Patient Information Leaflet

SCHEDULING STATUS: S4

VORISPORE 200 IV, 200 mg powder for solution for infusion

Voriconazole

Sugar free

Contains 88,74 mg sodium/vial

Read all of this leaflet carefully before you are given VORISPORE

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- VORISPORE has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What VORISPORE is and what it is used for

VORISPORE is an antifungal medicine. It works by killing or stopping the growth of the fungi that cause infections.

VORISPORE is used for the treatment of a wide variety of fungal infections in patients (adults and children over the age of 2).

VORISPORE may also be used for the prevention of fungal infections in high risk bone marrow transplant recipients.

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

VORISPORE should not be administered to you:

- if you are hypersensitive (allergic) to voriconazole or any ingredient in VORISPORE (listed in section 6);
- if you have prolonged QT-syndrome (a heart rhythm disorder);
- if your liver function is severely affected;
- if you are pregnant or breastfeeding;

A list of the medicines that may affect VORISPORE is shown in the section “Other medicines and VORISPORE”. However, the medicines in the following list must not be taken during your course of VORISPORE treatment:

- Astemizole (used for allergy)
- Cisapride (used for stomach problems)
- Pimozide (used for treating mental illness)
- Quinidine (used for irregular heartbeat)
- Ergot alkaloids (e.g. ergotamine, dihydroergotamine; used for migraine)
- Rifampicin, rifabutin (used for treating tuberculosis)
- Efavirenz (used for treating HIV) in doses of 400 mg and above once daily

- Carbamazepine (used to treat seizures)
- Phenobarbital (phenobarbitone) (used for severe insomnia and seizures)
- Ritonavir (used for treating HIV) in doses of 400 mg and more twice daily
- Sirolimus (used in transplant patients)
- St. John's Wort (herbal supplement used for depression).

Warnings and precautions

Women of childbearing potential

If you are a woman of childbearing potential you must always use effective contraception during treatment. See "Pregnancy and breastfeeding".

Tell your doctor or healthcare professional before being given VORISPORE, if you:

- are allergic to other azole type medicines (for example, fluconazole or ketoconazole which are antifungal medicines. Ask your doctor or pharmacist if you are unsure);
- if there is a possibility that you can get pregnant (if you are of childbearing age). VORISPORE cannot be used to treat patients who are pregnant or breastfeeding. Your doctor will advise you on effective contraception;
- are suffering from liver disease or have ever suffered from it. If you have liver disease, your doctor may prescribe a lower dose of VORISPORE. Your doctor should also monitor your liver function while you are being treated with VORISPORE by doing blood tests;
- you are known to have cardiomyopathy (diseased heart muscle), irregular heartbeat, slow heart rate or an abnormality of electrocardiogram (ECG) called 'long QTc syndrome';
- have a metabolic disorder such as low potassium, calcium or magnesium;

- have a kidney disease. Depending on the degree of kidney disease the doctor may decide to rather give you voriconazole tablets. Your doctor should monitor your renal function while you are being treated with VORISPORE by doing blood tests.

You should also know that:

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 VORISPORE, 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 VORISPORE.

VORISPORE can cause problems with your eyes and vision, including blurred vision, altered colour sensation and light sensitivity. You should wear sunglasses to protect your eyes from bright light. Tell your doctor immediately if you have any eye/vision problems.

If you had an organ transplant and receive VORISPORE, you may have inflammation and pain in the bones. See your doctor as soon as possible. He/she will decide if you should continue treatment with VORISPORE and will treat you as necessary.

Children

Sunburn or severe skin reaction following exposure to light or sun was experienced more frequently in children. If your child develops skin disorders, your doctor may refer your child to a dermatologist, who after consultation may decide that it is important for

your child to be seen on a regular basis. Elevated liver enzymes were also observed more frequently in children.

Other medicines and VORISPORE

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

Some medicines, when taken at the same time as VORISPORE, may affect the way VORISPORE works or VORISPORE may affect the way they work.

*VORISPORE **must not be used** if you are already taking any of the following list of medicines. Tell your doctor if you take:*

- Astemizole (used for allergy)
- Terfenadine (used for allergy)
- Cisapride (used for stomach problems)
- Pimozide (used for treating mental illness)
- Quinidine (used for irregular heartbeat)
- Carbamazepine (used to treat seizures)
- Phenobarbital (phenobarbitone) (used for severe insomnia and seizures)
- Efavirenz (used for treating HIV). Standard doses of VORISPORE and standard doses (400 mg or more) of efavirenz must not be given together
- Ergot alkaloids (e.g. ergotamine, dihydroergotamine; used for migraine)
- Rifampicin (used for treating tuberculosis)
- Ritonavir (used for treating HIV) in doses of 400 mg and more twice daily
- St. John’s Wort (herbal supplement used for depression)
- Sirolimus (used in transplant patients).

Tell your doctor if you are taking the following medicine, as treatment with VORISPORE at the same time should be avoided if possible:

- Ritonavir (used for treating HIV) in doses of 100 mg twice daily.
- Rifabutin (used for treating tuberculosis). If you are already being treated with rifabutin, VORISPORE is contraindicated and may not be administered.
- 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 VORISPORE and your dose may be adjusted.

Tell your doctor if you are taking any of the following medicines, as a dose adjustment or monitoring may be required to check that the medicines and/or VORISPORE are still having the desired effect:

- Everolimus (used for treating advanced kidney cancer and in transplant patients)
- Fluconazole (used for fungal infections)
- Warfarin (used to slow down clotting of the blood)
- Benzodiazepines (for example 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 VORISPORE while 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 (for example atorvastatin, simvastatin) (used for lowering cholesterol)
- Sulfonylureas (for example tolbutamide, glipizide, and glyburide) (used for diabetes)
- Vinca alkaloids (for example vincristine and vinblastine) (used in treating cancer)
- Other protease inhibitors (for example, saquinavir, amprenavir and nelfinavir)
- Non-nucleoside reverse transcriptase inhibitors (e.g. efavirenz, delavirdine, nevirapine) (used for treating HIV) (some doses of efavirenz can NOT be taken at the same time as VORISPORE)
- Indinavir and other HIV protease inhibitors (used for treating HIV).

Do not start taking or using a new medicine before you have discussed this with your doctor or pharmacist. Your doctor and pharmacist have more information on medicines to be careful with, or to avoid while you are given VORISPORE.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking VORISPORE.

You should not use VORISPORE when you are pregnant.

You must use effective contraception if you are of childbearing age. Contact your doctor immediately if you become pregnant while being treated with VORISPORE.

It is not known if VORISPORE is excreted in breastmilk. You should not breastfeed your baby if you receive VORISPORE.

Driving and using machines

VORISPORE may affect your vision and you may feel dizzy. You should not drive or operate machinery until you know how VORISPORE affects you.

VORISPORE contains sodium

Each vial of VORISPORE contains 225,6 mg sodium chloride, which provides 88,74 mg sodium (main component of cooking/table salt). Talk to your doctor or pharmacist if you need 6 or more vials daily for a prolonged period, especially if you have been advised to follow a low salt (sodium) diet.

3. How to use VORISPORE

VORISPORE should only be used under the supervision of a doctor.

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

Your doctor will decide what dose (depending on your weight) you should receive for your condition and also for how long you need to receive it. The dose and duration of treatment will depend on how your body and the infection reacts on the treatment.

Usually you will be given 6 mg VORISPORE per kg body mass, every 12 hours for the first 24 hours and thereafter 4 mg/kg every 12 hours as maintenance dose. If you use efavirenz (for HIV) or phenytoin (anti-seizure medicine), your doctor may adapt your dosage. See “Other medicines and VORISPORE”.

Your doctor or other healthcare provider will give you VORISPORE through a slow infusion (a drip for 1 to 2 hours) into one of your large veins.

Before it is used, VORISPORE powder for solution for infusion will be reconstituted and diluted to the correct concentration by your hospital pharmacist or nurse.

You may be switched from the intravenous infusion to tablets once your condition improves.

If you have the impression that the effect of VORISPORE is too strong or too weak, tell your doctor or pharmacist.

If you receive more VORISPORE than you should

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

If you missed a dose of VORISPORE

Since a healthcare provider will administer VORISPORE, it is unlikely that the dose will be missed.

If you stop using VORISPORE

It is important that you finish your treatment as prescribed by your doctor.

Do not expect to stop receiving VORISPORE just because you feel better. If you stop receiving treatment before the course is completed, the fungus causing the disease may become resistant to VORISPORE and your disease will get worse.

4. Possible side effects

VORISPORE can have side effects.

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

If any of the following happens, stop using VORISPORE and tell your doctor immediately:

- Serious allergic reactions, including a shock reaction. You may have swelling of the tongue and/or throat, difficulty in swallowing, difficulties in breathing, facial swelling, severe dizziness with very fast heartbeat and heavy sweating.

- Allergic skin reactions (sometimes severe), including 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, irritation of the skin and mucous membranes, life threatening skin condition that causes large portions of the epidermis, the skin's outermost layer, to detach from the layers of skin below.

These are all very serious side effects. If you have them, you may have had a serious reaction to VORISPORE. You may need urgent medical attention or further hospitalisation.

Tell your doctor immediately if you notice any of the following:

- Jaundice (yellowing of the eyes or skin, dark urine, upper stomach pain), liver failure, gallbladder disease, gallstones.
- Deterioration of brain function that is a serious complication of liver disease.
- Inflammation of the pancreas (abdominal pain, fever, rapid pulse, nausea, shivering).
- Severe diarrhoea and nausea with fever and weakness. This is a serious condition for which you may need urgent treatment.
- Heart rhythm disturbances, including very fast heartbeat, very slow heartbeat, conduction problems (sometimes life threatening), fainting.
- Double vision, serious conditions of the eye including pain and inflammation of the eyes and eyelids, abnormal eye movement, damage to the optic nerve resulting in vision impairment, optic disc swelling.
- Disorder of blood clotting system (clotting in the blood vessels). Some signs of a blood clot in your arm or leg may be swelling, pain, a warm sensation, reddish discolouration. Some signs of a blood clot in your lungs may be sudden shortness of breath, chest pain, heart pain and coughing. Some signs of a blood clot in your brain

may be sudden numbness or weakness in the face, arm or leg, confusion, trouble speaking.

- Guillain-Barre syndrome (the body's immune system attacks part of the peripheral nervous system, with resulting muscle weakness, beginning in the feet and hands).
- Liver injury, inflammation of the liver. Some signs may be yellowing of the skin and eyes, nausea and fever.
- Kidney failure, inflammation in the kidney, blood in the urine, problems urinating, changes in kidney function tests, protein in the urine.

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

Tell your doctor if you notice any of the following:

Frequent side effects

- Sinusitis (infection of the nasal passages).
- Low numbers of some types, including severe, of red (sometimes immune-related) and/or white blood cells (sometimes with fever), low numbers of cells called platelets that help the blood to clot (a blood test will be used to check these levels).
- You get more infections than usual. This could be because of a decrease in white blood cells. Your doctor will confirm this with a blood test.
- Low blood sugar, low blood potassium or low sodium in the blood (you will only know for sure that you have these deficiencies if you go for blood tests). Tell your doctor if you have muscle cramps and feel weak.
- Easy or excessive bruising, superficial bleeding into the skin, unexpected excessive bleeding, particularly if you also take or receive blood thinning medicines such as warfarin.
- Depression, problems falling asleep, anxiety, hallucinations (false perceptions).
- Sleepiness, feeling faint and/or dizzy.

- Convulsions (fits or jerks), muscle contractions, severe headache, loss of coordination.
- Tingling or abnormal skin sensations, increase in muscle tone, inability to flex the neck forward due to rigid neck muscles.
- Bleeding in the eye, blurred vision, change in colour vision, eyes sensitive for light, night blindness, a defect of vision in which objects appear greenish, colour blindness, a defect in vision where objects appear blue, eye problems, seeing bright circles that surround a light source, night blindness, seeing small specks, dots, circles, lines, a defect of vision in which objects appear yellowish.
- Shortness of breath, shortness of breath after exercise.
- Low blood pressure (you may feel faint or dizzy).
- Inflammation of a vein (phlebitis, a condition where the veins close to the surface of the body become swollen, tender, and red and may develop blood clots).
- Nausea (feeling sick), vomiting (being sick), diarrhoea (loose bowels), stomach pain, inflammation of the lips
- Liver problems (shown in laboratory tests)
- Constipation, indigestion
- Skin rashes, hair loss
- Back pain
- Feeling tired and generally weak
- Swelling around the eyes, lips, mouth, hands or feet.

Less frequent side effects

- Enlarged lymph glands (sometimes painful), failure of bone marrow, increased eosinophil
- High blood cholesterol (shown in laboratory tests)
- Overactive thyroid. If you have muscle weakness, have a rapid heartbeat and increased appetite, tell your doctor

- Underactive thyroid (some signs may be weight gain, fatigue and depression).
- Abnormal sense of taste
- Decreased sensitivity to touch
- Abnormal brain function, Parkinson-like symptoms, nerve injury resulting in numbness, pain, tingling or burning in the hands or feet
- Sudden behaviour changes, problems with thinking or speech
- Problems with balance or coordination, swelling of the brain
- Eye-rolling disorder where the eyes fix upwards
- Swelling and inflammation of nerves that transmit visual information to your eye or brain. Some signs are pain with eye movement and temporary vision loss in one eye.
- Ringing in the ears, dizziness, hearing loss
- Inflammation of certain internal organs – pancreas and duodenum, swelling and inflammation of the tongue
- Inflammation of the thin tissue that lines the inner wall of the abdomen and covers the abdominal organ (you may have signs like abdominal pain, bloating, fever, nausea)
- Bullous photosensitivity (skin blisters caused by sunlight)
- Freckles and pigmented spots
- Joint and muscle pains in the legs and arm
- Movement disorders (restlessness), parkinsonism (tremor, slow movement, impaired speech or muscle stiffness)
- Sleeplessness
- Flu-like illness
- Shivering, reactions at the site of the injection, including fever, reddening of the skin, pain, hardness or swelling
- Increased blood cholesterol

- Infusion site reaction (flushing, fever, sweating, increased heart rate and shortness of breath). Your doctor may stop the infusion if this occurs.

Other significant side effects whose frequency is not known, but should be reported to your doctor immediately:

- Skin cancer
- Inflammation of the tissue surrounding the bone
- Red, scaly patches or ring-shaped skin lesions that may be a symptom of an autoimmune disease called cutaneous lupus erythematosus
- Reactions on the infusion: flushing, fever, sweating, quick heartbeat, tight chest, shortness of breath, faintness, nausea, itching and rash.

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. You can also report side effects to SAHPRA on the SAHPRA website: www.sahpra.org.za. By reporting side effects, you can help provide more information on the safety of VORISPORE.

5. How to store VORISPORE

Store all medicines out of reach of children.

Store in the original carton at or below 25 °C.

Reconstituted solutions:

Once reconstituted, VORISPORE should be used immediately, but if necessary, may be stored for up to 72 hours at 2-8 °C or at room temperature (at or below 25 °C).

Reconstituted VORISPORE needs to be diluted with a compatible infusion solution first before it is infused. Your healthcare professional will prepare and store the solution according to the directions on the professional information.

6. Contents of the pack and other information

What VORISPORE contains

- The active substance is voriconazole.

  Each vial contains 200 mg voriconazole, equivalent to a 10 mg/ml solution when reconstituted by your hospital pharmacist or nurse.

- The other ingredients are hydroxypropyl-beta-cyclodextrin (HP-beta-CD), sodium chloride and hydrochloric acid (for pH adjustment).

What VORISPORE looks like and contents of the pack

A white to off-white, lyophilised powder.

The prepared solution is clear and without visible particles.

VORISPORE is packed in a single-use 25 ml clear, colourless, glass type I vial, closed with a grey rubber stopper and an aluminium cap with a red plastic flip-off seal. The vials are individually packed in cardboard boxes together with the patient information leaflet.

Holder of Certificate of Registration

Astral Pharma (Pty) Ltd

125 Meade Street

George

6529

South Africa

This leaflet was last revised in

Registration date: 21 January 2021

Registration number

49/20.1.7/1210

Access to the corresponding Professional Information

To be decided.