatic impairment due to infection, graft-versus-host disease, other liver disease or administration of hepatotoxic drugs have been successfully treated with **Ampholip**. In cases where serum bilirubin, alkaline phosphatase or serum transaminases increased, factors other than **Ampholip** were present and possibly accounted for the abnormalities. These factors included infection, hyperalimentation, concomitant hepatotoxic drugs and graft-versus-host disease.

Interactions with other medicaments :
Nephrotoxic Drugs :
Amphotericin B is a potentially nephrotoxic and particularly close monitoring of renal function is required in patients receiving nephrotoxic drugs concomitantly.

Zidovudine :
In dogs, exacerbated myelotoxicity and nephrotoxicity were observed when **Ampholip** was administered concomitantly with zidovudine. If concomitant treatment with zidovudine is required, renal and haematologic function should be closely monitored.

Cyclosporin :
Preliminary data suggest that patients receiving **Ampholip** concomitantly with high dose of cyclosporin experience an increase in serum creatinine. The data also suggest that the increase in serum creatinine is caused by cyclosporin and not by **Ampholip**.

Flucytosine :
The use of flucytosine with **Ampholip** has not been studied. While the synergy between Amphotericin B and flucytosine has been reported, Amphotericin B may enhance the toxicity of flucytosine by increasing its cellular uptake and impeding its renal excretion.

Conventional Amphotericin B has been reported to interact with antineoplastic agents, corticosteroids and corticotrophin (ACTH), antiarrhythmic agents digitalis glycosides and skeletal muscle relaxants.

Pregnancy and Lactation :
Conventional Amphotericin B has been used successfully to treat systemic fungal infections in pregnant women with no obvious effects on the foetus, but only a small number of cases have been reported. Reproductive toxicity studies of Amphotericin B in rats and rabbits showed no evidence of embryotoxicity, foetotoxicity or teratogenicity. However, safety for use in pregnant or lactating women has not been established for **Ampholip**. Therefore, **Ampholip** should be administered to pregnant or lactating women only for life-threatening disease when the likely benefit exceeds the risk to the mother and foetus.

Effect on Ability to Drive and Use Machines :
Ampholip is unlikely to affect the ability of an individual to drive or use machines, since adverse reactions are usually infusion-related. However, the clinical condition of patients who require **Ampholip** generally precludes driving or operating machinery.

Undesirable Effects :
Patients in whom significant renal toxicity was observed following conventional Amphotericin B frequently did not experience similar effects when **Ampholip** was substituted. Adverse reactions related to the administration of **Ampholip** have generally been mild or moderate, and have been most prevalent during the first 2 days of dosing.

Premedication (e.g. paracetamol) may be administered for the prevention of infusion related adverse events. The most common clinical adverse effects have been chills, fever, nausea and vomiting, which may occur during the first 2 days of treatment.

Decline in renal function, shown by increased serum creatinine, azotemia and hypokalaemia, have not typically required discontinuation of treatment. **Ampholip** has not been reported to directly cause changes in hepatic or haematologic function.

Adverse reaction that have been reported to occur with conventional Amphotericin B may occur with **Ampholip**. In general, the physician should monitor the patient for any type of adverse event associated with conventional Amphotericin B.
Metabolism and nutrition disorders
Frequency "common": Hyperkalaemia

Adverse reaction including fever chills and rigors may occur. Anaphylactoid reactions including hypotension, tachycardia bronchospasm, dyspnoea , hypoxia and hyperventilation have also been reported.

Overdose :
No serious acute reactions of cardio-respiratory arrest have been reported as found with the overdosage of Amphotericin B desoxycholate. If an overdosage is suspected, discontinue the therapy, monitor the patient closely and administer supportive therapy as required. **Ampholip** is not hemodialyzable.

PHARMACOLOGICAL INFORMATION :
Ampholip contains the antifungal agent, Amphotericin B, complexed with phospholipids. Amphotericin B is a macrocyclic, polyene, broad-spectrum antifungal antibiotic produced by Streptomyces nodosus. The lipophilic moiety of Amphotericin B allows molecules of the drug to be complexed in a ribbon-like structure with the phospholipids.

Pharmacodynamic properties :
Mechanism of action :
Amphotericin B, the active antifungal agent in **Ampholip**, may be fungistatic or fungicidal, depending on its concentration and on fungal susceptibility. The drug acts by binding to ergosterol in the fungal cell membrane causing subsequent membrane damage. As a result, cell contents leak from the fungal cell and ultimately, cell death occurs.

Microbiological activity :
Amphotericin B is active against many fungal pathogens in vitro, including Candida spp., Cryptococcus