Package Leaflet: Information for the Patient

Voriconazole 50 mg, 200 mg film-coated Tablets

Read all of this leaflet carefully before you start taking 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet (see section 4).

What is in this leaflet

1. What Voriconazole film-coated tablet is and what it is used for

Voriconazole film-coated tablet contains the active substance voriconazole. Voriconazole film-coated tablet 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).

Voriconazole film-coated tablet 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 taken under the supervision of a doctor.

2. What you need to know before you take Voriconazole film-coated tablet

Do not take Voriconazole film-coated tablet
If you are allergic to voriconazole or any of the other ingredients of this medicine (listed in section 6).

It is very important that you inform 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 course of Voriconazole film-coated tablet 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).
- 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 migraine).
- Sirolimus (used in transplant patients).
- Ritonavir (used for treating HIV) in doses of 400mg and more twice daily.
- St. John's Wort (herbal supplement).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking Voriconazole film-coated tablet if:

- You have had an allergic reaction to other azoles.
- You are suffering from, or have ever suffered from liver disease. If you have liver disease, your doctor may prescribe a lower dose of Voriconazole film-coated tablet. Your doctor should also monitor your liver function while you are being treated with Voriconazole film-coated tablet by doing blood tests.
- You are known to have cardiomyopathy, irregular heartbeat, slow heart rate or an abnormality of electrocardiogram (ECG) called 'long QTc syndrome'.

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 Voriconazole film-coated tablet:
- 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 Voriconazole film-coated tablet.

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

Children and adolescents
Voriconazole film-coated tablet should not be given to children younger than 2 years of age.

Other medicines and Voriconazole film-coated tablet
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 film-coated tablet, may affect the way Voriconazole film-coated tablet works or Voriconazole film-coated tablet may affect the way they work.

Tell your doctor if you are taking the following medicine, as treatment with Voriconazole film-coated tablet 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 film-coated tablet at the same time 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 film-coated tablet 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 film-coated tablet 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).
- Sulphonylureas (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 film-coated tablet 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 film-coated tablet).
- 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).

Pregnancy and breast-feeding
Voriconazole film-coated tablet must not be taken during pregnancy, 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 film-coated tablet. 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.

Driving and using machines
Voriconazole film-coated tablet 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 film-coated tablet contains lactose
Lactose is a type of sugar. If you have been told by your doctor that you have an intolerance to some sugars, tell your doctor before taking Voriconazole film-coated tablet.

3. How to take Voriconazole film-coated tablet

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 for the first 24 hours (Loading Dose)	400 mg every 12 hours for the first 24 hours	200 mg every 12 hours for the first 24 hours
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.

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
Dose for the first 24 hours (Loading Dose)	Your treatment will be started as an infusion	400 mg every 12 hours for the first 24 hours
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

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.

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

If you or your child are taking Voriconazole film-coated tablet for prevention of fungal infections, your doctor may stop giving Voriconazole film-coated tablet if you or your child develop treatment related side effects.

If you take more Voriconazole film-coated tablet 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 Voriconazole film-coated tablets with you. You may experience abnormal intolerance to light as a result of taking more Voriconazole film-coated tablet than you should.

If you forget to take Voriconazole film-coated tablet
It is important to take your Voriconazole film-coated tablet 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 stop taking Voriconazole film-coated tablet
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 Voriconazole film-coated tablet correctly, as described above.

Continue taking Voriconazole film-coated tablet 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.

When Voriconazole film-coated tablet treatment is stopped by your doctor you should not experience any effects.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible 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 Voriconazole film-coated tablet and see a doctor immediately
Rash, jaundice; changes in blood tests of liver function, pancreatitis.

Other side effects

Very common side effects (may affect more than 1 in 10 people)
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.

Common side effects (may affect up to 1 in 10 people)
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, fluid accumulation in the lungs, constipation, indigestion, inflammation of the lips, jaundice, inflammation of the liver, liver injury, redness of the skin, 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, itchiness, hair loss, back pain, kidney failure, blood in the urine, changes in kidney function tests.

Uncommon side effects (may affect up to 1 in 100 people)
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 and low white blood cells in blood), 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, 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, injection site reaction, allergic reaction or exaggerated immune response.

Rare side effects (may affect up to 1 in 1000 people)
Overactive thyroid gland, deterioration of brain function that is a serious complication of liver disease, loss of most fibres in the optic nerve resulting in vision impairment, 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'

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 film-coated tablet 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 film-coated tablet 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.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly by Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Voriconazole film-coated tablet

- Keep this medicine out of the sight and reach of children.
- 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.
- This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Voriconazole film-coated tablet contains
- The active substance is voriconazole.
  Each film-coated tablet contains either 50 mg voriconazole (for Voriconazole 50 mg

film-coated tablets) or 200 mg voriconazole (for Voriconazole 200 mg film-coated tablets). Also contains lactose monohydrate 67.80 mg per tablet (for Voriconazole 50 mg film-coated tablets) or 271.20 mg per tablet (for Voriconazole 200 mg film-coated tablets).

- The other ingredients are lactose monohydrate, pre-gelatinised starch, croscarmellose sodium, povidone, purified water, magnesium stearate which make up the tablet core and hypromellose, titanium dioxide (E171), lactose monohydrate, triacetin and purified water which make up the film-coat.

What Voriconazole film-coated tablet looks like and contents of the pack
Voriconazole 50 mg film-coated tablets are supplied as white to off-white, 7 mm round film-coated tablet, debossed with “BS 10” on one side and “50” on the other side. The tablets are available in 28 tablets (2 x 14)

Voriconazole 200 mg film-coated tablets are supplied as white to off-white, 15.8 x 8 mm capsule-shaped film-coated tablet, debossed with “BS 10” on one side and “200” on the other side. The tablets are available in 28 tablets (2 x 14)

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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Voriconazole 200 mg film-coated Tablets; MA Number: PL43801/0037

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