Patient Information Leaflet

SCHEDULING STATUS S4

VORZOL® IV (200 mg) powder for solution for infusion

Voriconazole

Sugar free

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.

What is in this leaflet

1. What VORZOL is and what it is used for

VORZOL contains a medicine called voriconazole. VORZOL is an antifungal medicine. It works by killing or stopping the growth of the fungi that cause infections.

It 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.),

- candidaemia (another type of fungal infection due to *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 *Scedosporium* sp. or *Fusarium* sp. (two different species of fungi).

VORZOL is intended for patients with worsening, possibly life-threatening, fungal infections.

Prevention of fungal infections in high risk bone marrow transplant recipients.

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

2. What you need to know before VORZOL is given to you

VORZOL should not be administered to you:

- If you are allergic to the active ingredient voriconazole, or to sulfobutyl ether beta-cyclodextrin sodium or any of the other ingredients of VORZOL (listed in section 6).

- It is very important that you tell 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 VORZOL 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)
- Ivabradine (used for symptoms of chronic heart failure)
- 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 treatment of migraine)
- 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)
- Rifabutin (used for treatment of tuberculosis)
- Ritonavir (used for treating HIV) in doses of 400 mg and more twice daily
- St. John's Wort (herbal supplement)
- Venetoclax (used to treat patients with blood cancers)

VORZOL cannot be used to treat patients who:

- Are pregnant or breastfeeding
- Have "long" QT syndrome (an abnormality of the electrocardiogram (ECG))
- Have severe impairment of the hepatic (liver) function.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before being given VORZOL if:

- You have had an allergic reaction to other azoles antifungal medicines.

- You are suffering from, or have ever suffered from liver disease. If you have liver disease, your doctor may prescribe a lower dose of VORZOL. Your doctor should also monitor your liver function while you are being treated with VORZOL 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 VORZOL:

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 VORZOL.

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, abdominal pain, please 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, 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, excessive sweating, please tell your doctor.

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

Children and adolescents

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

Other medicines and VORZOL

Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including those that are obtained without a prescription.
Some medicines, when taken at the same time as VORZOL, may affect the way VORZOL works or VORZOL may affect the way they work.

Tell your doctor if you are taking the following medicine, as treatment with VORZOL 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 drugs your doctor will monitor your heart rhythm frequently

Tell your doctor if you are taking either of the following medicines, as treatment with VORZOL at the same time should be avoided if possible, and a dose adjustment of VORZOL 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 VORZOL 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 VORZOL are still having the desired effect:

- 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 VORZOL 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)
- Tyrosine kinase inhibitors (e.g., 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)
- 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 VORZOL)
- 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 drugs (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)
- Tolvaptan (used to treat hyponatremia (low levels of sodium in your blood) or kidney function decline in patients with polycystic kidney disease)
- Letermovir (used for preventing cytomegalovirus (CMV) disease after bone marrow transplant)
- Naloxegol (used to treat constipation specifically caused by pain medicines, called opioids, e.g., morphine, oxycodone, fentanyl, tramadol, codeine)
- Ivacaftor (used to treat cystic fibrosis)
- Each vial of VORZOL IV contains 3 380,8 mg of sodium chloride per vial. This should be taken into account if you are on a strictly controlled sodium diet.

Pregnancy and breastfeeding

VORZOL 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 VORZOL.

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

Driving and using machines

VORZOL 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.

3. How VORZOL will be administered to you:

VORZOL powder for solution for infusion will be reconstituted and diluted to the correct concentration by your healthcare professional. The medicine 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 elderly patients) is as follows:

The recommended dose for adults (including elderly patients) is as follows: **Intravenous**	
Dose for the first 24 hours (Loading Dose)	6 mg/kg every 12 hours for the first 24 hours
Dose after the first 24 hours (Maintenance Dose) Prevention of breakthrough 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 liver disease.

Use in children (2 to 12 years of age) and adolescents:

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.

If you did not get VORZOL

Since a health care provider will administer VORZOL, it is unlikely that the dose will be missed.

Effects when treatment with VORZOL is stopped

VORZOL treatment will continue for as long as your doctor advises, however duration of treatment with VORZOL 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.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Not all side effects reported for VORZOL are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving VORZOL, please consult your doctor, pharmacist or other healthcare professional for advice.

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

Tell your doctor or nurse straight away if you notice any of the following serious side effects as you may need urgent medical attention. Patient will be given VORZOL IV and therefore need to alert hospital personnel if they notice serious side effects. Administration will be stopped by the nurse.

- Rash, itching, swelling of your face or throat or difficulty breathing with wheezing.

- Yellowing of the skin and eyes, dark urine, and tiredness which may be symptoms of liver problems. Changes in blood tests of liver function.
- Upper abdominal pain, fever, rapid pulse and tenderness when touching the abdomen, which may be signs of pancreatitis

Other side effects

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
- 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)
- Acute breathing difficulty, chest pain, swelling of the face (mouth, lips and around eyes), fluid accumulation in the lungs
- Constipation, indigestion, inflammation of the lips
- Jaundice, inflammation of the liver and liver injury
- Skin rashes which may lead to severe blistering and peeling of the skin characterised 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:

- 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 organs
- Enlarged lymph glands (sometimes painful), failure of blood marrow, increased eosinophils
- 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
- Very fast heart rate or skipped heartbeats, sometimes with erratic electrical impulses
- Abnormal electrocardiogram (ECG)
- 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

Frequency unknown:

- 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
- Heart rhythm or conduction problems (sometimes life threatening)
- Life threatening allergic reaction
- 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’
- 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

Reactions during the infusion have occurred less frequently with VORZOL (including flushing, fever, sweating, increased heart rate and shortness of breath). Your doctor may stop the infusion if this occurs.

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://sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of VORZOL.

Suspected adverse reaction can also be reported directly to the HCR via Patientsafety.sacg@novartis.com

5. How to store VORZOL

Store all medicines out of reach of children.

- Before reconstitution, store below 30 °C.
- Do not use this medicine after the expiry date which is stated on the label. The expiry date refers to the last day of that month.
- Once reconstituted, VORZOL should be used immediately, but if necessary may be stored for up to 24 hours at 2 °C to 8 °C (in a refrigerator) or at 20 °C to 30 °C for 3 hours.
- Reconstituted VORZOL needs to be diluted with a compatible infusion solution first before it is infused.
- Do not throw away any medicines via wastewater or household waste.
- Ask your pharmacist how to throw away medicines you no longer required. These measures will help protect the environment.

6. Contents of the pack and other information

What VORZOL contains

The active substance is voriconazole.

The other ingredients are sulfobutyl ether beta-cyclodextrin sodium and nitrogen.

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

What VORZOL looks like and contents of the pack

VORZOL powder for solution for infusion will be packed in single 25 ml clear, glass vials, type I, closed with red chlorobutyl rubber stoppers and sealed with aluminium flip-off seals with plastic disc. The sealed vial is packed in an outer cardboard carton.

Pack Size: 1 vial.

Holder of Certificate of Registration

Sandoz South Africa (Pty) Ltd.

Magwa Crescent West

Waterfall City

Jukskei View

Midrand

2090

This leaflet was last revised in

30 May 2022

Registration number

49/20.1.7/1011

Access to the corresponding Professional Information

Not applicable

[1]Company Reg. No.: 1990/001979/07