PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Voriconazole Teva New

Film-coated tablets

Composition

Each film-coated tablet contains:

Voriconazole 200 mg

For information regarding inactive ingredients and allergens, see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for your treatment. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.

1. What is the medicine intended for?

Voriconazole Teva is a broad-spectrum antifungal medicine intended for the treatment of:

- Invasive aspergillosis (an infection caused by fungi of the Aspergillus type).
- Candida infections in the blood system (candidemia) in non-neutropenic patients.
- Invasive Candida infections that are resistant to fluconazole (another antifungal medicine), including C. Krusei.
- Severe fungal infections caused by fungi of the Scedosporium and Fusarium types.

Voriconazole Teva is intended for patients with severe, possibly life-threatening, fungal infections.

Voriconazole Teva is intended for the prevention of invasive fungal infections in high-risk bone marrow transplant recipients.

Therapeutic class:

Antifungal from the triazole class. It works by killing or stopping the growth of the different fungi that cause infections.

2. Before using the medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the additional ingredients the medicine contains, listed in section 6.
- Do not take this medicine with terfenadine (for allergy), astemizole (for allergy), cisapride (for stomach problems), pimozide (for mental problems), quinidine (for heart rate problems), ivabradine (for the treatment of chronic heart failure), rifabutin (for the treatment of tuberculosis), rifampicin (for treatment of tuberculosis), carbamazepine (for the treatment of convulsions), phenobarbital (for the treatment of convulsions and severe insomnia), ergot derivatives (ergotamine, dihydroergotamine; for the treatment of migraines), sirolimus (in transplant patients), efavirenz, at a dosage of 400 mg and more given once a day (for the treatment of HIV), ritonavir at a dosage of 400 mg and more each time, given twice a day (for the treatment of HIV), the Hypericum herb (St. John's Wort), naloxegol (for the treatment of constipation caused mainly by the use of opioid type pain relievers (e.g. morphine, oxycodone, fentanyl, tramadol, codeine)), tolvaptan (used to treat hyponatremia (low levels of sodium in the blood) or used to slow down the decline in kidney function in patients with polycystic kidney disease), lurasidone (for the treatment of depression), venetoclax (for treating patients with chronic lymphocytic leukemia – CLL).

Before treatment with Voriconazole Teva, tell the doctor if:

- You suffer or have suffered in the past from an allergic reaction to preparations from the azole class.
- You suffer from a disease of the heart muscle (cardiomyopathy), irregular or slow heart rate or an electrocardiogram (ECG) abnormality called 'long QTc syndrome'.
- You suffer or have suffered in the past from a liver disease. The doctor will monitor your liver function by performing blood tests.

Special warnings regarding the use of the medicine

- Avoid any sunlight and sun exposure while using the medicine. It is important to cover sun exposed areas of skin and to use sunscreen with a high sun protection factor (SPF), as an increased sensitivity of the skin to sunlight (UV) may occur. This warning is also applicable to children.
- While taking the medicine, tell the doctor immediately if you develop: sunburn, a severe skin rash or blisters, bone pain.
- If one of these skin effects occurs, the doctor may refer you to a dermatologist. There is a small chance of developing skin cancer with long-term use of Voriconazole Teva.
- If you develop signs of 'adrenal insufficiency', a medical condition in which 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 the doctor.
- If you develop symptoms of "Cushing's syndrome" in which the body produces an excess of the hormone cortisol, which may lead to symptoms such as: weight gain, fatty tissue between the shoulders, a rounded face, darkening of the skin on the abdomen, knees, breasts and arms, thin skin, tendency to bruise easily, high blood sugar, excessive hairiness, excessive sweating, please tell the doctor.
- The doctor will monitor liver and kidney function by performing blood tests during the course of treatment with Voriconazole Teva.
- Before starting and during the course of treatment you should be monitored for disturbances in electrolyte levels, such as low levels of potassium, magnesium and calcium.

Children and adolescents

This medicine is not intended for children and infants under the age of two years.

Tests and follow-up

As Voriconazole Teva affects the liver and kidneys, the doctor will monitor your liver and kidney function by performing blood tests. Please tell the doctor if you experience abdominal pain or if there is a change in the texture of your stools.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist. Especially if you are taking:

Medicines you should avoid taking in combination with Voriconazole Teva if possible, and a dosage adjustment is required if given together:

- Phenytoin (for treatment of epilepsy). If you are taking this medicine, your phenytoin blood level should be monitored.
- Ritonavir (for the treatment of HIV) at a low dosage of 100 mg twice a day. Certain dosages of ritonavir cannot be taken with Voriconazole Teva. See "Do not use this medicine if" in this section.
- Glasdegib (for the treatment of cancer) – if you are required to use both medicines, your doctor will monitor your heart rate more often.

Combining Voriconazole Teva with the following medicines may require dosage adjustment and monitoring to ensure that the medicines and/or Voriconazole Teva still have the desired effect:

- Warfarin and other anticoagulants (e.g. phenprocoumon, acenocoumarol)
- Cyclosporine, tacrolimus (for transplant patients)
- Sulfonylurea type medicines (e.g. tolbutamide, glipizide and glyburide) (for the treatment of diabetes)
- Statins (e.g. atorvastatin, simvastatin, lovastatin) (for lowering cholesterol levels)
- Benzodiazepines (e.g midazolam, alprazolam and triazolam) (for the treatment of severe insomnia and as a tranquilizer)
- Omeprazole (for the treatment of stomach ulcer)
- Birth control pills (side effects such as nausea and menstrual disorders may occur)
- Vinca derivatives (e.g. vincristine, and vinblastine) (for the treatment of cancer)
- Tyrosine kinase inhibitors (e.g. axitinib, bosutinib, cabozantinib, ceritinib, cobimetinib, dabrafenib, dasatinib, nilotinib, sunitinib, ibrutinib, ribociclib) (for the treatment of cancer)
- Tretinoin (for the treatment of leukemia)
- Indinavir and other HIV protease inhibitors (for the treatment of HIV)
- NNRTI medicines for the treatment of HIV (e.g. delavirdine, nevirapine, efavirenz) (certain dosages of efavirenz cannot be taken with Voriconazole Teva, see "Do not use this medicine if" in this section)
- Methadone (for the treatment of addiction)
- Short-acting opiates (e.g. alfentanil, fentanyl, sufentanil) (pain relievers in surgical procedures)
- Oxycodone and hydrocodone (to relieve moderate to severe pain)
- Non-steroidal anti-inflammatory drugs (e.g. ibuprofen and diclofenac) (for the treatment of pain and inflammation)
- Fluconazole (for the treatment of fungal infections)
- Everolimus (for the treatment of advanced kidney cancer and in transplant patients)
- Letermovir (for preventing cytomegalovirus (CMV) induced disease after bone marrow transplant)
- Ivacaftor (for the treatment of cystic fibrosis (CF))

For a list of medicines not to be taken concomitantly with Voriconazole Teva, please see "Do not use this medicine if" in this section.

Pregnancy and breastfeeding

Do not use this medicine if you are pregnant, unless you have received an explicit instruction from the doctor. Women of childbearing age should use effective contraceptives when using the medicine. If you become pregnant while taking Voriconazole Teva refer to your doctor immediately.

If you are pregnant or breastfeeding, think you might be pregnant or are planning to become pregnant, consult the doctor before taking this medicine.

Driving and operating machinery

Voriconazole Teva may cause blurred vision or sensitivity to light. If you are affected by this, do not drive or operate dangerous machinery. Children should be cautioned against riding a bicycle or playing near a road etc.

Important information about some of the ingredients of the medicine

- The tablet contains lactose, therefore if you have been told by your doctor that you have an intolerance to certain sugars, refer to the doctor before taking this medicine.
- The tablet contains less than 1 mmol (23 mg) of sodium, and is therefore considered "sodium-free".

3. How should you use the medicine?

Always use the medicine according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the medicine.

The dosage and treatment regimen will be determined only by the doctor. The dosage will be determined depending on your weight and the type of your infection.

Depending on your response to the treatment, the doctor may increase or decrease your daily dosage. If you have a liver disease, the doctor may decrease your dosage.

Do not exceed the recommended dose!

If you or your child are taking Voriconazole Teva to prevent fungal infections, your doctor may stop the treatment if you or your child develop treatment-related side effects.

- Tablets should only be given if the child is capable of swallowing tablets.

Take the tablet at least one hour before or one hour after a meal. The tablet should be swallowed whole with some water.

In the absence of a score line – the tablet must not be halved. No information is available regarding crushing/chewing.

If you accidentally took a higher dosage

If you took an overdose or if a child swallowed this medicine by mistake, proceed immediately to a hospital emergency room and bring the package of the medicine with you. You may experience increased sensitivity to light as a result of taking an overdose.

If you forgot to take the medicine

It is important to take the medicine at the same time every day.

If you forgot to take this medicine at the required time, take the next dose at the usual time, but never take a double dose to compensate for a forgotten dose. Follow the treatment as recommended by the doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting a doctor.

If you stop taking the medicine

Continue taking the medicine until the doctor instructs you to stop. If you stop taking the medicine early, your infection may continue or recur. Patients with a weakened immune system or those with difficult infections may require long-term treatment to prevent the infection from returning.

Do not take medicines in the dark! Check the label and the dose <u>every time</u> you take the medicine. Wear glasses if you need them.

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using Voriconazole Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Serious side effects – discontinue use of the medicine and refer to the doctor immediately in the following cases:

- Rash
- Jaundice; change in blood test results for liver function
- Inflammation of the pancreas (pancreatitis)

Additional side effects

Very common side effects (may occur in more than 1 out of 10 people):

- Visual impairment (changes in vision, including: blurry vision, color alterations, increased sensitivity to light, color blindness, eye impairment, seeing a halo, night blindness, swinging vision, seeing sparks, seeing aura, reduced visual acuity, blinding brightness, narrowed field of vision, blotches/spots in the field of vision)
- High fever
- Rash
- Nausea, vomiting, diarrhea
- Headache
- Limb swelling
- Abdominal pain
- Breathing difficulties
- Increased liver enzymes

Common side effects (may occur in up to 1 out of 10 people):

- Sinusitis, gum inflammation, chills, weakness
- Low level, including severely low, of some red and/or white blood cells (sometimes accompanied by fever), low level of platelets that help the blood to clot
- Low blood sugar level, low level of potassium in the blood, low blood sodium level
- Anxiety, restlessness, depression, confusion, sleeping difficulties, hallucinations
- Convulsions, tremor or involuntary muscle movements, tingling or abnormal skin sensations, increase in muscle tone (tension), sleepiness, dizziness
- Bleeding in the eye
- Heart rhythm problems including very fast/very slow heartbeat, fainting
- Low blood pressure, inflammation of the veins (phlebitis)
- Acute breathing difficulties, chest pain, swelling of the face (mouth, lips and around the eyes), fluid retention in the lungs
- Constipation, digestive difficulties, inflammation of the lips
- Jaundice, inflammation of the liver (hepatitis) and liver damage
- Skin rashes which may lead to severe peeling and blistering of the skin characterized by a flat and red area on the skin covered with small confluent bumps, redness in the skin
- Itching
- Hair loss
- Back pain
- Renal failure, blood in the urine, changes in kidney function tests

Uncommon side effects (may occur in up to 1 out of 100 people):

- Flu-like symptoms, irritation and inflammation of the gastrointestinal tract, inflammation of the gastrointestinal tract causing diarrhea, inflammation of the lymphatic vessels
- Inflammation of the thin tissue which is located in the inner wall of the abdomen and covers the abdominal cavity
- Enlarged lymph glands (sometimes painful), failure of bone marrow, increased eosinophil level in the blood
- Decreased function of the adrenal gland, underactive thyroid gland
- Abnormal brain function, Parkinson-like symptoms, nerve injury resulting in numbness, pain, tingling or burning sensation in the limbs
- 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 causing vision disturbance, optic disc swelling
- Decreased sensitivity to touch
- Changes in the sense of taste
- Hearing disturbances, ringing in the ears, vertigo (sensation of giddiness)
- Inflammation of certain internal organs – pancreas and intestines, swelling and inflammation of the tongue
- Enlarged liver, liver failure, gallstones or gallbladder disease
- Arthritis, inflammation of the veins accompanied by the formation of a blood clot (thrombosis)
- Inflammation of the kidney, protein in the urine, damage to the kidney
- Very fast heart rate or skipped heartbeats – sometimes accompanied by irregular electrical impulses
- Changes in the electrocardiogram (ECG)
- Elevated blood cholesterol levels, increased level of blood urea
- Allergic skin reactions (sometimes severe), including life-threatening conditions of the skin, which cause the appearance of painful blisters, sores/warts on the skin and mucous membranes, especially in the mouth, skin inflammation, hives, sunburn or severe skin reactions as a result of exposure to light or sun, red and irritated skin, red or purple spots on the skin due to a decrease in the blood platelet count, eczema
- Allergic reaction or abnormal immune response

Rare side effects (may occur in up to 1 out of 1,000 people):

- Overactive thyroid
- Deterioration of brain function (a serious complication of liver disease)
- Severe damage to the optic nerve, cloudy cornea, involuntary eye movements
- Appearance of blisters as a result of sensitivity/exposure to light
- 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 the blood clotting system
- Allergic skin reactions (sometimes severe) including rapid swelling (edema) of the skin, itchy or sore patches of thick, red skin with scales, itching of the skin and mucous membranes – a 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 and scaly skin patches, sometimes thickened with 'horns'

Side effects with unknown frequency (effects whose frequency has not yet been determined):

- Freckles and pigmented spots

Side effects with unknown frequency (effects whose frequency has not yet been determined), but which are significant and need to be reported to the treating doctor immediately:

- Skin cancer
- Inflammation of the tissue surrounding the bone
- Red and peeling areas of skin or ring-shaped skin lesions that may be a symptom of an autoimmune disease called cutaneous lupus erythematosus

There have been reports of skin cancer development in patients who have taken voriconazole for a long period of time.

Sunburn or a severe skin reaction, as a result of exposure to light or sun, was observed more frequently in children. If you/your child develop skin disorders, your treating doctor may refer you to a dermatologist, who after consultation may decide whether it is important for you/your child to come for monitoring on a regular basis. An increase in liver enzymes has also been observed more frequently in children.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- **Store below 25°C.**

6. Additional information

In addition to the active ingredient the medicine also contains:

Lactose monohydrate, pregelatinised maize starch, croscarmellose sodium, povidone, magnesium stearate, hypromellose, titanium dioxide, glycerol

What does the medicine look like and what are the contents of the package:

A white, film-coated, oblong tablet, debossed with "V" on one side and with "200" on the other side.

The medicine is marketed in a blister package containing 14, 28 or 30 film-coated tablets.

Not all package sizes may be marketed.

Name and address of marketing authorization holder and manufacturer:

Teva Israel Ltd.

124 Dvora HaNevi'a St., Tel Aviv 6944020

The leaflet was revised in December 2021 in accordance with the Ministry of Health guidelines.

Registration number of the medicine in the national drug registry of the Ministry of Health: 168-68-36179-00

VORICONAZOLE TABS PIL MW1221

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