
30 YEARS
GILEAD
I Am confident reconstituting AmBisome®
(liposomal amphotericin B)
Key information for reconstituting with dextrose and administering AmBisome®
This document has been created and funded by Gilead.
Please refer to the AmBisome® Summary of Product Characteristics for full information on storage, dosing, reconstitution and dilution. Prescribing Information can be found on back cover.
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AmBisome®
Liposomal amphotericin B 50mg

Calculating how much AmBisome® your patient requires

The information shown here provides a useful example of how to make the 4 key calculations:

1. How much AmBisome® does your patient need?
2. How many vials?
3. How much reconstituted AmBisome® is needed for your patient's dosage?
4. How much dextrose solution is needed for the required concentration?

Typical daily dose of AmBisome® for empirical treatment of febrile neutropenia: **3 mg/kg per day**

Typical diluted concentration range of AmBisome®: **0.2 to 2 mg/ml**

A guide to making up 0.2 and 2 mg/ml concentrations for the weight examples shown (based on an AmBisome® dose of 3 mg/kg/day in dextrose 5% solution for infusion)

Weight (kg)	10	25	40	55	70	85
Number of vials	1	2	3	4	5	6
Amount AmBisome® (mg) to be withdrawn for further dilution	30	75	120	165	210	255
Volume of reconstituted AmBisome® (ml)	7.5	18.75	30	41.25	52.5	63.75
To make up 0.2 mg/ml concentration						
Volume of 5% dextrose needed (ml)	142.5	356.25	570	783.75	997.5	1211.25
Total volume (ml)	150	375	600	825	1050	1275
To make up 2.0 mg/ml concentration						
Volume of 5% dextrose needed (ml)	7.5	18.75	30	41.25	52.5	63.75
Total volume (ml; AmBisome® plus 5% dextrose)	15	37.5	60	82.5	105	127.5

For the typical doses for mycoses, mucormycosis and visceral leishmaniasis, please refer to the Summary of Product Characteristics.

Calculation example for a patient with bodyweight of 70 kg

Dose given: 3 mg/kg/day

AmBisome needed: 70x3=210 mg

Each AmBisome® vial contains 50 mg of amphotericin

Vials needed: 210 divided by 50=4.2; thus 5 vials needed

The volume of reconstituted AmBisome® to be withdrawn for further dilution in 5% dextrose is calculated by dividing 210 (dose of AmBisome®) by 4 (concentration of the reconstituted AmBisome®)= 52.5 ml

I Am ready to administer AmBisome®

What to check before you start

Every time you prepare to administer AmBisome® to a patient, you should first carry out these important checks.

The prescription is for AmBisome®

AmBisome® is not interchangeable with other amphotericin products

Sterile water is available

AmBisome® must be reconstituted using sterile water (without a bacteriostatic agent)

Dextrose solution is available

AmBisome® must be diluted in dextrose 5%, 10% or 20% solution - **not saline**

AmBisome® is not mixed with saline

AmBisome® cannot be mixed with other drugs or electrolytes for reconstitution

Essential equipment needed to administer AmBisome®

Use the information on the opposite page to calculate how much AmBisome® your patient requires, and then gather the equipment shown here.

The number of vials you calculated for your patient

5-micron filter for each vial

Swabs, syringes and needles

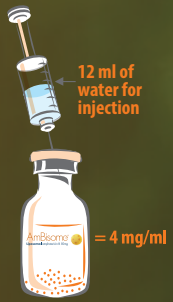
Sterile water for injection

Infusion bag with adequate volume of 5%, 10% or 20% dextrose solution

The 3 simple steps to reconstitute and dilute AmBisome®

STEP 1 – Reconstitution

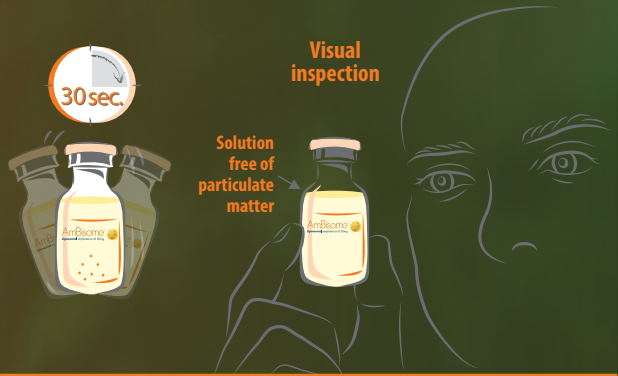
- Remove plastic cap from AmBisome® vial and clean rubber stopper
- Check vial is free from foreign or particulate matter
- Add 12 ml of sterile water for injection to AmBisome® vial using the syringe



STEP 2 – Dispersion and inspection

- **Immediately** after water is added, **shake vial vigorously** for 30 seconds
- A yellow, translucent dispersion should be produced
- Inspect vial for particulate matter
- Continue shaking until complete dispersion occurs

Do not use if you see evidence of precipitation or foreign matter



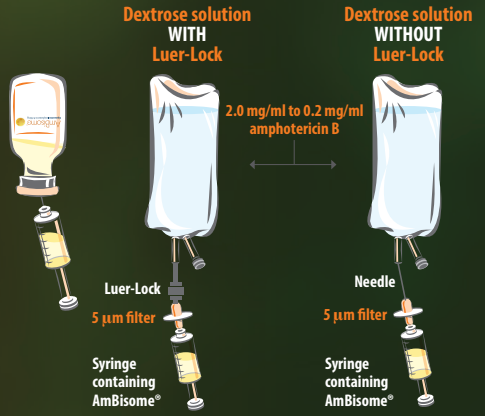
Repeat steps 1 & 2. Repeat this whole process for each vial needed, until all are fully reconstituted and dispersed.

STEP 3 – Dilution and filtration

- Withdraw the calculated amount of reconstituted AmBisome® using a new sterile syringe
- Add 5-micron filter to syringe
- Add required amount of AmBisome® to dextrose infusion bag
- When AmBisome® is thoroughly mixed, it is ready for administration

Important: use a new sterile syringe and 5-micron filter for each vial

Remember: AmBisome® should never be reconstituted or diluted with saline. If you are administering AmBisome® using an existing IV line, make sure to flush the line thoroughly with dextrose prior to initiation of AmBisome® treatment. If this isn't possible, AmBisome® should be administered through a separate line. Please refer to the SmPC for infusion times.



Key AmBisome® storage information

It is important to follow this advice at all times in order to preserve the quality of the AmBisome® solution.

- Do not store unopened AmBisome® above 25 °C
- Do not freeze reconstituted AmBisome®
- Do not store partially used AmBisome® vials
- Never reuse AmBisome® vials
- Use AmBisome® immediately after reconstitution whenever possible
- Ambient light exposure (25+/-2 °C) for up to 24 hours is acceptable

Be ready to use AmBisome® for treatment of the next infection

Further information can be found in the AmBisome® Summary of Product Characteristics and Reconstitution video.
The Reconstitution video can be accessed at www.medicines.org.uk/emc/product/1022/video

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.