

VORITROP

Voriconazole Tablets (50 mg and 200 mg)

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What VORITROP tablets are used for:

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 *Candida* infections including infection in the esophagus,
- Serious invasive *Candida* sp.infections when the fungus is resistant to fluconazole (another Anti-fungal medicine),
- Serious fungal infections caused by *Scedosporium* sp.or *Fusarium* sp. (two different species of fungi).

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

Prevention of breakthrough fungal infections in febrile high-risk neutropenic patients.

Prevention of fungal infections in high risk bone marrow transplant in patients ≥ 12 years old..

How VORITROP tablets works

VORITROP contains the active substance voriconazole. Voriconazole is an antifungal medicine. It works by killing or stopping the growth of the fungi that cause infections.

Before you use VORITROP tablets

- When you must not take it

Voriconazole must not be taken during pregnancy or breastfeeding, unless indicated by your doctor. Effective contraception must be used in women of childbearing potential. Contact your doctor immediately if you become pregnant while taking Voriconazole. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

If you are allergic to voriconazole or any of the other ingredients of this medicine.

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

- terfenadine, astemizole, cisapride, pimozide, quinidine, rifampicin, efavirenz, carbamazepine, phenobarbital, ergot alkaloids, sirolimus, ritonavir and St. John's Wort.

- Before you start to take it

Please tell your doctor or pharmacist if:

- you have had an allergic reaction to other azoles.
- you are suffering from or have ever suffered from liver disease.
- you are known to have cardiomyopathy irregular heartbeat slow heart rate or an abnormality of the electrocardiogram (ECG) called 'long QTc syndrome'.

You should avoid any sunlight and sun exposure while being treated. It is important to cover sub exposed areas of the skin and use sunscreen with high sub protection factor (SPF) as an increased sensitivity of skin to the sun's UV rays can occur.

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 Voriconazole, may affect the way Voriconazole works or Voriconazole may affect the way they work.

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

- Taking other medicines

Tell your doctor if you are taking the following medicine, as treatment with Voriconazole 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 at the same time

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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 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 Voriconazole 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 Voriconazole 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)

- 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).

How to use VORITROP tablets

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

- How much to use

Always take this medicine 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.

The recommended dose for adults (including elderly patients) is as follows:

	Tablets	
	Patients 40 kg and above	Patients less than 40 kg
Dose after the first 24 hours (Maintenance Dose)	200 mg twice a day	100 mg twice a day

Depending on your response to treatment, your doctor may increase the daily dose to 300 mg twice a day. For patients less than 40 kg, the dose may be increased to 150 mg twice a day.

The doctor may decide to decrease the dose if you have mild to moderate cirrhosis.

Use in children and adolescents: The recommended dose for children and teenagers is as follows:

	Tablets	
	Children aged 2 to less than 12 years and teenagers aged 12 to 14 years weighing less than 50 kg	Teenagers aged 12 to 14 years weighing 50 kg or more; and all teenagers older than 14

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Dose after the first 24 hours (Maintenance Dose)	9 mg/kg twice a day (a maximum dose of 350 mg twice daily)	200 mg twice a day
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Depending on your response to treatment, your doctor may increase or decrease the daily dose.

Tablets must only be given if the child is able to swallow tablets.

If you or your children are taking Voriconazole for prevention of fungal infections, your doctor may stop giving Voriconazole if you or your child develops treatment related side effects.

- When to use it

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

- How long to use it

Continue taking VORITROP for as long as your doctor recommends.

- If you forget to take it

It is important to take your VORITROP 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.

- If you take too much (overdose)

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 VORITROP tablets with you. You may experience abnormal intolerance to light as a result of taking more Voriconazole than you should.

While you are using VORITROP tablets

- Things you must do

Take your medicine exactly as your doctor has told you.

Tell all the doctors, dentists and pharmacists that are treating you that you are taking VORITROP.

Tell your doctor immediately if you become pregnant while taking this medication.

- Things you must not do

Do not stop taking the medicine unless advised by your doctor.

Do not take any new medicines without consulting your doctor.

Do not give VORITROP to anyone else, even if they have the same symptoms or condition as you.

- Things to be careful of

Voriconazole 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 contains lactose:

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

Side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

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

Serious side effects – Stop taking VORITROP and see a doctor immediately.

- Rash

- Jaundice; Changes in blood tests of liver function.

- Pancreatitis.

Other side effects

Very common:

Visual impairment (change in vision including blurred vision, visual color 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.

Common:

- Inflammation of the sinuses, inflammation of the gums, chills, weakness.

- Low numbers of some types, including severe, of red (sometimes immune-related)

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and/or white blood cells (sometimes with fever), low numbers of cells called platelets that help the blood to clot.

- Allergic reaction or exaggerated immune response
- 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 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

Uncommon:

- 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
- Problem 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

Rare:

- Overactive thyroid gland
- Deterioration of brain function that is a serious complication of liver disease
- Loss of most fibers 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 sub mucosal 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'

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Side effects with frequency not known:

- Freckles and pigmented spots
- Other significant side effects whose frequency is not known, but should be reported to your doctor immediately:
- 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 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 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 any of these side effects persist or are troublesome, please tell your doctor.

This is not a complete list of all possible side effects. If you get any side effects talk to your doctor or pharmacist.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my [Consumers → Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)]

Storage and disposal of VORITROP tablets

- Storage

Keep out of the reach and sight of children.

Store below 30 °C.

Do not use your medicine after the expiry date which is stated on the pack after 'EXP'. The expiry date refers to the last day of that month.

- Disposal

Medicines should not be disposed of via waste water or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Product description

- What it looks like

VORITROP 50 are supplied as White to off white, round, film coated tablets, debossed with 'V50' on one side and plain on the other side.

VORITROP 200 are supplied as White to off white, oval, film coated tablets, debossed with 'V200' on one side and plain on the other side.

- Ingredients

- Active Ingredient
Voriconazole

- Inactive Ingredient
Lactose Monohydrate,
Pregelatinized Starch,
Croscarmellose Sodium,
Povidone K 25, Magnesium Stearate,

Film Coating (50 mg):
Hypromellose, Lactose monohydrate, Tricetin & Titanium Dioxide.

Film Coating (200 mg):
Opadry II White 30K580005

- MAL number:

VORITROP 50:
MAL21066022AZ
VORITROP200:
MAL21066023AZ

Manufacturer

Intas Pharmaceuticals Ltd.
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Product Registration Holder

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