PRESCRIBING INFORMATION

Consult Summary of Product Characteristics (SmPC) before prescribing.

AMBISOME® Liposomal amphotericin B 50 mg Powder for dispersion for infusion.

PRESENTATION: Sterile, powder for dispersion for infusion. Each vial contains 50mg of amphotericin B (50,000 units), encapsulated in liposomes.

INDICATIONS (adults and children aged 1 month to 18 years: 1) Severe systemic and/or deep mycoses 2) Visceral leishmaniasis in immunocompetent patients 3) Empirical treatment of presumed fungal infections in febrile neutropenic patients, where the fever has failed to respond to broad-spectrum antibiotics and appropriate investigations have failed to define a bacterial or viral cause. Infections successfully treated with AmBisome include: disseminated candidiasis, aspergillosis, mucormycosis, chronic mycetoma, cryptococcal meningitis and visceral leishmaniasis. AmBisome should not be used to treat the common clinically inapparent forms of fungal disease which show only positive skin or serologic tests. **DOSAGE/ADMINISTRATION**: *Preparation*: Follow reconstitution instructions exactly as per SmPC. *Administration*: intravenous infusion over a 30 – 60 min period, or over a 2 hour period for doses greater than 5mg/kg/day. Recommended concentration is 0.2mg/ml - 2.0mg/ml. *Non-equivalence of amphotericin products:* Different amphotericin products (sodium deoxycholate, liposomal, lipid complex) are not equivalent in terms of pharmacodynamics, pharmacokinetics and dosing and so the products should not be used interchangeably without accounting for these differences. Both the trade name, common name and dose should be verified pre-administration. There is a risk of under-dose if AmBisome is administered at a dose recommended for amphotericin B deoxycholate. *Posology* - Administration of a test dose is advisable before a new course of treatment. A small amount of an AmBisome infusion (e.g. 1 mg) can be administered for about 10 minutes and then stopped and the patient observed carefully for the next 30 minutes. If there have been no severe allergic or anaphylactic/anaphylactoid reactions the infusion of AmBisome dose can be continued. Mycoses: Usually instituted at a daily dose of 1.0mg/kg of body weight, and increased stepwise to 3.0mg/kg. Data presently insufficient to define total dosage requirements and duration of treatment. However, a cumulative dose of 1.0 – 3.0g over 3 – 4 weeks has been typical. Dosage must be adjusted to the specific requirements of each patient. Mucormycosis: Recommended starting dose is 5 mg/kg/daily. Duration determined on an individual basis. Courses of up to 6-8 weeks are commonly used in clinical practice. Longer durations may be required for deep seated infections or during prolonged courses of chemotherapy or neutropenia. Doses greater than 5 mg/kg and up to a maximum of 10 mg/kg have been used in clinical trials and clinical practice, however data on safety and efficacy are limited. Therefore a benefit:risk assessment should be made to determine whether the potential benefits are considered to outweigh known risks of toxicity at these higher doses. Visceral leishmaniasis: Total dose of 21.0 – 30.0 mg/kg of body weight over 10-21 days. Particulars as to the optimal dosage and eventual development of resistance yet incomplete. To be administered under strict medical supervision. Empirical treatment of febrile neutropenia: Recommended dose is 3mg/kg body weight per day. Treatment should be continued until recorded temperature is normalised for 3 consecutive days. Treatment should be discontinued after maximum of 42 days. *Special populations/Dose Adjustments*: **Children <1 month:** Not recommended due to lack of data on safety and efficacy. Elderly: No dose adjustment. Renal Impairment: No dose adjustment unless clinically significant reduction in renal function where consideration should be given to dose reduction, treatment interruption or discontinuation. Hepatic Impairment*:* No data available, no dose recommendation**. CONTRAINDICATIONS**: Hypersensitivity to active substance/any of the excipients, unless the condition requiring treatment is life threatening and amenable only to AmBisome therapy. **WARNINGS/PRECAUTIONS:** Anaphylactic/anaphylactoid or severe allergic reactions: Administration of a test dose is advisable. If severe reaction occurs, infusion should be immediately stopped and the patient should not receive any further infusion. Infusion related-reaction: Precautionary measures are advisable. Slower infusion rates of over 2 hours or routine administration of diphenhydramine, paracetamol, pethidine and/or hydrocortisone have been reported to be successful in their prevention or treatment. Renal toxicity: Caution advised for prolonged therapy. Laboratory evaluation of serum electrolytes, particularly potassium and magnesium, as well as renal, hepatic and haematopoietic function should be performed at least weekly, and particular attention should be given to patients receiving concomitant nephrotoxic medicines. Refer to SmPC for full information on interactions with other medicines. Potassium supplementation may also be required. If renal function deteriorates significantly, consideration should be given to dosage reduction, treatment interruption or discontinuation. Pulmonary toxicity: Acute pulmonary toxicity has been reported in patients given amphotericin B (as sodium deoxycholate complex) during or shortly after leukocyte transfusions. It is recommended that these infusions are separated by as long a period as possible and pulmonary function should be monitored. Diabetic patients: Each vial of AmBisome contains approximately 900mg of sucrose. Renal dialysis patients: Haemodialysis or peritoneal dialysis does not appear to affect the elimination of AmBisome. No dose adjustment required, however administration should be avoided during haemodialysis procedure. **INTERACTIONS:** No interaction studies have been performed with AmBisome, however some medicinal products known to interact with amphotericin B may interact with AmBisome. See SmPC for full list. **PREGNANCY/LACTATION**: Safety not established, risk/benefit assessment should be considered. **DRIVING/USING MACHINERY:** No studies have been performed. Some side effects of AmBisome may impact the ability to drive and use machines. **SIDE EFFECTS**: Refer to SmPC for full information on side effects. Very common(≥1/10): nausea, vomiting, hypokalaemia, pyrexia, rigors. Common(≥1/100, <1/10): tachycardia*, headache, dyspnoea*, diarrhoea, abdominal pain, increased creatinine, blood urea increased, rash, back pain*, hypomagnesaemia, hypocalcaemia, hyperglycaemia, hyponatraemia, vasodilatation, flushing*, hypotension*, chest pain*, liver function tests abnormal, hyperbilirubinaemia, alkaline phosphatase increased. Uncommon (≥1/1,000, <1/100): thrombocytopenia, convulsion, bronchospasm*, anaphylactoid reaction. Unknown frequency: cardiac arrest, arrhythmia, anaemia, angioneurotic oedema, anaphylactic reactions, hypersensitivity renal failure, renal insufficiency, rhabdomyolysis (associated with hypokalaemia), musculoskeletal pain* (described as arthralgia or bone pain). Chest tightness and the side effects marked * may be infusion-related reactions and these resolve rapidly when stopping the infusion. False elevations of serum phosphate may occur when samples from patients receiving AmBisome are analysed using the PHOSm assay. In a double-blind study involving 687 patients, nephrotoxicity with AmBisome was approximately half that for conventional amphotericin B. In another double-blind study involving 244 patients, the incidence of nephrotoxicity with AmBisome was approximately half that for amphotericin B lipid complex. **OVERDOSE**: Stop administration immediately and carefully monitor serum electrolytes, hepatic, renal and haematopoietic function. **PHARMACEUTICAL PRECAUTIONS**: Do not store above 25°C. Keep the container in the outer carton. AmBisome does not contain any bacteriostatic agent, the reconstituted and diluted product should be used immediately. In-use storage not normally longer than 24 hours at 2 – 8°C, unless reconstitution and dilution has taken place in controlled and validated aseptic conditions. Chemical and physical stability has been demonstrated for 24 hours at 25°C ± 2 and 7 days at 2 – 8°C for reconstituted product. Following dilution with 5% dextrose, chemical and physical stability have been shown for 24 - 48 hours at 25°C ± 2 and 4 – 7 days at 2 – 8°C (dependent upon final concentration). DO NOT STORE partially used vials. DO NOT RECONSTITUTE AMBISOME WITH SALINE, OR MIX WITH OTHER medicinal products. AmBisome is not equivalent to other amphotericin products. **LEGAL CATEGORY**: POM. **PACK:** Carton of 10 vials. **PRICE:** £821.87. **MARKETING AUTHORISATION NUMBER**: PL 16807/0001. **FURTHER INFORMATION**: Gilead Sciences Ltd, 280 High Holborn, London, WC1V 7EE, UK. Telephone: +44 (0) 8000 113700. E-mail: ukmedinfo@gilead.com. AmBisome is a trademark.

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Adverse events should be reported. For the UK, reporting forms and information can be found at www.mhra.gov.uk/yellowcard or via the Yellow Card app (download from the Apple App Store or Google Play Store). Adverse events should also be reported to Gilead to safety_FC@gilead.com or +44 (0) 1223 897500.