PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

VFEND 50 mg film-coated tablets

VFEND 200 mg film-coated tablets

Voriconazole

Contains sugar (**lactose monohydrate)**

Each VFEND 50 mg film-coated tablet contains 63,42 mg lactose monohydrate.

Each VFEND 200 mg film-coated tablet contains 253,675 mg lactose monohydrate.

Read all of this leaflet carefully before you start taking VFEND

- 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.
- VFEND 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 VFEND is and what it is used for
2. What you need to know before you take VFEND
3. How to take VFEND
4. Possible side effects
5. How to store VFEND
6. Contents of the pack and other information

1. What VFEND is and what it is used for

VFEND belongs to a group of medicines called triazole antifungal medicines and works by killing or stopping the growth of the fungi that cause infections.

VFEND is used to treat a wide variety of fungal infections and for the prevention of fungal infections in high risk bone marrow transplant recipients.

VFEND has been prescribed for you. Do not allow anyone else to take it.

VFEND should only be taken under the supervision of a doctor.

2. What you need to know before you take VFEND

Do not take VFEND

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

A list of the medicines that may affect VFEND is shown in the section ‘Other medicines and VFEND’. However, the medicines in the following list *must not* be taken during your course of VFEND treatment:

- Terfenadine (used for allergy)
- Astemizole (used for allergy)
- Cisapride (used for stomach problems)
- Pimozide (used for treating mental illness)
- Quinidine (used for irregular heartbeat)
- Ivabradine (used for symptoms of chronic heart failure)
- Rifampicin (used for treating tuberculosis)
- Carbamazepine (used to treat seizures)
- Phenobarbital (used for severe insomnia and seizures)

- St John's Wort (herbal supplement)
- 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 treating tuberculosis)
- Naloxegol (used to treat constipation specifically caused by pain medicines, called opioids, e.g., morphine, oxycodone, fentanyl, tramadol, codeine)
- Tolvaptan (used to treat hyponatremia (low levels of sodium in your blood) or to slow kidney function decline in patients with polycystic kidney disease)
- Lurasidone (used to treat depression)
- Venetoclax (used to treat patients with chronic lymphocytic leukaemia - CLL)

VFEND cannot be used by patients who

- are pregnant or breastfeeding
- have 'long QT syndrome' (an abnormality of the electrocardiogram (ECG))
- have severe impairment of hepatic (liver) function

Warnings and precautions

Take special care with VFEND:

Before being treated with VFEND, tell your doctor:

- if you have had an allergic reaction to other azoles, antifungals.
- if you are known to have cardiomyopathy, irregular heartbeat, slow heart rate or an abnormality of electrocardiogram (ECG) called 'long QTc syndrome'.
- 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 VFEND. Your doctor should also monitor your liver function while you are being treated with VFEND by doing blood tests.

- if you are suffering from or have ever suffered from kidney disease. Your doctor should monitor your renal function while you are being treated with VFEND 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. This may be further increased by other medicines that sensitise the skin to sunlight, like methotrexate. These precautions are also applicable to children.

While being treated with VFEND:

- tell your doctor immediately if you develop
  - sunburn
  - severe skin rash or blisters

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 VFEND**.**

Tell your doctor if you develop signs of 'adrenal insufficiency' (where the adrenal glands do not produce adequate amounts of certain steroid hormones such as cortisol) which may lead to symptoms such as chronic or long lasting fatigue, muscle weakness, loss of appetite, weight loss and abdominal pain.

Tell your doctor if you develop signs of 'Cushing's syndrome', where the body produces too much of the hormone cortisol, which may lead to symptoms such as weight gain, a fatty hump between the shoulders, a rounded face, darkening of the skin on the stomach, thighs, breasts, and arms, thinning skin, bruising easily, high blood sugar, excessive hair growth and excessive sweating.

Your doctor should monitor the function of your liver and kidney by doing blood tests.

Children and adolescents

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

Other medicines and VFEND

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 VFEND, may affect the way VFEND works or VFEND may affect the way they work. Tell your doctor if you are taking any of the following medicines, as VFEND must not be taken if you are already taking any of these medicines:

- Astemizole (used for allergy)
- Cisapride (used for stomach problems)
- Pimozide (used for treating mental illness)
- Quinidine (used for irregular heartbeat)
- Ivabradine (used for symptoms of chronic heart failure)
- Terfenadine (used for allergy)
- Carbamazepine (used to treat seizures)
- Phenobarbital (used for severe insomnia and seizures)
- Ergot alkaloids (including but not limited to ergotamine, dihydroergotamine; used for migraine)
- Rifabutin (used for treating tuberculosis).
- 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)
- Naloxegol (used to treat constipation specifically caused by pain medicines, called opioids, e.g., morphine, oxycodone, fentanyl, tramadol, codeine)

- Tolvaptan (used to treat hyponatremia (low levels of sodium in your blood) or to slow kidney function decline in patients with polycystic kidney disease)
- Lurasidone (used to treat depression)
- Venetoclax (used to treat patients with chronic lymphocytic leukaemia – CLL)

Tell your doctor if you are taking any of the following medicines, as treatment with VFEND at the same time should be avoided if possible:

- Ritonavir (used for treating HIV) in doses of 100 mg twice daily
- Glasdegib (used for treating cancer) – if you need to use both medicines your doctor will monitor your heart rhythm frequently

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

- Phenytoin (used to treat epilepsy)

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

- Warfarin and other anticoagulants (including but not limited to, phenprocoumon, acenocoumarol; used to slow down clotting of the blood)
- Ciclosporin (used in transplant patients)
- Tacrolimus (used in transplant patients)
- Sulphonylureas (including but not limited to tolbutamide, glipizide, and glyburide) (used for diabetes)
- Statins (used for lowering cholesterol)
- Benzodiazepines (including but not limited to midazolam, triazolam and alprazolam) (used for severe insomnia and stress)
- Omeprazole (used for treating ulcers)
- Oral contraceptives (if you take VFEND whilst using oral contraceptives, you may get side effects

such as nausea and menstrual disorders)

- Vinca alkaloids (including but not limited to vincristine and vinblastine) (used in treating cancer)
- Tyrosine kinase inhibitors (including but not limited to axitinib, bosutinib, cabozantinib, ceritinib, cobimetinib, dabrafenib, dasatinib, nilotinib, sunitinib, ibrutinib, ribociclib) (used for treating cancer)
- Tretinoin (used to treat leukaemia)
- Indinavir and other HIV protease inhibitors (used for treating HIV)
- Other non-nucleoside reverse transcriptase inhibitors (including but not limited to delavirdine, nevirapine) (used for treating HIV)
- Methadone (used to treat heroin addiction)
- Efavirenz (used for treating HIV) (some doses of efavirenz cannot be taken at the same time as VFEND)
- Alfentanil, fentanyl and other opiates (painkillers used for surgical procedures)
- Oxycodone and other long acting opiates
- Non-steroidal anti-inflammatory drugs (including but not limited to ibuprofen, diclofenac) (used for treating pain and inflammation)
- Fluconazole (used for fungal infections)
- Everolimus (used for treating advanced kidney cancer and in transplant patients)
- Letermovir (used for preventing cytomegalovirus (CMV) disease after bone marrow transplant)
- Flucloxacillin (antibiotic used against bacterial infections)
- Ivacaftor (used to treat cystic fibrosis)
- Corticosteroids, including inhaled corticosteroids and intranasal corticosteroids, including but not limited to prednisolone, budesonide (used to reduce inflammation)

VFEND with food and drink

VFEND tablets must be taken at least one hour before or one hour after a meal.

Pregnancy and breastfeeding

VFEND 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 VFEND.

Do not take VFEND while you are breastfeeding your baby.

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 health care provider for advice before taking this medicine.

Driving and using machines

VFEND 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.

It is not always possible to predict to what extent VFEND may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which VFEND affects them.

VFEND contains lactose and sodium

If you have been told by your doctor that you have an intolerance to some sugars, tell your doctor before taking VFEND.

VFEND 50 mg and 200 mg tablets contain less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

3. How to take VFEND

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

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

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

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

Your doctor will tell you how long your treatment with VFEND will last. Continue taking VFEND 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.

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

If you take more VFEND than you should

If you take more tablets than prescribed (or if someone else takes your tablets) you must seek medical advice or go to the nearest hospital casualty department immediately. Take your box of VFEND tablets with you.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take VFEND

It is important to take your VFEND 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 forgotten individual

doses.

Effects when treatment with VFEND 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 VFEND correctly, as described above.

When VFEND treatment is stopped by your doctor you should not experience any effects. However, if you were taking medicines containing ciclosporin or tacrolimus you must mention this to your doctor, as the dose will need to be adjusted.

4. Possible side effects

VFEND can have side effects.

Not all side effects reported for VFEND are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking VFEND, please consult your health care provider for advice.

If any side effects occur, most are likely to be minor and temporary. However, some may be serious and need medical attention.

Frequent side effects

- Sinusitis
- Anaemia
- Low numbers of cells called platelets that help the blood to clot
- Low numbers of some types of white blood cells or of all types of blood cells

- Red or purple discoloration of the skin which may be caused by low platelet count, other blood cell changes
- Swelling of the extremities
- Low blood sugar
- Low blood potassium
- Depression
- Hallucinations and other nervous symptoms
- Anxiety
- Inability to sleep
- Agitation
- Confusion
- Headache
- Fainting
- Trembling
- Increase in muscle tone
- Tingling or abnormal skin sensations
- Sleepiness
- Dizziness
- Visual disturbances (change in vision)
- Bleeding in the eye
- Heart rhythm problems including very fast heartbeat, very slow heartbeat
- Low blood pressure
- Inflammation of a vein (which may be associated with the formation of a blood clot)
- Breathing difficulty
- Fluid accumulation in the lungs
- Diarrhoea

- Vomiting
- Stomach pains
- Nausea
- Swelling of the lips
- Dyspepsia (heartburn/indigestion)
- Constipation
- Gingivitis (inflammation of the gums)
- Gastroenteritis (inflammation of gastrointestinal tract)
- Changes in blood tests of liver function
- Jaundice (yellowing of the skin and/or whites of the eyes)
- Hepatitis (inflammation of the liver)
- Rash
- Redness and peeling of the skin
- Hair loss
- Purple spots on the skin due to small blood vessels bursting
- Rash characterised by a flat, red area on the skin that is covered with small bumps that join each other
- Itchiness
- Sunburn or severe skin reaction following exposure to light or sun
- Back pain
- Kidney failure
- Blood in the urine
- Fever
- Chest pain
- Swelling of the face
- Weakness

- Chills
- Flu-like symptoms
- Changes in blood tests of kidney function

Less frequent side effects

- Inflammation of the large intestine (colon) causing diarrhoea
- Failure of blood marrow to produce sufficient healthy blood cells
- Enlarged lymph glands (sometimes painful)
- Increase in a type of white blood cell which may be associated with allergic reaction
- Disorder of blood clotting system
- Allergic reaction or exaggerated immune response
- Depressed function of the adrenal gland
- Underactive thyroid gland
- Overactive thyroid gland
- Manifestation (signs) of swelling of the brain
- Abnormal brain function
- Parkinson-like symptoms
- Nerve injury resulting in numbness, pain, tingling or burning in the hands or feet
- Problem with balance or coordination
- Decreased sensitivity to touch
- Abnormal sense of taste
- Involuntary repetitive movement of the eye
- Decline in brain function that occurs as a result of severe liver disease
- Muscle weakness caused by an abnormal immune system response
- Damage to the optic nerve, swelling of the optic disc or scarring of the cornea resulting in vision impairment
- Prolonged involuntary upward gaze of the eyes

- Double vision
- Pain and inflammation of the eyes and eyelids
- Hearing difficulties
- Sensation that you, or the environment around you, is spinning
- Ringing in the ears
- Very fast heart rate or skipped heartbeats, sometimes with erratic electrical impulses
- Abnormal electrocardiogram (ECG)
- Heart rhythm or conduction problems (sometimes life threatening)
- Inflammation of the lymphatic system (e.g. swelling of tonsils, lymph nodes)
- Peritonitis (inflammation of the lining of the abdominal cavity)
- Pancreatitis (inflammation of the pancreas)
- Swelling and inflammation of the tongue
- Inflammation of upper small intestine
- Liver failure
- Enlarged liver
- Gallbladder disease
- Gallstones
- Allergic skin reactions (sometimes severe), including
    - a life-threatening skin condition causing peeling skin, fever, body aches, a flat red rash, and blisters and sores on the mucosal membranes
    - hives
    - swelling under the skin (usually of the face, lips, tongue, and throat)
    - blistering of skin exposed to sun
    - patches of red, raised skin that often look like a bulls-eye
    - thick scaly rash, ranging in color from red to purple
    - life-threatening skin condition that causes large portions of the epidermis, the skin’s outermost layer, to detach from the layers of skin below

- Eczema (red, itchy skin)
- Psoriasis (scaly, itchy, dry patches of skin)
- Joint pain
- Damage to the kidney
- Proteins in the urine
- Inflammation of the kidney
- Increased blood urea
- Increased blood cholesterol

Other side effects

- Low sodium in the blood
- Skin cancer
- Red, scaly patches or ring-shaped skin lesions that may be a symptom of an autoimmune disease called cutaneous lupus erythematosus
- Symptoms of a serious hypersensitivity reaction called DRESS, including skin rash, fever, swollen glands, increase in a type of white blood cell (eosinophilia) and inflammation of the internal organs
- Inflammation of the periosteum, a layer of connective tissue that surrounds bone (periostitis)

As VFEND 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.

If any of these side effects persist or are troublesome, please tell your doctor.

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 or pharmacist or nurse. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reactions 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 VFEND.

5. How to store VFEND

Store all medicines out of reach of children.

VFEND tablets must be stored at or below 25 °C.

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

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 VFEND contains

The active substance in this medicine is voriconazole.

VFEND 50 mg and 200 mg tablets

Each tablet contains 50 mg and 200 mg voriconazole respectively.

The other ingredients are croscarmellose sodium, lactose monohydrate, magnesium stearate, povidone and 16ypromellose16d starch which make up the tablet core and glycerol triacetate, 16ypromellose, lactose monohydrate and titanium dioxide, which make up the film-coat.

What VFEND looks like and contents of the pack

VFEND 50 mg tablets are white to off-white, round convex tablets, engraved with "Pfizer" on one side and "VOR50" on the other.

VFEND 200 mg tablets are white to off-white, capsule-shaped tablets, engraved with "Pfizer" on one

side and “VOR200” on the other.

VFEND tablets are available in transparent PVC/Aluminium blister packs.

The blister packs are contained in cardboard cartons with pack sizes of 2, 10, 14, 20, 28, 30, 50, 56 or 100 tablets.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

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