

## PATIENT CARE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

### VORICONAZOLE-TRIMA

Film-coated tablets

Each film-coated tablet contains: voriconazole 200 mg  
For a list of inactive ingredients and allergens: See the subsection 'Important information about some of this medicine's ingredients' and section 6 'Additional information'.

**Read this leaflet carefully in its entirety before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist. This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours. This medicine is not intended for children and infants under the age of two years.

**1. WHAT IS THIS MEDICINE INTENDED FOR?**  
VORICONAZOLE-TRIMA is an anti-fungal preparation. It works by killing or stopping the growth of different fungi that cause infections. The preparation is intended for patients with severe, possibly even life-threatening, infections. In addition, the preparation serves to prevent fungal infections in bone marrow transplant patients who are at high risk. The preparation should be used only under medical supervision.

#### Therapeutic group:

Anti-fungal from the triazole group.

### 2. BEFORE USING THE MEDICINE

#### **X Do not use the medicine if:**

- X** You are sensitive (allergic) to the active ingredient or to any of the additional ingredients contained in the medicine, listed in section 6.
- X** 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), rifampicin (for treating tuberculosis), carbamazepine (for treating seizures), phenobarbital (for treating seizures and severe insomnia), ergot derivatives (ergotamine, dihydroergotamine; for treating migraines), sirolimus (for transplant patients), efavirenz at a dosage of 400 mg and more once a day (for treating HIV), ritonavir at dosages given twice a day of 400 mg and more each time (for treating HIV), the Hypericum herb (St. John's Wort).

**Before starting treatment with VORICONAZOLE-TRIMA, tell the doctor if:**

- you suffer, or have suffered in the past, from an allergic reaction to preparations from the azole group.
- you suffer from cardiomyopathy or a heart rate impairment.
- you suffer, or have suffered in the past, from a liver disease. Your doctor will monitor your liver function by performing blood tests.

#### Special warnings regarding use of the medicine

**I** Avoid any sun exposure while using the medicine. It is important to cover areas of the body that may be exposed to the sun and to use sunscreen with a high sun protection factor (SPF), as an increased sensitivity of the skin to the sun's rays may occur. This warning is also applicable to children.

**I** During use of the medicine, tell the doctor immediately if you get a

sunburn, develop a severe skin rash or blisters, pain in the bones. If you develop one of these skin effects, your doctor may refer you to a dermatologist. There is a small chance of developing skin cancer upon long-term use of VORICONAZOLE-TRIMA.

**I** Your doctor will monitor liver and kidney function by performing blood tests during the course of treatment with VORICONAZOLE-TRIMA. Please tell your doctor if you experience abdominal pain or if there is any change in the texture of your stools.

**I** Before starting and during the course of treatment, monitor for disturbances in electrolyte levels, such as hypokalemia, hypomagnesemia, hypocalcemia.

**I** **Other medicines and VORICONAZOLE-TRIMA**  
**If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.** In particular, if you are taking:

Medicines whose administration in combination with VORICONAZOLE-TRIMA should be avoided if possible and a dosage adjustment is required if given together:

- Phenytoin (to treat epilepsy). If you are taking this medicine, the blood level of phenytoin should be monitored.
- Ritonavir (to treat HIV) at a low dosage of 100 mg twice a day. Certain dosages of ritonavir cannot be taken with VORICONAZOLE-TRIMA, see "Do not use the medicine if", in this section.
- Rifabutin (to treat tuberculosis). If you are being treated with rifabutin, you must perform a blood count and side effects to rifabutin should be monitored regularly.

Medicines that, when taken with VORICONAZOLE-TRIMA, may require a dosage adjustment and monitoring that the medicines and/or VORICONAZOLE-TRIMA are still having the desired effect:

- Warfarin and other anticoagulants (e.g., phenprocoumon, acenocoumarol)
- Cyclosporin, tacrolimus (for transplant patients)
- Sulfonylureas (e.g., tolbutamide, glipizide, and glyburide) (to treat diabetes)

- Statins (e.g., atorvastatin, simvastatin, lovastatin) (to treat high cholesterol level)
- Benzodiazepines (e.g., midazolam, alprazolam, and triazolam) (for severe insomnia and as a tranquilizer)
- Omeprazole (to treat peptic ulcers)
- Oral contraceptives

- Vinca alkaloids (e.g., vincristine and vinblastine) (to treat cancer)
- Indinavir and other HIV protease inhibitors (to treat HIV)
- NNRTI medicines to treat AIDS, e.g., delavirdine, nevirapine, efavirenz (some dosages of efavirenz cannot be taken with VORICONAZOLE-TRIMA; see section "Do not use the medicine if" in this section)

- Methadone (to treat addiction)
- Short-acting opiates (e.g., alfentanil, fentanyl and sufentanil) (painkillers for surgical procedures)

- Oxycodone and hydrocodone (to relieve moderate to severe pain)
- Non-steroidal anti-inflammatory drugs (e.g., ibuprofen and diclofenac) (to treat pain and inflammation)
- Fluconazole (to treat fungal infections)
- Everolimus (to treat advanced kidney cancer and in transplant patients)

**I** **Pregnancy and breastfeeding**  
Do not use this medicine if you are pregnant, unless you received an explicit instruction from the doctor. Women of childbearing age must use effective contraceptives when using the medicine. Refer

to your doctor immediately if you become pregnant while taking VORICONAZOLE-TRIMA.

If you are pregnant or breastfeeding, think you are pregnant or are planning a pregnancy, refer to a doctor before taking the medicine.

**I** **Driving and use of machinery**  
VORICONAZOLE-TRIMA may cause blurring of vision or sensitivity to light. If you are affected by it, do not drive or operate dangerous machinery. Children should be cautioned against riding a bicycle or playing near the road and the like.

**I** **Important information about some of the ingredients of VORICONAZOLE-TRIMA**

The tablets contain lactose; therefore, if you have been told by a doctor that you have an intolerance to certain sugars, refer to a doctor before taking the medicine.

### 3. HOW SHOULD YOU USE THE MEDICINE?

Always use this preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

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

Depending on your response to treatment, your doctor may increase or decrease your daily dosage.

#### Do not exceed the recommended dose!

- Only give this medicine to children if they are able to swallow tablets (and in any case not children under 6 years old).

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

Take the tablet at least one hour before or one hour after a meal. Swallow the tablet whole with a little water. As there is no score line, do not split the tablet. There is no information about crushing/chewing.

#### If you accidentally took a higher dosage

If you took an overdose, or if a child has accidentally swallowed the medicine, 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 forget to take the medicine

It is important that you take the medicine at the same time every day. If you forgot to take the medicine at the required time, take the next dose at the scheduled time, **but never take a double dose** to compensate for a forgotten dose.

Adhere to the treatment regimen recommended by the doctor. Even if there is an improvement in your health condition, do not stop treatment with the medicine without consulting your doctor.

#### If you stop taking the medicine

If you stop taking the medicine early, your infection may continue or recur.

Patients with a weakened immune system or those with severe 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 each time you take medicine. Wear glasses if you need them.**

**If you have further questions regarding use of the medicine, consult the doctor or pharmacist.**

### 4. SIDE EFFECTS

As with any medicine, using VORICONAZOLE-TRIMA may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

**Serious side effects - stop taking the medicine and refer to the doctor immediately**

- rash
- jaundice and/or change in blood test results for liver function
- pancreatitis

#### Additional side effects

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

- visual impairment (change in vision including blurred vision, color alterations, increased sensitivity to light, color blindness, eye disorder, halo, night blindness, swinging vision, seeing sparks, aura, reduced visual acuity, blinding brightness, narrowed field of vision, blotches/spots in the field of vision)
- fever
- rash
- nausea, vomiting, diarrhea
- headache
- swelling in the extremities
- stomach pain
- breathing difficulties
- increased liver enzymes

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

- sinusitis, inflammation of the gums, chills, weakness
- low level, including severe, of certain 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 blood potassium level, low blood sodium level
- anxiety, agitation, depression, confusion, sleep difficulties, hallucinations
- seizures, tremor or involuntary muscle movements, tingling or abnormal skin sensations, increase in muscle tone, sleepiness, dizziness
- bleeding in the eye
- heart rhythm problems including very fast/very slow heartbeat, fainting
- low blood pressure, inflammation of the veins (which may be associated with the formation of a blood clot)
- acute breathing difficulties, chest pain, swelling of the face (mouth, lips and around the eyes), fluid retention in the lungs
- constipation, indigestion, 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 red area on the skin 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

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

- feeling sick, irritation and inflammation of the gastrointestinal tract, inflammation of the gastrointestinal tract causing diarrhea, inflammation of the lymphatic system

- inflammation of the thin tissue that lines 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 in the brain
- double vision, serious conditions of the eye including: pain and/or inflammation of the eyes and eyelids, abnormal eye movement, damage to the optic nerve causing vision disturbance, optic disc swelling

- decreased sensitivity to touch
- change in sense of taste
- hearing disturbances, ringing in the ears, vertigo (dizzy sensation)
- inflammation of certain internal organs - pancreas and duodenum, swelling and inflammation of the tongue
- enlarged liver, liver failure, gallstones or gallbladder disease
- joint inflammation, inflammation of the veins (which may be associated with the formation of a blood clot)
- inflammation of the kidney, protein in the urine, damage to the kidney
- very fast heart rate or skipped heartbeats, sometimes accompanied by irregular electric impulses
- changes in the electrocardiogram (E.C.G)
- increase in level of blood cholesterol, increased level of blood urea
- allergic skin reactions (sometimes severe), including life-threatening conditions of the skin, which cause onset of painful blisters, sores/ warts on the skin and mucous membranes, especially in the mouth, inflammation of the skin, hives, sunburn or severe skin reactions as a result of exposure to light or sun, skin redness and irritation, 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 in 1,000 people):**

- overactive thyroid gland
- deterioration of brain function (a serious complication of liver disease)
- severe damage to the optic nerve, cloudy cornea, involuntary eye movement
- 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 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 thick with "horns"

**Side effects of unknown frequency (effects whose frequency has not been determined):**

- freckles and pigmented spots

**Side effects of unknown frequency (effects whose frequency has not been determined), but are significant and need to be reported to the attending doctor immediately:**

- skin cancer
- inflammation of the tissue surrounding the bone
- red and scaly areas on the skin or ring-shaped skin lesions, may be a symptom of an autoimmune disease called cutaneous lupus erythematosus

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

Sunburn or a severe skin reaction, following exposure to light or sun, was observed more frequently in children. If you/your child develop skin disorders, your 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 the leaflet, consult with the doctor. Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage ([www.health.gov.il](http://www.health.gov.il)) that directs you to the online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il>

You can also report side effects by email to [Safety@trima.co.il](mailto:Safety@trima.co.il)

### 5. How Should the Medicine be Stored?

**Avoid poisoning!** This medicine, and any other medicine, should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

- Storage conditions: Store in a dry place below 25°C.

### 6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains: Lactose monohydrate, croscarmellose sodium, povidone, pregelatinized starch, magnesium stearate, HPMC, titanium dioxide, polyethylene glycol.

Each tablet contains 248.5 mg lactose monohydrate.

**What the medicine looks like and the contents of the package:**

Each package contains 14 or 28 elongated, white film-coated tablets.

**Manufacturer and license holder:** Trima Israel Pharmaceutical Products Maabarot Ltd., Maabarot, 4023000, Israel.

This leaflet was checked and approved by the Ministry of Health in March 2014 and was updated in accordance with the Ministry of Health guidelines in August 2019.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 151.41.33937.00

Maabarot 4023000  
Israel Pharmaceutical Products  
Maabarot Ltd.



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