SCHEDULING STATUS S4

VORICONAZOLE 50 mg VIATRIS film-coated tablets

VORICONAZOLE 200 mg VIATRIS film-coated tablets

Voriconazole

Contains sugar: lactose monohydrate 64,20 mg per tablet (50 mg) / lactose monohydrate 256,40 mg per tablet (200 mg)

Read all of this leaflet carefully before you start receiving VORICONAZOLE VIATRIS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- VORICONAZOLE VIATRIS 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 VORICONAZOLE VIATRIS is and what it is used for
2. What you need to know before you receive VORICONAZOLE VIATRIS
3. How to receive VORICONAZOLE VIATRIS
4. Possible side effects
5. How to store VORICONAZOLE VIATRIS
6. Contents of the pack and other information

1. What VORICONAZOLE VIATRIS is and what it is used for

VORICONAZOLE VIATRIS contains the active substance voriconazole.

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

VORICONAZOLE VIATRIS 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 a fungus named *Aspergillus sp*).
- Candidaemia (another type of fungal infection due to a fungus named *Candida sp*) in non-neutropenic patients (patients without abnormally low white blood cells count).
- Serious invasive *Candida sp.* infections when the fungus is resistant to fluconazole (another antifungal medicine). Serious fungal infections caused by fungi named *Scedosporium sp.* or *Fusarium sp*. (two different species of fungi).
- VORICONAZOLE VIATRIS is intended for patients with worsening and possibly life-threatening fungal infections.
- VORICONAZOLE VIATRIS should only be taken under the supervision of a doctor. Serious fungal infections caused by a fungus named *Scedosporium sp.* or *Fusarium sp*.

2. What you need to know before you receive VORICONAZOLE VIATRIS

Do not take VORICONAZOLE VIATRIS:

- if you are allergic (hypersensitive) to voriconazole or any other ingredients of VORICONAZOLE VIATRIS (listed in section 6).

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.

The medicines in the following list must not be taken during your course of VORICONAZOLE VIATRIS treatment:

- Terfenadine (used for allergy)

- Astemizole (used for allergy)
- Cisapride (used for stomach problems)
- Pimozide (used for treating mental illness)
- Quinidine (used for irregular heart beat)
- Rifampicin (used for treating tuberculosis)
- Efavirenz (used for treating HIV) in doses of 400 mg and above once daily
- Carbamazepine (used to treat seizures)
- Phenobarbital (used for severe insomnia and seizures)
- Ergot alkaloids (e.g., ergotamine, dihydroergotamine; used for migraine)
- Sirolimus (used in transplant patients)
- Ritonavir (used for treating HIV) in doses of 400mg and more twice daily
- St. John's Wort (herbal supplement).
- Rifabutin (voriconazole is likely to increase plasma concentration significantly)
- Prolonged QT syndrome
- Pregnancy and lactation
- Severe impairment of liver function

Warnings and precautions

Take special care with VORICONAZOLE VIATRIS:

- if you have had an allergic reaction to other azoles.
- 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 VORICONAZOLE VIATRIS. Your doctor should also monitor your liver function while you are being treated with VORICONAZOLE VIATRIS by doing blood tests.
- if you are known to have heart problems, including cardiomyopathy (a disease of the heart muscle), irregular heartbeat, slow heart rate or an abnormality of electrocardiogram (ECG)

called ‘long QTc syndrome’.

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 VORICONAZOLE VIATRIS:

  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 possibility that skin cancer could develop with long-term use of VORICONAZOLE VIATRIS.
- Your doctor should monitor the function of your liver and kidney by doing blood tests.

Children and adolescents

VORICONAZOLE VIATRIS should not be given to children younger than 2 years of age.

Other medicines and VORICONAZOLE VIATRIS

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

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

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

- Ritonavir (used for treating HIV) in doses of 100 mg twice daily.

Tell your doctor if you are taking either of the following medicines, as treatment with VORICONAZOLE VIATRIS at the same time should be avoided if possible, and a dose adjustment of voriconazole may be required:

- 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.
- 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 VORICONAZOLE VIATRIS and your dose may be adjusted.

Tell your doctor if you are taking either of the following medicines, as treatment with VORICONAZOLE VIATRIS at the same time should be avoided if possible, and a dose adjustment of voriconazole may be required:

- Warfarin and other anticoagulants (e.g., phenprocoumon, acenocoumarol; used to slow down clotting of the blood)
- Ciclosporin (used in transplant patients)
- Tacrolimus (used in transplant patients)
- Sulfonylureas (e.g., tolbutamide, glipizide, and glyburide) (used for diabetes)
- Statins (e.g., atorvastatin, simvastatin) (used for lowering cholesterol)
- Benzodiazepines (e.g. midazolam, triazolam) (used for severe insomnia and stress)
- Omeprazole (used for treating ulcers)
- Oral contraceptives (if you take VORICONAZOLE VIATRIS whilst using oral

contraceptives, you may get side effects such as nausea and menstrual disorders)

- Vinca alkaloids (e.g., vincristine and vinblastine) (used in treating cancer)
- Indinavir and other HIV protease inhibitors (used for treating HIV)
- 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 VORICONAZOLE VIATRIS)
- Methadone (used to treat heroin addiction)
- Alfentanil and fentanyl and other short-acting opiates such as sufentanil (painkillers used for surgical procedures)
- Oxycodone and other long-acting opiates such as hydrocodone (used for moderate to severe pain)
- Non-steroidal anti-inflammatory medicines (e.g., ibuprofen, diclofenac) (used for treating pain and inflammation)
- Fluconazole (used for fungal infections)
- Everolimus (used for treating advanced kidney cancer and in transplant patients).

Pregnancy, breastfeeding and fertility

Pregnancy

VORICONAZOLE VIATRIS must not be taken during pregnancy. Effective contraception must be used in women of childbearing potential. Contact your doctor immediately if you become pregnant while taking VORICONAZOLE VIATRIS.

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

Breast-feeding

You should not breast-feed while you are taking VORICONAZOLE VIATRIS.

Driving and using machines

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

VORICONAZOLE VIATRIS contains lactose

VORICONAZOLE VIATRIS contains lactose which may have an effect on the control of your blood sugar with diabetes mellitus. Patients with the rare hereditary conditions of lactose/fructose or galactose intolerance should not take VORICONAZOLE VIATRIS.

3. How to take VORICONAZOLE VIATRIS

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

Always take VORICONAZOLE VIATRIS exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. It is important to keep taking VORICONAZOLE VIATRIS every day.

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

You must take your tablets twice a day, 12 hours apart.

VORICONAZOLE VIATRIS tablets must only be given if a child is able to swallow tablets. Take your tablet at least one hour before, or one hour after a meal. Swallow the tablet whole with some water.

VORICONAZOLE VIATRIS should not be given to children younger than 2 years of age.

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

If you take more VORICONAZOLE VIATRIS than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, seek help at the nearest hospital or poison control centre. You may experience abnormal intolerance to light as a result of taking more VORICONAZOLE VIATRIS than you should.

If you missed a dose of VORICONAZOLE VIATRIS:

It is important to take your VORICONAZOLE VIATRIS tablets regularly at the same time each day. If you forget to take one dose, take your next dose when it is due. Do not take a double dose to make up for a forgotten dose.

Effects when treatment with VORICONAZOLE VIATRIS is stopped

It has been shown that taking all doses at the appropriate times may greatly increase the effectiveness of your medicine. Therefore, unless your doctor instructs you to stop treatment, it is important to keep taking VORICONAZOLE VIATRIS correctly, as described above.

Continue taking VORICONAZOLE VIATRIS until your doctor tells you to stop. Do not stop treatment early because your infection may not be cured. Patients with a weakened immune system or those with difficult infections may require long term treatment to prevent the infection from returning.

When VORICONAZOLE VIATRIS treatment is stopped by your doctor you should not experience any effects.

4. Possible side effects

VORICONAZOLE VIATRIS can have side effects.

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

If any of the following happens, stop taking VORICONAZOLE VIATRIS and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, tongue and 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 reaction to VORICONAZOLE VIATRIS. You may need urgent medical attention or hospitalisation.

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

- 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),
- very fast heart rate or skipped heartbeats, sometimes with erratic electrical impulses,
- abnormal electrocardiogram (ECG),
- heart rhythm or conduction problems (sometimes life threatening),
- jaundice, inflammation of the liver and liver injury (yellowing of the skin and eyes),

- pancreatitis, inflammation of the pancreas.

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- visual impairment (change in vision including blurred vision, visual colour alterations, abnormal intolerance to visual perception of light, colour blindness, eye disorder, halo vision, night blindness, swinging vision, seeing sparks, visual aura, visual acuity reduced, visual brightness, loss of part of the usual field of vision, spots before the eyes),
- fever, rash,
- nausea, vomiting, diarrhoea,
- headache,
- swelling of the extremities,
- stomach pains,
- breathing difficulties,
- elevated liver enzymes,
- inflammation of the sinuses, inflammation of the gums, chills, weakness,
- 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,
- 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,

- constipation, indigestion, inflammation of the lips,
- 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, redness of the skin,
- itchiness,
- hair loss,
- back pain,
- kidney failure, blood in the urine, changes in kidney function tests.

Less frequent side effects:

- flu-like symptoms, irritation and inflammation of the gastrointestinal tract, inflammation of the gastrointestinal tract causing antibiotic associated diarrhoea, inflammation of the lymphatic vessels,
- inflammation of the thin tissue that lines the inner wall of the abdomen and covers the abdominal organ,
- enlarged lymph glands (sometimes painful), failure of blood marrow, increased eosinophil,
- depressed function of the adrenal gland, underactive thyroid gland,
- 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, abnormal eye movement, damage to the optic nerve resulting in vision impairment, optic disc swelling,
- decreased sensitivity to touch,

- abnormal sense of taste,
- hearing difficulties, ringing in the ears, vertigo,
- inflammation of certain internal organs- pancreas and duodenum, swelling and inflammation of the tongue,
- enlarged liver, liver failure, gallbladder disease, gallstones,
- joint inflammation, inflammation of the veins under the skin (which may be associated with the formation of a blood clot),
- inflammation of the kidney, proteins in the urine, damage to the kidney,
- blood cholesterol increased, blood urea increased,
- allergic skin reactions (sometimes severe), including life-threatening skin condition that causes painful blisters and sores of the skin and mucous membranes, especially in the mouth, inflammation of the 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,
- infusion site reaction,
- allergic reaction or exaggerated immune response,
- overactive thyroid gland,
- deterioration of brain function that is a serious complication of liver disease,
- loss of most fibres in the optic nerve, clouding of the cornea, involuntary movement of the eye,
- bullous photosensitivity,
- a disorder in which the body’s immune system attacks part of the peripheral nervous system,
- disorder of blood clotting system,
- 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,

- small dry scaly skin patches, sometimes thick with spikes or ‘horns’.

Side effects with frequency not known:

- freckles and pigmented spots,
- 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.

As VORICONAZOLE VIATRIS has been known to affect the liver and the kidney, your doctor should monitor the function of your liver and kidney by doing blood tests. Please advise your doctor if you have any stomach pains or if your stools have a different consistency.

There have been reports of skin cancer in patients treated with VORICONAZOLE VIATRIS for long periods of time.

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 via the "6.04 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 VORICONAZOLE VIATRIS.

5. How to store VORICONAZOLE VIATRIS

Store all medicines out of reach of children.

Store at or below 25°C.

Keep the blisters in the carton until required for use.

Do not use after the expiry date stated on the carton label or on the blister pack.

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 VORICONAZOLE VIATRIS contains

The active substance is voriconazole.

Each VORICONAZOLE VIATRIS 50 mg and 200 mg film-coated tablets contain voriconazole 50 mg and 200 mg respectively.

The other ingredients are: Croscarmellose sodium, lactose monohydrate, magnesium stearate, povidone (K29/32), pregelatinised starch {colourant: Opadry II white: lactose monohydrate; HPMC 2910/hypromellose 15cP; titanium dioxide, triacetin }

What VORICONAZOLE VIATRIS looks like and contents of the pack

VORICONAZOLE 50 mg VIATRIS:

A white to off-white, film-coated, oval, biconvex tablet debossed with “V26” on one side of the tablet and blank on the other side.

VORICONAZOLE 200 mg VIATRIS:

A white to off-white, film-coated, capsule shaped, biconvex tablet debossed with “M164” on one side of the tablet and blank on the other side.

Contents of the pack:

PVC/Aluminium blister pack (30’s) comprises of clear, transparent PVC film on one side and hard tempered aluminium foil with heat seal lacquer on the other side.

Suitable number of blister strips will be placed in an outer cardboard carton.

The number of tablets per blister strip and the number of blister strips in each carton shall be based on commercial requirement.

Holder of Certificate of Registration

Viatris South Africa (Pty) Ltd

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Republic of South Africa

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Registration numbers

VORICONAZOLE 50 mg VIATRIS: 48/20.1.7/0620

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Access to the corresponding Professional Information

To follow