

1.3.2 Patient Information Leaflet

SCHEDULING STATUS: S5

Vorispore 50 FC, film-coated tablet

Vorispore 200 FC, film-coated tablet

Voriconazole

Contains sugar (lactose monohydrate)

Each Vorispore 50 FC tablet contains 58,77 mg lactose monohydrate and each Vorispore 200 FC tablet contains 235,08 mg lactose monohydrate.

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 or your pharmacist.
- 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
2. What you need to know before you use Vorispore
3. How to use Vorispore
4. Possible side effects
5. How to store Vorispore
6. Contents of the pack and other information

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 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 when the fungus is resistant to fluconazole (another antifungal medicine),

- serious fungal infections caused by *Scedosporium sp.* or *Fusarium sp.* (two different species of fungi).Vorispore may also be used for the prevention of fungal infections in high risk bone marrow transplant recipients.

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

2. What you need to know before you use 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.

It is very important that you inform your doctor or pharmacist if you are taking or have taken any other medicines, even those that are obtained without a prescription, or herbal medicines. There are many medicines that must **not** be taken during your course of Vorispore treatment. (See comprehensive list below, under “Other medicines and Vorispore “Vorispore **must not be** used if you are already taking any of the following list of medicines”).

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Warnings and precautions

Tell your doctor or healthcare provider before you take Vorispore, if you:

- are allergic to other azole type medicines (for example, fluconazole or ketoconazole. Ask your doctor or pharmacist if you are unsure);
- 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. 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 and light sensitivity. You should wear sunglasses to protect your eyes from bright light.

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

Vorispore is not recommended for use in children below the age of 2 years because there is insufficient data on safety and effectiveness in this age group.

Other medicines and Vorispore

Always tell your healthcare provider if you are taking any other medicine. (This includes all complimentary 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 (used for severe insomnia and seizures)
- Efavirenz (used for treating HIV) in doses of 400 mg and above once daily
- 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)
- 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 your blood counts and side effects to rifabutin will need to be monitored. A dose adjustment of Vorispore may be required
- 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 and other anticoagulants (e.g., phenprocoumon, acenocoumarol; 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)

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- 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.

Adequate information is not available on the use of Vorispore in pregnant women. Studies in animals have toxic effects on the developing foetus. The potential risk to humans is unknown. Vorispore should not be used during pregnancy.

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 (see section 4). If this happens, you should not drive or handle tools or machinery.

Vorispore contains lactose

Vorispore contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to use Vorispore

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

Always take Vorispore exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor will decide what dose 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.

The usual dose for adults (including elderly patients) is as follows:

	Body weight 40 kg and more	Body weight below 40 kg
Dose for the first 24 hours (Loading dose)	400 mg every 12 hours for the first 24 hours	200 mg every 12 hours for the first 24 hours

Dose after the first 24 hours (Maintenance dose)	200 mg twice a day	100 mg twice a day
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Depending on your response to treatment, your doctor may increase the daily dose to 300 mg twice a day. The doctor may decide to decrease the dose if you have mild to moderate cirrhosis.

Take your tablet at least one hour before, or one hour after a meal. Swallow the tablet whole with some water.

Use in children and adolescents

Tablets must only be given if the child is able to swallow tablets.

Your child's doctor will work out the dose for your child, based on his/her mass.

He/she will tell you how long the treatment with Vorispore will last.

Take your tablet at least one hour before, or one hour after a meal. Swallow the tablet whole with some water.

The usual dose for children and teenagers is as follows:

	Children aged 2 - 12 years
Dose for the first 24 hours (Loading dose)	6 mg/kg every 12 hours. Your treatment will be started as an infusion
Dose after the first 24 hours (Maintenance dose)	4 mg/kg every 12 hours.

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

Do not receive a double dose to make up for forgotten individual doses.

PIL Guideline

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.

PIL Guideline

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.
- 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)

- 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).
- Kidney failure, inflammation in the kidney, blood in the urine, problems urinating, changes in kidney function tests, proteins in the urine. These are all very serious side effects. If you have them, you may have had a serious reaction to Vorispor. You may need urgent medical attention or hospitalisation. Tell your doctor if you notice any of the following:

Also 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
- 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), severe headache, loss of coordination
- Tingling or abnormal skin sensations, increase in muscle tone

- Bleeding in the eye
- 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
- Constipation, indigestion
- Skin rashes, hair loss
- Back pain
- Feeling tired and generally weak.

Less frequent side effects

- Enlarged lymph glands (sometimes painful), failure of bone marrow, increased eosinophil
- Disorder of blood clotting system
- 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
- 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
- Bullous photosensitivity
- Freckles and pigmented spots
- Joint and muscle pains in the legs and arm.
- Flu-like illness
- Increased blood cholesterol.

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. Some side effects such as temporary blood, cholesterol, kidney or liver problems can only be detected when your doctor orders blood or urine tests to check your progress.

Children

Sunburn or severe skin reaction following exposure to light or sun was experienced more frequently in children. If you or your child develops skin disorders, your doctor may refer you to a dermatologist, who after consultation may decide that it is important for you or your child to be seen on a regular basis. Elevated liver enzymes were also observed more frequently in children.

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 pack at or below 25 °C.

Do not use after the expiry date stated on the label and carton.

Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What Vorispore contains

- The active substance is voriconazole.

Each tablet contains 50 mg or 200 mg voriconazole.

- The other ingredients are pregelatinised starch, lactose monohydrate, povidone K30, croscarmellose sodium, colloidal anhydrous silica and magnesium stearate. The tablet coating, Opadry II White OY-LS-28908, contains titanium dioxide (E171), lactose monohydrate, hypromellose (E464) and macrogol/PEG (E1521).

What Vorispore looks like and contents of the pack

Film-coated tablets.

Vorispore 50 FC is presented as a white to off-white round biconvex film-coated tablet with code V50 on one side.

Vorispore 200 FC is presented as a white to off-white oval biconvex film-coated tablet with code V200 on one side.

The tablets are packed in:

Transparent PVC blisters with aluminium foil packed in cartons of 2, 7, 10, 14, 20, 28, 30, 50, 56 or 100 film-coated tablets together with the professional information and patient information leaflets.

White HDPE bottles with child-resistant PP screw caps with an induction seal liner packed in cartons with 2, 7, 10, 14, 20, 28, 30, 50, 56 or 100 film-coated tablets together with the professional information and patient information leaflets.

Not all pack sizes may be marketed at one time.

Holder of Certificate of Registration

Astral Pharma (Pty) Ltd

125 Meade Street

George

6529

South Africa

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Access to the corresponding Professional Information

To be decided.