

## Package leaflet: information for the user

### AmBisome

Liposomal Amphotericin B 50 mg  
Powder for Concentrate for Dispersion for Infusion

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

### What is in this leaflet

1. What AmBisome is and what it is used for
2. Before you are given AmBisome
3. How AmBisome is used
4. Possible side effects
5. How to store AmBisome
6. Contents of the pack and other information

#### 1. What AmBisome is and what it is used for

**AmBisome is an antifungal antibiotic.** The active ingredient in AmBisome is amphotericin B.

**AmBisome is given as an infusion** into a vein (a drip) by a doctor or nurse.

AmBisome has been studied in patients aged one month and above.

AmBisome is used to treat serious infections caused by fungi:

- **Fungal infections of one or more organs inside the body**
- **Suspected fungal infections** in patients who have a **raised temperature and a low white blood cell count called *neutropenia*.**  
Before you are given AmBisome your doctor will check that your fever is not due to bacteria or viruses and will try and treat the infection with a course of antibiotics.
- **Visceral leishmaniasis**, a disease caused by a parasite.

AmBisome is not used to treat common fungal infections that are not serious, for example skin infections

#### 2. Before you are given AmBisome

##### Before your first treatment

Before your first treatment your doctor may give you a small amount of AmBisome. They will then wait for approximately 30 minutes to see whether you have an allergic reaction, before continuing the infusion of the full dose.

**Your doctor will not give you AmBisome:**

- **If you are allergic** (hypersensitive) to amphotericin B or any other ingredients of this medicine (listed in section 6). However, if **your condition is life-threatening** you may be given AmBisome if your doctor believes that only AmBisome can help you.
  - **If you have previously had a severe allergic reaction** (*anaphylactic* or *anaphylactoid*) to AmBisome. Symptoms of such immediate and life-threatening allergic reactions include: flushing, itching, sickness, swelling of the face, mouth, tongue and airways, often enough to cause difficulty breathing.
- ➔ Tell your doctor if any of these applies to you, you must not be given AmBisome

## Warnings and precautions

### Your doctor will take special care with AmBisome:

- **If you have a severe allergic (*anaphylactic* or *anaphylactoid*) reaction.** If this happens your doctor will stop the infusion.
- **If you get other reactions related to the infusion.** If this happens, your doctor may slow down the infusion, so you receive AmBisome over a longer period of time (approximately 2 hours). Your doctor may also give you medicines to prevent or treat infusion-related reactions, such as diphenhydramine (an antihistamine), paracetamol, pethidine (for pain relief) and/or hydrocortisone (an anti-inflammatory medicine that works by reducing the response of your immune system).
- **If you are taking other medicines that may cause kidney damage,** see the section *Other medicines and Ambisome*. AmBisome may cause damage to the kidney. Your doctor or nurse will take blood samples to measure your *creatinine* (a chemical in the blood that reflects kidney function), and electrolyte levels (particularly potassium and magnesium) before and during the treatment with AmBisome because both of these can be abnormal if you have changes in your kidney function. This is particularly important if you have previous renal damage or are taking other medicines that can affect the way your kidney functions. The blood samples will also be tested for changes in your liver, and your body's ability to produce new blood cells and platelets. **If blood tests show a change in kidney function,** or other important changes your doctor may give you a lower dose of AmBisome or stop treatment.
- **If blood tests show that your potassium levels are low.** If this happens, your doctor may prescribe a potassium supplement for you to take while you are treated with AmBisome.
- **If blood test shows that your potassium levels are high** you may suffer irregular heartbeat, sometimes severe.
- **If you are receiving or recently had a white blood cell transfusion.** Sudden and severe problems in the lungs can happen if you are given AmBisome infusion during or shortly after a white blood cell transfusion. Your doctor will recommend that the infusions are separated by as long a period as possible. This will reduce the risk of lung problems, and your lungs will be monitored.
- **If you have kidney failure and are having dialysis.** Your doctor may start AmBisome treatment after the procedure has ended.
- **If you have diabetes.** AmBisome contains approximately 900 mg of sucrose (sugar) in each vial. Tell your doctor if you have diabetes.

### Other medicines and AmBisome

**Tell your doctor** if you are taking any other medicines, or have recently taken any. This includes medicines and herbal products you bought without a prescription.

### Medicines that may cause kidney damage:

- **Medicines that suppress the immune system** (*immunosuppressants*), such as ciclosporin.
  - **Certain antibiotics** called *aminoglycosides* (including gentamicin, neomycin and streptomycin).
  - **Pentamidine** a medicine used to treat pneumonia in people with AIDS and leishmaniasis.
- ➔ **Tell your doctor if you are taking any of these medicines.** AmBisome may make any kidney damage caused by the medicine worse. If you are taking any of these medicines, your doctor or nurse will take regular blood samples to check your kidneys.

#### **Medicines that may lower your potassium levels:**

- **Corticosteroids**, anti-inflammation medicines that work by reducing the response of your immune system.
  - **Corticotropin** (ACTH), used to control the amount of corticosteroid produced by your body. The body produces corticosteroid in response to stress.
  - **Diuretics**, medicines that increase the amount of urine your body produces. This includes furosemide.
  - **Digitalis glycosides**, medicines produced from the foxglove plant and used to treat heart failure. AmBisome may worsen the side effects of digitalis, such as heart rhythm changes.
  - **Muscle relaxants** usually used during surgery, such as tubocurarine. AmBisome may increase the muscle relaxant effect.
- ➔ **Tell your doctor if you are taking any of these medicines** or have had recent surgery where these drugs may have been used.

#### **Other medicines:**

- **Antifungal medicines**, such as flucytosine. AmBisome may worsen the side effects of flucytosine. This includes changes in the body's ability to produce new blood cells. This may be seen in blood tests.
  - **Certain cancer medicines**, such as methotrexate, doxorubicin, carmustine and cyclophosphamide. Taking this type of medicine with AmBisome may cause kidney damage, wheezing or trouble breathing and low blood pressure.
  - **White blood cell transfusions.** Sudden and severe problems in the lungs can happen if you are given AmBisome infusion during or shortly after a white blood cell transfusion. Your doctor will recommend that the infusions are separated by as long a period as possible. This will reduce the risk of lung problems and your lungs will be monitored.
- ➔ **Tell your doctor if you are taking any of these medicines** or receiving such transfusions.

#### **Pregnancy and breast-feeding**

**Tell your doctor before you are given AmBisome if you are pregnant,** planning to become pregnant, or if you are breast-feeding. Your doctor will only prescribe AmBisome if they think the benefits of treatment outweigh the risks to you and your unborn child or your baby.

#### **Driving and using machines**

Do not drive or use machinery

Some of the possible side effects of AmBisome could affect your ability to drive or use machines safely, See Section 4, *Possible side effects*.

### **AmBisome contains sugar**

Tell your doctor if you have an intolerance to sucrose or other sugars

Tell your doctor if you have diabetes. AmBisome contains approximately 900 mg of sugar (sucrose) in each vial.

### **Important information about some of the ingredients of AmBisome**

AmBisome contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially 'sodium-free'.

AmBisome contains soya oil. If you are allergic to peanut or soya, do not use this medicinal product.

## **3. How AmBisome is used**

AmBisome is always given to you by a doctor or nurse. It is given as an infusion into a vein (a drip).

### **AmBisome must not be given by any other method.**

To prepare the infusion AmBisome must be dissolved in sterile water for injection and then diluted with a solution containing dextrose. AmBisome must not be mixed with saline (salt) solutions or with other drugs or electrolytes.

AmBisome is not interchangeable with other amphotericin products.

### **Before your first treatment**

Before your first treatment your doctor may give you a small amount of AmBisome. They will then wait for approximately 30 minutes to see whether you have an allergic reaction, before continuing the infusion of the full dose.

### **Use in adults and in elderly people**

Your dose of AmBisome will depend on your body weight and your own particular needs.

- **Fungal infections of one or more organs of the body:**

Treatment is normally started at 1 mg per kg of body weight, every day over 3 to 4 weeks. Your doctor may decide to increase the amount you receive to as high as 3 mg per kg body weight.

For mucormycosis the starting dose is normally 5 milligrams per kilogram body weight per day. The duration of therapy will be determined on an individual basis by your Doctor

- **Suspected fungal infections in patients with a raised temperature and neutropenia:**

Treatment is normally started at 1 mg per kg body weight, per day. Your doctor may decide to increase the amount you receive to as high as 3 mg per kg body weight.

- **Visceral leishmaniasis:**

The usual dose is 1 to 1.5 mg per kg body weight, per day for 21 days, or 3 mg per kg body weight for 10 days.

If you have a severely weakened immune system (for instance, if you are HIV positive), the dose is 1 to 1.5 mg per kg body weight for 21 days. Due to the risk of re-infection, on-going treatment or a further course of treatment may be needed.

#### **Use in children**

AmBisome has been used to treat children. The dose of AmBisome for a child is calculated per kg of body weight in the same way as for adults.

AmBisome is not recommended in babies under 1 month old.

#### **Use in patients with kidney problems**

No change in dose or frequency of infusion is required. Your doctor or nurse will take regular blood samples to test for changes in kidney function during AmBisome treatment.

#### **How long will the infusion take?**

Normally the infusion will take 30 to 60 minutes. For doses greater than 5 mg per kg of body weight per day, the infusion could take up to 2 hours.

#### **If you receive a higher dose of AmBisome than you should**

You should tell your doctor immediately if you think you received too much AmBisome.

If you have any further questions on the use of this medicine, ask your doctor.

### **4. Possible side effects**

Like all medicines, AmBisome can cause side effects, although not everybody gets them.

Tell your doctor immediately if you have a severe allergic reaction, chest pain, develop an irregular heart beat or kidney problems (signs include tiredness and passing less urine). Severe allergic reaction side effects may include: skin rash, difficulty breathing, wheezing, chest tightness, swelling of the airways/tongue/face/hands or feet, loss of consciousness, confusion or dizziness, rapid or irregular heart beat, vomiting and nausea.

#### **Side effects during the infusion**

*You may get side effects during the infusion:*

- **Very common** (*may affect more than 1 in 10 people treated*): fever, chills, and shivering.
- **Less frequent infusion-related side effects include:** chest tightness, chest pain, breathlessness, difficulty breathing (possibly with wheezing), flushing, a faster heart rate than normal, low blood pressure and musculoskeletal pain (described as joint pain, back pain, or bone pain).

These side effects clear up quickly when the infusion is stopped. These reactions may not happen with future infusions of AmBisome or with a slower infusion (over 2 hours). Your doctor may give you other medicines to prevent infusion-related reactions, or to treat the symptoms if you do get them. If you have a severe infusion-related reaction, your doctor will stop the AmBisome infusion and you should not receive this treatment in the future.

#### **Very common side effects**

*(may affect more than 1 in 10 people treated)*

- Low blood potassium levels, leading to feeling tired, confused, having muscle weakness or cramps
- Feeling sick or being sick
- Fever, chills or shivering.

### **Common side effects**

*(may affect up to 1 in 10 people treated)*

- Low magnesium, calcium or sodium blood levels, leading to feeling tired, confused, muscle weakness or cramps
- High blood sugar levels
- Headache
- A faster heart rate than normal
- Widening of the blood vessels, causing low blood pressure and flushing
- Breathlessness
- Diarrhoea
- Stomach pain
- Rash
- Chest pain
- Back pain
- Abnormal results for liver or kidney function showing up in blood tests or urine tests
- High blood potassium levels

### **Uncommon side effects**

*(may affect up to 1 in every 100 people treated)*

- Bleeding into the skin, unusual bruising and bleeding for a long time after injury
- Fits or seizures (*convulsions*)
- Difficulty breathing, possibly with wheezing
- Pain and swelling around the vein where AmBisome has been infused.

### **Other side effects**

It is not yet clear how frequently these side effects occur:

- low red blood cell levels (*anaemia*), with symptoms of excessive tiredness, being out of breath after light activity, and a pale complexion
- Heart attacks
- Kidney failure
- Severe swelling of the skin around the lips, eyes or tongue
- Breakdown of muscle
- Bone pain and joint pain

### **Interference with Phosphorus blood test results.**

This medicine may interfere with a particular blood test that measures levels of phosphorus (called the PHOSm assay). Please tell your doctor that you are receiving this medicine before such blood tests.

### **Reporting of side effects**

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system:

#### **Ireland**

*HPRA Pharmacovigilance*

*Earlsfort Terrace*

*IRL - Dublin 2*

*Tel: +353 1 6764971*

*Fax: +353 1 6762517*  
*Website: [www.hpra.ie](http://www.hpra.ie)*  
*e-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).*

By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store AmBisome**

AmBisome is stored in the pharmacy.

Keep this medicine out of the sight and reach of children.

Do not use AmBisome after the expiry date which is stated on the label after {EXP}. The expiry date refers to the last day of the month.

Do not store above 25 °C. Do not store partially used vials for future patient use.

AmBisome is a single dose, unpreserved, sterile, freeze-dried yellow powder to be dissolved in water for injection and diluted with a dextrose solution before infusion into a vein. From a microbiological point of view, the product should be used immediately once dissolved and diluted. If it is not used immediately, in-use storage times and conditions prior to use are the responsibility of the doctor or pharmacist and would normally not be longer than 24 hours at 2°C to 8°C unless reconstitution (dissolving the powder in water for injection) and dilution have taken place in controlled conditions to prevent microbial contamination.

Where reconstitution (dissolving the powder in water for injection) and dilution with dextrose solution are carried out under controlled conditions the storage time varies depending on the concentration of dextrose used and the storage temperature. Please refer to the Summary of Product Characteristics for further information.

Do not use AmBisome if there is any evidence of deterioration or foreign matter.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

## **6. Content of the pack and other information**

### **What AmBisome contains**

**The active substance is** amphotericin B. Each vial contains 50 mg of amphotericin B enclosed inside liposomes (small fat particles).

**The other ingredients are:** hydrogenated soy phosphatidylcholine, cholesterol, distearoylphosphatidylglycerol, alpha tocopherol, sucrose (sugar), disodium succinate hexahydrate, sodium hydroxide and hydrochloric acid.

### **What AmBisome looks like and contents of the pack**

AmBisome is a sterile, bright yellow Powder for Concentrate for Dispersion for infusion.

It is presented in a 15 ml, 20 ml or 30 ml glass vial.

Each vial contains 50 mg of the active ingredient amphotericin B.

The closure consists of a rubber stopper and an aluminium ring seal fitted with a removable plastic cap.

Each carton contains 10 vials and 10 filters.

Not all pack sizes may be marketed.

### **Marketing Authorisation Holder and Manufacturer**

#### **Marketing authorisation holder**

Gilead Sciences Ireland UC  
Ida Business & Technology Park  
Carrigtohill  
Co Cork  
Ireland

#### **Manufacturer**

Gilead Sciences Ireland UC,  
IDA Business & Technology Park,  
Carrigtohill,  
County Cork,  
Ireland

For any information about this medicine or for alternative formats of this leaflet for the visually impaired, please contact the local representative of the Marketing Authorisation Holder:

#### **Ireland**

Gilead Sciences Ireland UC  
Tel: +353 214 825 999

**This leaflet was last revised in 02/2024**

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**The following information is intended for healthcare professionals only:**

**READ THIS ENTIRE SECTION CAREFULLY BEFORE BEGINNING RECONSTITUTION.**

**AmBisome is NOT interchangeable with other amphotericin products.**

**AmBisome must be reconstituted using Sterile Water for Injection (without a bacteriostatic agent) and diluted in Dextrose solution (5%, 10% or 20%) for infusion only.**

The use of any solution other than those recommended, or the presence of a bacteriostatic agent (e.g. benzyl alcohol) in the solution, may cause precipitation of AmBisome.

AmBisome is NOT compatible with saline and must not be reconstituted or diluted with saline or administered through an intravenous line that has previously been used for saline



unless first flushed with dextrose solution (5%,10% or 20%) for infusion. If this is not feasible, AmBisome should be administered through a separate line.

Do NOT mix AmBisome with other drugs or electrolytes.

Aseptic technique must be observed in all handling, since no preservative or bacteriostatic agent is present in AmBisome, or in the material specified for reconstitution and dilution.

Vials of AmBisome Containing 50 mg of Amphotericin B are Prepared as Follows:

1. Add 12 ml of Water for Injection to each AmBisome vial, to yield a preparation containing 4 mg/ml amphotericin B.

**Step 1**



2. IMMEDIATELY after the addition of water, SHAKE THE VIAL VIGOROUSLY for 30 seconds to completely disperse the AmBisome. After reconstitution the concentrate is a translucent, yellow dispersion. Visually inspect the vial for particulate matter and continue shaking until complete dispersion is obtained. Do not use if there is evidence of precipitation of foreign matter.

**Step 2**



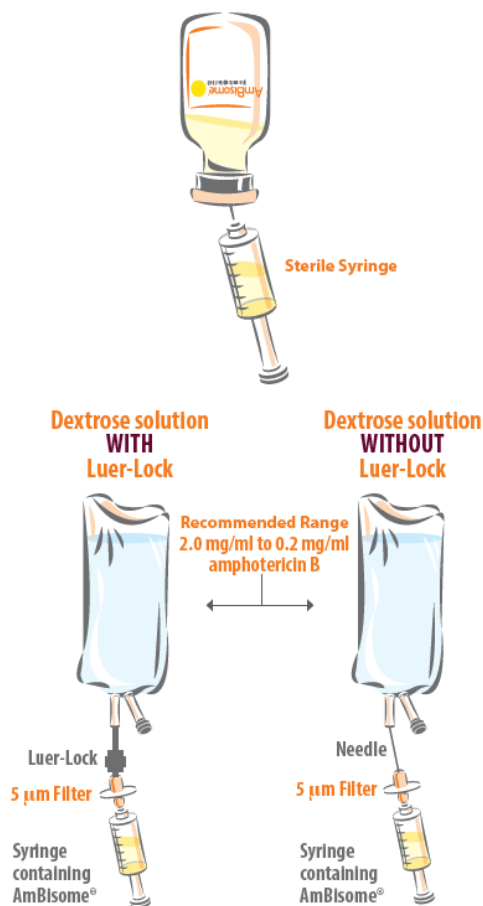
3. Calculate the amount of reconstituted AmBisome (4 mg/ml) to be further diluted (see table below).

4. The infusion solution is obtained by dilution of the reconstituted AmBisome with between one (1) and nineteen (19) parts dextrose solution (5%, 10% or 20%) for infusion by volume, to give a final concentration in the recommended range of 2.00mg/ml to 0.20mg/ml amphotericin B as AmBisome (see table below).

5. Withdraw the calculated volume of reconstituted AmBisome into a sterile syringe. Using the 5-micron filter provided, instill the AmBisome preparation into a sterile container with the correct amount of Dextrose solution (5%, 10% or 20%) for infusion.

An in-line membrane filter may be used for intravenous infusion of AmBisome. However, the mean pore diameter of the filter should not be less than 1.0 micron.

### Step 5



### Preparation of AmBisome for Infusion

An example is provided in the table below of the preparation of AmBisome dispersion for infusion at a dose of **3mg/kg/day** in dextrose 5% solution for infusion. Note that this table relates to doses of **3mg/kg/day** only, however other doses than this may be prescribed for a patient. If a dose other than **3mg/kg/day** has been prescribed for a patient, then the appropriate calculations must be undertaken and the table cannot be used.

Table 2: Example of the preparation of AmBisome dispersion for infusion at a dose of **3mg/kg/day** in dextrose 5% solution for infusion

Weight of patient (kg)	Number of vials required to prepare dose*	Amount of AmBisome required by the patient (to be withdrawn for further dilution) (mg)	Volume of reconstituted AmBisome to be withdrawn for further dilution (ml)**	To make up a 0.2mg/ml final concentration (1 in 20 dilution)		To make up a 2.0mg/ml final concentration (1 in 2 dilution)	
				Volume of 5% dextrose needed (ml)	Total volume (ml; AmBisome plus 5% dextrose)	Volume of 5% dextrose needed (ml)	Total volume (ml; AmBisome plus 5% dextrose)
10	1	30	7.5	142.5	150	7.5	15
25	2	75	18.75	356.25	375	18.75	37.5
40	3	120	30	570	600	30	60
55	4	165	41.25	783.75	825	41.25	82.5
70	5	210	52.5	997.5	1050	52.5	105
85	6	255	63.75	1211.25	1275	63.75	127.5

\* The full contents of a vial(s) may not be required to prepare a dose for a patient.

\*\* Each vial of AmBisome (50mg) is reconstituted with 12ml Water for Injection to provide a concentration of 4mg/ml Amphotericin B.

For single use only. Discard any unused contents.

Any unused product or waste material should be disposed of in accordance with local requirements.