PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

VORIFEND IV (200 mg) lyophilised powder for solution for infusion.

Voriconazole.

Sugar free.

Read all of this leaflet carefully before you are given **VORIFEND IV.**

- 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

1. What VORIFEND IV is and what it is used for

2. What you need to know before you take VORIFEND IV

3. How to take VORIFEND

4. Possible side effects

5. How to store VORIFEND

6. Contents of the pack and other information

1. What VORIFEND IV is and what it is used for

VORIFEND IV contains a medicine called voriconazole. It belongs to a group of medicines called antifungals.

It works by killing or stopping the growth of the fungi that cause infections.

VORIFEND IV is used for the treatment of patients (adults and children over the age of 2) with:

- Invasive aspergillosis (a type of fungal infection due to *Aspergillus sp.*),
- Serious invasive *Candida sp*. infections
- Serious fungal infections caused by *Scedosporium sp*. or *Fusarium sp*. (two different species of fungi).

VORIFEND IV is also used in the prevention of fungal infections in high risk patients, e.g. bone marrow transplant recipients or relapsed leukaemia patients.

This product should only be used under the supervision of a doctor.

2. What you need to know before you are given VORIFEND IV

VORIFEND IV should not be administered to you:

- If you are allergic to voriconazole, to hydroxypropyl betacyclodextrin or any of the other ingredients of VORIFEND IV (listed in section 6).
- If you are known to have an abnormality of electrocardiogram (ECG) called 'long QTc syndrome'.
- If you are pregnant or breastfeeding.
- If you have severe liver impairment.

Tell your doctor, nurse or pharmacist if you are taking any of the following medicines:

- astemizole (used for allergy).
- cisapride (used for stomach problems).
- pimozide (used for treating mental illness).
- quinidine (used for irregular heartbeat).
- terfenadine (used for allergy).
- rifampicin (used for treating tuberculosis).
- carbamazepine (used to treat seizures).
- phenobarbitone (used for severe insomnia and seizures).

- efavirenz (used for treating HIV) in doses of 400 mg and above once daily.
- ritonavir (used for treating HIV) in doses of 400 mg and more twice daily.
- ergot alkaloids (e.g. ergotamine, dihydroergotamine; used for migraine).
- sirolimus (used in transplant patients).
- rifabutin (used for treatment of tuberculosis).
- St John's Wort (herbal supplement).

VORIFEND IV must not be co-administered with these medicines.

Warnings and precautions

Tell your doctor or healthcare professional before being given VORIFEND IV:

- If you have had an allergic reaction to other azoles antifungal medicines.
- If you are known to have cardiomyopathy, irregular heartbeat, or slow heart rate.
- If you are suffering from or have ever suffered from liver disease. If you have liver disease, your doctor may prescribe a lower dose of VORIFEND IV. Your doctor should also monitor your liver function while you are being treated with VORIFEND IV by doing blood tests.

You should avoid any sunlight and sun exposure while being treated. It is important to cover sun exposed areas of skin and use sunscreen with high sun protection factor (SPF), as an increased sensitivity of skin to the sun's UV rays can occur.

These precautions are also applicable to children.

While being treated with VORIFEND IV:

Tell your doctor immediately if you develop:

- Sunburn.
- Severe skin rash or blisters.
- Bone pain.

If you develop skin disorders as described above, your doctor may refer you to a dermatologist, who after consultation may decide that it is important for you to be seen on a regular basis. There is a small chance that skin cancer could develop with long term use of VORIFEND IV.

Children and adolescents

VORIFEND IV should not be given to children younger than 2 years of age.

Other medicines and VORIFEND IV:

Always tell your healthcare professional if you are taking any other medicine
(This includes complementary or traditional medicines).

- Everolimus (used for treating advanced kidney cancer and in transplant patients).
- Fluconazole (used for fungal infections).
- Phenytoin (used to treat epilepsy). If you are already being treated with phenytoin your blood concentration of phenytoin will need to be monitored during your treatment with VORIFEND IV and your dose may be adjusted.
- Warfarin and other anticoagulants (e.g. phenprocoumon, acenocoumarol; used to slow down clotting of the blood).
- Benzodiazepines (e.g midazolam, triazolam) (used for severe insomnia and stress)
- Ciclosporin (used in transplant patients)
- Tacrolimus (used in transplant patients)
- Oxycodone and other long acting opiates such as hydrocodone (used for moderate to severe pain)
- Methadone (used to treat heroin addiction)
- Non-steroidal anti-inflammatory drugs (e.g. ibuprofen, diclofenac) (used for treating pain and inflammation)
- Omeprazole (used for treating ulcers)

- Oral contraceptives (if you take voriconazole whilst using oral contraceptives, you may get side effects such as nausea and menstrual disorders)
- Alfentanil and fentanyl and other short acting opiates such as sufentanil (painkillers used for surgical procedures)
- Statins (e.g. atorvastatin, simvastatin) (used for lowering cholesterol)
- Sulphonylureas (e.g. tolbutamide, glipizide, and glyburide) (used for diabetes)
- Vinca alkaloids (e.g. vincristine and vinblastine) (used in treating cancer)
- Indinavir and other HIV protease inhibitors (e.g. saquinavir, amprenavir and nelfinavir) used for treating HIV
- Non-nucleoside reverse transcriptase inhibitors (e.g. delavirdine, nevirapine) (used for treating HIV)
- Cimetidine (used for heartburn and peptic ulcers)
- Digoxin (used to treat various heart conditions
- Macrolide antibiotics (e.g. erythromycin)
- Mycophenolic acid (used in transplant patients)
- Prednisolone (used to treat certain types of allergies, inflammatory conditions, autoimmune disorders and cancers)
- Ranitidine (used to treat peptic ulcers and gastric reflux)

Pregnancy, breastfeeding and fertility

VORIFEND IV must not be used during pregnancy. Effective contraception must be used in women of childbearing potential. Contact your doctor immediately if you become pregnant while being treated with VORIFEND IV.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Driving and using machines

VORIFEND IV may cause blurring of vision or uncomfortable sensitivity to light. While affected, do not drive or operate any tools or machines. Tell your doctor if you experience this.

VORIFEND IV contains sodium

Each vial of VORIFEND IV contains 225,60 mg of sodium chloride per vial. This should be taken into consideration if you are on a strictly controlled sodium diet.

3. How VORIFEND IV will be administered

VORIFEND IV powder for solution for infusion will be reconstituted and diluted to the correct concentration by your healthcare professional.

This will be given to you by intravenous infusion (into a vein in your arm with a needle) at a maximum rate of 3 mg/kg per hour over 1 to 2 hours.

Your doctor will determine your dose depending on your weight and the type of infection you have.

Your doctor may change your dose depending on your condition.

The recommended dose for adults (including older people and adolescents 12 to 16 years of age) is as follows:

Dose for the first 24 hours (Loading dose): 6 mg/kg every 12 hours.

Dose after the first 24 hours (Maintenance dose): 4 mg/kg twice a day.

Dose after the first 24 hours (Maintenance dose), when used to prevent fungal infections: 3 mg/kg twice a day.

Depending on your response to treatment, your doctor may decrease the dose to 3 mg/kg twice daily.

The doctor may decide to decrease the dose if you have mild to moderate liver disease.

The recommended dose for children (2 to 12 years of age) is as follows:

Dose for the first 24 hours (Loading dose): 6 mg/kg every 12 hours.

Dose after first 24 hours (Maintenance dose): 4 mg/kg every 12 hours.

Depending on your response to treatment, your doctor may increase or decrease the daily dose.

If you missed a dose of VORIFEND IV:

As you will be given this medicine under close medical supervision, it is unlikely that a dose would be missed. However, tell your doctor or pharmacist if you think that a dose has been forgotten.

If your treatment with VORIFEND IV is stopped

VORIFEND IV treatment will continue for as long as your doctor advises, however duration of treatment with VORIFEND IV powder for solution for infusion should be no more than 6 months.

Patients with a weakened immune system or those with difficult infections may require long term treatment to prevent the infection from returning. You may be switched from the intravenous infusion to tablets once your condition improves.

When VORIFEND IV treatment is stopped by your doctor you should not experience any effects.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or other healthcare professional.

4. Possible side effects

VORIFEND IV can have side effects.

Not all side effects reported for VORIFEND IV are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving VORIFEND IV, please consult your doctor, pharmacist or other healthcare professional for advice.

Tell your doctor or nurse straight away if you notice any of the following side effects. These are very serious side effects and you may need urgent medical treatment:

- rash, itching, swelling of your face, lips or throat or difficulty breathing with wheezing.
- serious breathing difficulties.
- yellowing of the skin and eyes, dark urine, and tiredness which may be symptoms of liver problems.

Other frequent side effects include:

- Flu-like symptoms, irritation and inflammation of the gastrointestinal tract, inflammation of the sinuses, inflammation of the gums, chills, weakness.
- Low numbers of some types of red or white blood cells, low numbers of cells called platelets that help the blood to clot.
- Low blood sugar, low blood potassium, low sodium in the blood.
- Anxiety, depression, confusion, agitation, inability to sleep, hallucinations.
- Seizures, tremors or uncontrolled muscle movements, tingling or abnormal skin sensations, increase in muscle tone, sleepiness, dizziness.
- Bleeding in the eye.
- Heart rhythm problems including very fast heartbeat, very slow heartbeat, fainting.
- Low blood pressure, inflammation of a vein (which may be associated with the formation of a blood clot).
- Breathing difficulty, chest pain, swelling of the face, fluid accumulation in the lungs.

- Nausea, vomiting, diarrhoea, abdominal pain, constipation, indigestion, inflammation of the gums.
- Jaundice, redness of the skin
- Skin rashes which may lead to severe blistering and peeling of the skin characterized by a flat, red area on the skin that is covered with small confluent bumps, itchiness or hair loss.
- Back pain
- Fever, chills, chest pain

Other less frequent side effects include:

- Swelling or inflammation of the large intestine (colon).
- Blood cell changes (increased eosinophil and low white blood cells in blood).
- Allergic reaction or exaggerated immune response.
- Depressed function of the adrenal gland, underactive thyroid gland.
- High amount of cholesterol in the blood.
- Abnormal brain function, Parkinson-like symptoms, nerve injury resulting in numbness, pain, tingling or burning in the hands or feet, problems with balance or coordination, swelling of the brain.
- Double vision, serious conditions of the eye including: pain and inflammation of the eyes and eyelids, involuntary movement of the eye, abnormal eye movement, damage to the optic nerve resulting in vision impairment, optic disc swelling.
- Hearing difficulties, ringing in ears, vertigo.
- Very fast heart rate or skipped heartbeats, abnormal electrocardiogram (ECG).
- Inflammation of the walls of the lymphatic vessels.
- Inflammation of certain internal organs-pancreas and duodenum, swelling and inflammation of the tongue.
- Enlarged liver, liver failure, gallbladder disease, gallstones.

- Allergic skin reactions (sometimes severe), including widespread blistering rash and skin peeling, inflammation of the skin, the rapid swelling (oedema) of the dermis, subcutaneous tissue, mucosa and submucosal tissues, itchy or sore patches of thick, red skin with silvery scales of skin, hives, sunburn or severe skin reaction following exposure to light or sun, skin redness and irritation, red or purple discoloration of the skin which may be caused by low platelet count, eczema.
- Arthritis.

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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the **Adverse Drug Reaction Reporting Form**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store VORIFEND IV

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Unopened vials must be stored at or below 25 °C in the original package to protect from light. Once reconstituted, VORIFEND IV should be used immediately, but if necessary may be stored for up to 24 hours at 2°C - 8°C (in a refrigerator). Your doctor, nurse or pharmacist knows how to prepare and store the drip (solution for infusion) properly.

- Do not use after the expiry date printed on the label or carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What VORIFEND IV contains

The active substance is voriconazole.

Each VORIFEND IV vial contains 200 mg Voriconazole. When reconstituted as directed, each ml contains 10 mg Voriconazole.

The other ingredients are hydroxypropylbetadex, sodium chloride, hydrochloric acid and water for injection.

What VORIFEND IV looks like and contents of the pack

Before reconstitution, VORIFEND IV is a white to off white lyophilised powder.

The reconstituted solution is clear, colourless and free from visible particles.

Vorifend IV powder for solution for infusion is packed in a 25 ml type I colourless glass vial, sealed with a grey rubber stopper and an aluminium cap with plastic sub-cap of red colour. Supplied in packs of 1 vial packed in a cardboard box accompanied with an instruction leaflet.

Holder of Certificate of Registration and Manufacturer

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