1.3.2 Patient Information Leaflet

SCHEDULING STATUS:

S4

AmBisome® (intravenous infusion)

Amphotericin B 50 mg (50 000 units) per vial (after reconstitution, the concentrate contains 4 mg/mL amphotericin B).

Contains sucrose 900 mg

Read all of this leaflet carefully before you are given AmBisome

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.

What is in this leaflet

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1. What AmBisome is and what it is used for

- AmBisome contains an antifungal antibiotic, which is a medicine used to treat serious infections caused by fungi.
- AmBisome is also used for the treatment of visceral leishmaniasis, a disease caused by a parasite.

2. What you need to know before you are given AmBisome

AmBisome should not be administered to you:

- If you suffer from known allergic or hypersensitive reactions to the active ingredient amphotericin B or any of the other ingredients (see above).
- If you are allergic to peanut or soya, do not receive AmBisome, since AmBisome contains soya oil.
- If you have previously experienced a severe anaphylactic or anaphylactoid reaction to AmBisome (an immediate, life-threatening allergic reaction with symptoms including flushing, itching, sickness, swelling of the face, mouth, tongue and airways, often enough to cause difficulty breathing).

Warnings and precautions

Tell your doctor or healthcare provider before being given the injection if:

Your doctor will take special care with AmBisome:

- If you experience other reactions that are thought to be related to the infusion. If this happens, your doctor might slow down the infusion so you receive AmBisome over a longer

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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. AmBisome may cause damage to the kidneys. Your doctor will take regular samples to test creatinine (a chemical in the blood that reflects kidney function) and electrolyte levels which can be abnormal due to reduced kidney function.
- If the results of your blood tests show that the level of potassium in your blood is low.
- If the results of your blood tests show a change in kidney function or other important changes.
- If you are receiving or have just received a leukocyte (white blood cell) transfusion.
- If you are receiving haemodialysis or filtration for kidney function.
- If you are diabetic. AmBisome contains approximately 900 mg of sucrose in each vial (see 'AmBisome contains sucrose').

Other medicines and AmBisome:

If you are taking other medicines on a regular basis, including complementary or traditional medicines, concomitant use of **AmBisome** may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare provider for advice.

Tell your doctor if you are taking any of the following medicines:

- Medicines that may cause kidney damage, including:

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- Immunosuppressant agents (medicines that supress the immnune system) such as cyclosporine;
- Any of the group of antibiotics known as aminoglycosides including gentamycin, neomycin and streptomycin;
- Pentamidine (a medicine used to treat pneumonia in people with AIDS and leishmaniasis);

• Medicines that may lower your potassium levels:

- Corticosteroids (anti-inflammation medicines) and corticotrophin (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) for example furosemide;
- Digitalis glycosides used to treat heart failure. AmBisome may worsen the side effects of digitalis;
- Skeletal muscle relaxants used in anaesthesia during surgery.

• Other medicines:

- Antifungals such as flucytosine;
- Anticancer agents 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;
- Leukocyte 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.

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Pregnancy and breastfeeding and fertility:

If you are pregnant or breastfeeding your baby while receiving AmBisome, please consult your doctor, pharmacist or other healthcare professional for advice.

The safety of AmBisome during pregnancy and whilst breastfeeding is not known.

It is not known whether AmBisome passes into breast milk.

Before you begin using any new medicine (prescription or non-prescription) or if you develop any new medical problem while you are being given this medicine, check with your doctor, nurse, or pharmacist.

Driving and using machinery:

AmBisome may cause headache and chest tightness or pain (see 'Possible side effects'), but have minimal effect on mental and/or physical abilities to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision.

It is not always possible to predict to what extent AmBisome may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which AmBisome affects them.

AmBisome contains sucrose

AmBisome contains sucrose which may have an effect on the control of your blood sugar if you have diabetes mellitus.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before receiving AmBisome.

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3. HOW AmBisome IS GIVEN:

Do not share medicines prescribed for you with any other person.

The usual dose is:

- AmBisome is always given to you by a doctor or nurse.
- The dosage of AmBisome is dependent on body weight and is adjusted to meet the needs of each individual patient.
- Your doctor will decide on the appropriate dosage for you.
- Children:

  AmBisome has been used to treat children aged from 1 month to 18 years old.

  AmBisome has not been studied in babies under 1 month old.
- Elderly*:*

  No change in dose or frequency of infusion is required for elderly patients.
- Patients with reduced kidney function:

  No change in dose or frequency of infusion is required. Your doctor will take regular blood samples to test for changes in kidney function.
- If you have the impression that the effect of AmBisome is too strong or too weak, talk to your doctor or pharmacist. The dose will be controlled in regular intervals by your doctor and adapted if necessary.

The route of administration:

You will not be expected to give yourself AmBisome. It will be given to you by a person who is qualified to do so.

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If you received more AmBisome than you should:

Since a healthcare professional will administer AmBisome, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you missed a dose of AmBisome:

Since a healthcare professional will administer AmBisome, it is unlikely that the dose will be missed.

4. Possible side effects

AmBisome can have side effects.

Not all side effects reported for AmBisome are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking AmBisome, please consult your healthcare professional for advice.

If any of the following happens, stop receiving AmBisome and tell your doctor immediately:

- Swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing;
- rash or itching;
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to AmBisome. You may need urgent medical attention.

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Side effects during the infusion

- Fever, chills and shivering are the most common infusion related reactions expected to occur during the infusion;
- less frequent infusion related sideeffects can include back pain, chest tightness, chest pain, breathlessness, difficulty in breathing, flushing, a faster than normal heart rate and low blood pressure.

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.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Feeling tired or confused or having muscle weakness or cramps caused by low magnesium, calcium or sodium levels in the blood;
- abnormal results for liver or kidney function showing up in blood or urine tests;
- high blood sugar levels;
- breathlessness.

These are all serious side effects. You may need urgent medical attention.

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Tell your doctor if you notice any of the following:

The following adverse events occurred more commonly during treatment with AmBisome:

- Feeling tired or confused or having muscle weakness or cramps caused by low potassium levels in the blood;
- feeling sick or being sick;
- fever, chills or shivering.

The following adverse events occurred less commonly during treatment with AmBisome:

- Headache;
- a faster heart rate than normal;
- widening of the blood vessels, low blood pressure and flushing;
- diarrhoea, abdominal pain;
- abnormal results for liver or kidney function showing up in blood or urine tests;
- pain in the chest or back;
- Bleeding into the skin, unusual bruising and bleeding for a long time after injury (thrombocytopenia);
- Fits or seizures (*convulsions*);
- Pain and swelling around the vein where AmBisome has been infused (phlebitis).

The following side effects have been reported but the frequency is unknown:

- low red blood cell levels (*anaemia*), with symptoms of excessive tiredness, being out of breath after light activity, and a pale complexion;
- Heart attacks (cardiac arrest);

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- Kidney failure (renal failure);
- Breakdown of muscle (rhabdomyolysis);
- 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.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/. By reporting side effects, you can help provide more information on the safety of AmBisome.

5. How to store AmBisome

- The shelf life is printed on the label.
- Do not use this medication after the date printed on the label.
- Do not store above 25 °C .

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- As the product does not contain any bacteriostatic agent, from a microbiological point of view, the reconstituted or diluted product should be used immediately.
- In-use storage times and conditions prior to administration are the responsibility of the user and would normally not be longer than 24 hours at 2 °C - 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.
- However, the physical and chemical stability of AmBisome has been demonstrated for up to 24 hours at 2 °C – 8 °C, following reconstitution with sterile water for injection.
- When diluted with 5 %, 10 % or 20 % dextrose, AmBisome should be administered as soon as possible.
- Keep all medicines out of the reach of children
- Store in the original package / container.
- Do not store in a bathroom.
- Do not use after the expiry date stated on the label / carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).
- Do not use AmBisome if there is any evidence of deterioration or foreign matter.

6. Contents of the pack and other information

What AmBisome contains

- The active substance is:

Each vial contains 50 mg Amphotericin B (50 000 units) encapsulated in liposomes as the active ingredient.

- The other inactive ingredients are:

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Hydrogenated soy phosphatidylcholine, cholesterol, distearoylphosphatidylglycerol, alpha tocopherol, sucrose, disodium succinate hexahydrate, sodium hydroxide and hydrochloric acid.

Contains sugar: sucrose 900 mg per vial.

Contains soya oil.

What AmBisome looks like and contents of the pack

Yellow lyophilised cake or powder, free of visible evidence of contamination.

Reconstituted solution: Translucent, yellow emulsion, essentially free of visible contamination or agglomerates.

AmBisome is presented in 15 ml or 20ml sterile, clear, colourless, Type I glass vials. The closure consists of butyl rubber stoppers and aluminium ring seals fitted with removable plastic caps. Single-dose vials are packed ten per carton with 10 sterile disposable 5 micron syringe filters included.

Holder of Certificate of Registration and Manufacturer

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Access to the corresponding Professional Information

Can be obtained on the SAHPRA website

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