Package leaflet: Information for the patient

Fungizone 50mg
Powder for Sterile Concentrate

Amphotericin B

Please read all of this leaflet carefully before you start taking your medicine because it contains important information for you.

- **Please keep this leaflet. You may need to read it again.**
- **If you have any further questions, ask your doctor.**

This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What Fungizone 50mg Powder for Sterile Concentrate is and what it is used for

The name of your medicine is Fungizone 50mg Powder for Sterile Concentrate. It contains the active ingredient amphotericin B, which belongs to a group of medicines called anti-fungal antibiotics.

Fungizone 50mg Powder for Sterile Concentrate is used to treat serious infections caused by yeasts and certain fungi.

2. What you need to know before being given your medicine

You should not be given this medicine if you:

- are **allergic** (hypersensitive) to amphotericin B or any of the other ingredients in this medicine.

Take special care with Fungizone 50mg Powder for Sterile Concentrate if you:

- have any **kidney** or **liver problems**

If this applies to you, talk to your doctor before being given Fungizone 50mg Powder for Sterile Concentrate.

Taking other medicines

Always tell your doctor or pharmacist about other medicines you may be taking or have recently taken including those obtained without a prescription.

This is especially important if you are taking:

- any anti-cancer medicines (e.g. methotrexate, cyclophosphamide, cisplatin)
- any medicines which affect your kidney function (e.g. gentamicin, vancomycin)
- any muscle relaxants (e.g. baclofen, dantrolene, diazepam)
- any corticosteroids (e.g. beclomethasone) or corticotrophins
- any medicines to treat heart failure (e.g. digoxin)
- a medicine called flucytosine used to treat fungal infections

If you have recently had a specific type of transfusion called a leukocyte transfusion, please tell your doctor.

Pregnancy and breast-feeding

If you are pregnant, think you may be pregnant, or if you are breast-feeding, speak to your doctor before being given Fungizone 50mg Powder for Sterile Concentrate.

Driving and using machinery

Fungizone 50mg Powder for Sterile Concentrate should not affect your ability to drive.

Fungizone contains sodium

This medicinal product contains less than 1mmol sodium (23mg) per dose, i.e. essentially ‘sodium-free’.

3. How you will be given your medicine
Fungizone 50mg Powder for Sterile Concentrate will be given to you in hospital by a doctor or nurse.
The daily dose is 0.25-1.0mg per kg of your body weight. In some cases your doctor may consider it necessary to increase this dose to 1.5mg/kg. If you are given too much of this medicine, you may experience life-threatening heart or lung problems. If you have any concerns about the amount of medicine you have been given, please speak to the person who has given you the infusion for further advice.

It will be given to you slowly through a drip into a vein (an infusion). This will usually take between 2-6 hours.

A test dose may be given before you start treatment with this medicine. Several months of treatment is usually necessary to get rid of the infection completely.

In some patients, the doctor may give other medicines to help reduce other unwanted effects.

These include:

- medicines to help stop you feeling sick or being sick,
- aspirin,
- an anti-allergy medicine (antihistamine),
- a corticosteroid
- a medicine to stop your blood from clotting (anticoagulant).

4. Possible side effects
Like all medicines, Fungizone 50mg Powder for Sterile Concentrate can cause side effects, although not everybody gets them.

Treatment with Fungizone 50mg Powder for Sterile Concentrate may affect your blood cells, kidneys, liver or heart. For this reason, your doctor will want to monitor all these things before, during and after giving you this medicine.

If you notice any of the following, contact your doctor **immediately**:
- swelling of the face, lips, or tongue
- skin reactions including severe rash and itching
- difficulty breathing

As these may be signs of an allergic reaction.

There have been reports of blood disorders which may be characterised by fever or chills, sore throat, ulcers in the mouth or throat, unusual tiredness or weakness, unusual bleeding or unexplained bruises. Tell your doctor **immediately** if you notice any of these symptoms.

The following side effects have been seen in some patients receiving Fungizone by spinal injection: severe stinging/burning pain in the spine, spinal cord injury, impaired movement and loss of ability to move or feel anything.

Fungizone 50mg Powder for Sterile Concentrate can cause kidney problems. If you notice that you are more thirsty, need to go to the toilet more frequently, or the volume of urine increases, tell your doctor **immediately.**
Patients treated with Fungizone have reported the following side effects:

Very Common side effects (affects more than 1 user in 10):
- Feeling sick and being sick
- High temperature (sometimes with shaking chills)
- Decrease in potassium in the blood
- Increase in creatinine in the blood
- Kidney problems which may lead to abnormal urine production, kidney stones and imbalances of substances in the blood (e.g. potassium)
- Difficulty in breathing
- Low blood pressure

Common side effects (affects 1 to less than 10 users in 100):
- Anaemia-low level of red blood cells
- Abnormal liver function shown by abnormal liver function tests
- Decreased magnesium in the blood
- Headache
- Diarrhoea
- Rash
- Decreased appetite
- Sudden loss of kidney function
- Pain at the injection site with or without swollen veins or a blood clot

Uncommon side effects (affects 1 to less than 10 users in 1,000):

- A rare form of anaemia where there is a low level of white blood cells
- Low counts of white blood cells in the blood
- Low counts of platelets in the blood
- Impaired sensation or movement
- Irregular heartbeat, sometimes severe
- Spasm of the lungs
- Pain in the stomach
- Yellowing of the skin and eyes
- Pain in muscles
- Impaired or abnormal kidney function
- Flushing

Rare side effects (affects 1 to less than 10 users in 10,000):

- Abnormal blood clotting
- High counts of white blood cells in the blood
- Allergic reactions
- Increased potassium in the blood
- Altered mental state
- Convulsion
- Vision blurred or double vision
- Hearing loss, ringing in the ears
- Short-lived spinning sensation (vertigo)
- Heart attack or heart not working properly
- High blood pressure
- Shock
- Inflammation of the lungs and fluid in the lungs
- Stomach cramps, indigestion
- Bleeding in intestines, resulting in black faeces
- Loss of liver function
- Rash – characterised by a flat red area on the skin that is covered with small bumps
- Itching
- Flu like symptoms followed by a painful red or purple spreading rash
- Skin conditions including skin coming off in layers
- Pain in joints
- Abnormal kidney function with increased or decreased amounts of urine produced
- Pain and tiredness
- Decreased weight

Reporting of side effects
If you get any 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 directly via:

HPRA Pharmacovigilance
Earlsfort Terrace
IRL- Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie.

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

5. How to store your medicine

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

Unopened product will be stored in a refrigerator (2-8°C) in the pharmacy and should not be used after the expiry date shown on the carton/label.

This medicine will be prepared in a special area before the doctor or nurse gives it to you. After being mixed together the medicine will be kept for no more than 8 hours at room temperature (25°C) or 24 hours in a refrigerator (2-8°C). It should be stored protected from light.

6. Contents of the pack and other information

What Fungizone 50mg Powder for Sterile Concentrate contains
The active substance is amphotericin B (50 mg per vial). The other ingredients are desoxycholic acid, concentrated phosphoric acid, sodium hydroxide, disodium phosphate dodecahydrate, monosodium phosphate dihydrate, water.

What Fungizone 50mg Powder for Sterile Concentrate looks like and contents of the pack
Fungizone 50mg Powder for Sterile Concentrate is a yellow to orange, fluffy powder and is supplied in glass vials.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
CHEPLAPHARM Arzneimittel GmbH
Ziegelhof 24
17489 Greifswald
Germany

Manufacturer
Delpharm Saint Remy
Usine de Saint-Remy
Rue de l'Isle
28380 Saint-Remy-Sur-Avre
France

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PLEASE DETACH BEFORE HANDING ABOVE SECTION TO THE PATIENT

INFORMATION FOR HEALTH PROFESSIONALS

Below is a summary of the dosage, administration, reconstitution and storage details for Fungizone 50mg Powder for Sterile Concentrate. Reference should be made to the Summary of Product Characteristics for full prescribing information.

ADMINISTRATION
Posology
Fungizone should be administered by intravenous infusion over a period of 2-6 hours (in rare instances infusion times of up to 6 hours may be necessary). Reduction of the infusion rate may reduce the incidence of side effects. Initial daily dose should be 0.25 mg/kg of body weight gradually increasing to a level of 1.0 mg/kg of body weight depending on individual response and tolerance. Within the range of 0.25-1.0 mg/kg the daily dose should be maintained at the highest level which is not accompanied by unacceptable toxicity. In seriously ill patients the daily dose may be gradually increased up to a total of 1.5 mg/kg. Since amphotericin B is excreted slowly, therapy may be given on alternate days in patients on the higher dosage schedule. Several months of therapy are usually necessary; a shorter period of therapy may produce an inadequate response and lead to relapse.
When commencing all new courses of treatment, it is advisable to administer a test dose immediately preceding the first dose. A volume of the infusion containing 1mg (i.e. 10mL) should be infused over 20-30 minutes and the patient carefully observed for at least a further 30 minutes. It should be noted that patient responses to the test dose may not be predictive of subsequent severe side effects.

Whenever medication is interrupted for a period longer than seven days, therapy should be resumed by starting with the lowest dosage level, i.e. 0.25 mg/kg of body weight and increased gradually.

CAUTION:
Under no circumstances should a total daily dose of 1.5 mg/kg be exceeded. The recommended concentration for intravenous infusion is 10 mg/100 mL.

Amphotericin B may be the only effective treatment available for potentially life threatening fungal disease. In each case, its possible life saving benefit must be balanced against its untoward and dangerous side effects.

Paediatric population
Safety and effectiveness in paediatric patients have not been established through adequate and well-controlled studies. Systemic fungal infections have been treated in paediatric patients without reports of unusual side effects.

Older people
No specific dosage recommendations or precautions.

RECONSTITUTION:
Reconstitute as follows: An initial concentrate of 5 mg amphotericin B per ml is first prepared by rapidly expressing 10ml sterile water for injection, without a bacteriostatic agent, directly into the lyophilized cake, using a sterile needle (minimum diameter: 20 gauge) and syringe. Shake the vial immediately until the colloidal solution is clear. The infusion solution, providing 10mg/100ml is obtained by further dilution (1:50) with 5% Glucose Injection of pH above 4.2. The pH of each container of Glucose Injection should be ascertained before use. Commercial Glucose Injection usually has a pH above 4.2; however, if it is below 4.2 then 1 or 2 ml of buffer should be added to the Glucose Injection before it is used to dilute a concentrated solution of amphotericin. The recommended buffer has the following composition:

Dibasic sodium phosphate (anhydrous) 1.59 g
Monobasic sodium phosphate (anhydrous) 0.96 g
Water for Injections BP q.s. to 100 mL

The buffer should be sterilised before it is added to the Glucose Injection, either by filtration through a bacterial filter, or by autoclaving for 30 mins at 15 lb pressure (121°C).

CAUTION:

Aseptic technique must be strictly observed in all handling, since no preservative or bacteriostatic agent is present. Do not reconstitute with saline solutions.
The use of any diluent other than the ones recommended or the presence of a bacteriostatic agent in the diluent may cause precipitation of the amphotericin B. Do not use the initial concentrate or the infusion solution if there is any evidence of precipitation of foreign matter.
An in-line membrane filter may be used for intravenous infusion of amphotericin; however the mean pore diameter of the filter should not be less than 1.0 micron in order to assure passage of the amphotericin dispersion.
Other preparations for injection should not be added to the infusion solution or administered via the cannula being used to administer Fungizone.

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

The use of Fungizone by other routes has been documented in the published literature:

Bladder irrigation/instillation (eg candiduria): Continuous irrigation with 50mg Fungizone in 1 litre sterile water each day until urinary cultures are negative. Intermittent use of volumes of 100-400mL (concentrations of 37.5-200 mcg/mL) has also been reported. The urine should be alkalinized (with potassium citrate) and antifungal ointment applied to the perineal area.

Lung inhalation (eg pulmonary aspergillosis): 8-40 mg amphotericin B (nebulized in sterile water or 5% Glucose) has been given daily in divided doses. Concurrent eradication of oral and intestinal yeast reservoirs is recommended.

Intrathecal (eg coccidiodal meningitis): Patients who do not respond to fluconazole or itraconazole would be candidates for intrathecal amphotericin B therapy with or without continuation of azole treatment. The intrathecal dosage of amphotericin B normally ranges between 0.1mg and 1.5mg per dose, administered at intervals ranging from daily to weekly, beginning at a low dosage and increasing the dosage until the appearance of patient intolerance. Amphotericin B is irritating when injected into the CSF
Reports of neurological events such as arachnoiditis, myelopathy, paresis and paralysis have been associated with the intrathecal route of administration

Other: Other uses of solutions prepared using Fungizone include local instillations for the treatment of fungal infections of the ear, eye, peritoneum, lung cavities and joint spaces.

SPECIAL PRECAUTIONS FOR STORAGE
Vials of powder for reconstitution should be stored in a refrigerator
Reconstituted: After reconstitution with 10 mL sterile Water for Injections the concentrate (5 mg/ml) should be stored protected from light. Chemical and physical in-use stability has been demonstrated for 8 hours at up to 25 °C and 24 hours at 2-8 °C.

From a microbiological point of view, due to the absence of any microbial preservative, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the

responsibility of the user. These would normally not be longer than 24 hours at 2-8 °C unless reconstitution has taken place in controlled and validated aseptic conditions. It is not intended as a multidose vial. Any unused material should be discarded. Solutions prepared for intravenous infusion (i.e. 10 mg or less amphotericin per 100 mL) should be used promptly after preparation.