VORY® Tablet
(Voriconazole)

QUALITATIVE AND QUANTITATIVE COMPOSITION

VORY® 200mg Tablet
Each film coated tablet contains:
Voriconazole USP.....200mg

PHARMACEUTICAL FORM

Tablet

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS: Voriconazole is a broad-spectrum, triazole antifungal agent and is indicated in adults and children aged 2 years and above as follows:
● Treatment of invasive aspergillosis. ● Treatment of candidemia in non-neutropenic patients. ● Treatment of fluconazole-resistant serious invasive *Candida* infections (including *C. krusei)*. ● Treatment of serious fungal infections caused by *Scedosporium* spp. and *Fusarium* spp. ● Voriconazole should be administered primarily to patients with progressive, possibly life-threatening infections. ● Prophylaxis of invasive fungal infections in high-risk allogeneic haematopoietic stem cell transplant (HSCT) recipients.

POSOLOGY AND METHOD OF ADMINISTRATION: Posology: Electrolyte disturbances such as hypokalaemia, hypomagnesemia, and hypocalcemia should be monitored and corrected, if necessary, prior to initiation and during voriconazole therapy. **Treatment:** ***Adults:*** Therapy must be initiated with the specified loading dose regimen of either intravenous or oral voriconazole to achieve plasma concentrations on Day 1 that are close to a steady state. On the basis of the high oral bioavailability, switching between intravenous and oral administration is appropriate when clinically indicated. Detailed information on dose recommendations is provided in the following table:

	Intravenous	Oral	
		Patients 40kg and above*	Patients less than 40kg*
Loading dose regimen (first 24 hours)	6mg/kg every 12 hours	400mg every 12 hours	200mg every 12 hours
Maintenance dose (after first 24 hours)	4mg/kg twice daily	200mg twice daily	100mg twice daily

*This also applies to patients aged 15 years and older.

Duration of treatment: Treatment duration should be as short as possible depending on the patient's clinical and mycological response. Long-term exposure to voriconazole greater than 180 days (6 months) requires careful assessment of the benefit-risk balance. ***Dose adjustment (Adults):*** If patient response to treatment is inadequate, the maintenance dose may be increased to 300mg twice daily for oral administration. For patients less than 40kg the oral dose may be increased to 150mg twice daily. If the patient is unable to tolerate treatment at a higher dose, reduce the oral dose by 50mg steps to 200mg twice daily (or 100mg twice daily for patients less than 40kg) maintenance dose. In case of use as prophylaxis, refer below:
Children (2 to <12 years) and young adolescents with low body weight (12 to 14 years and <50kg): Voriconazole should be dosed as children as these young adolescents may metabolize voriconazole more similarly to children than to adults. The recommended dosing regimen is as follows:

	Intravenous	Oral
Loading Dose Regimen (first 24 hours)	9mg/kg every 12 hours	Not recommended
Maintenance Dose (after first 24 hours)	8mg/kg twice daily	9mg/kg twice daily (a maximum dose of 350mg twice daily)

It is recommended to initiate the therapy with the intravenous regimen and the oral regimen should be considered only after there is a significant clinical improvement. It should be noted that an 8mg/kg intravenous dose will provide voriconazole exposure approximately 2-fold higher than a 9mg/kg oral dose. Considering the assumed limited gastro-enteric transit time in paediatric patients, the absorption of tablets may be different in paediatric compared to adult patients. It is therefore, recommended to use the oral suspension formulation in children aged 2 to <12. All other adolescents (12 to 14 years and ≥50kg; 15 to 17 years regardless of body weight). Voriconazole should be dosed as adults. ***Dose adjustment (Children [2 to <12 years] and young adolescents with low body weight [12 to 14 years and <50kg]):*** If patient response to treatment is inadequate, the dose may be increased by 1mg/kg steps (or by 50mg steps if the maximum oral dose of 350mg was used initially). If the patient is unable to tolerate treatment, reduce the dose by 1mg/kg steps (or by 50mg steps if the maximum oral dose of 350mg was used initially). Use in paediatric patients aged 2 to <12 years with hepatic or renal insufficiency has not been established. **Prophylaxis in Adults and Children:** Prophylaxis should be initiated on the day of the transplant and may be administered for up to 100 days. Prophylaxis should be as short as possible depending on the risk of developing invasive fungal infection (IFI) as defined by neutropenia or immunosuppression. It may only be continued up to 180 days after transplantation in case of continuing immunosuppression or graft versus host disease (GvHD). ***Dose:*** The recommended dosing regimen for prophylaxis is the same as for treatment in the respective age groups. Please refer to the treatment tables above. ***Duration of prophylaxis:*** Use of voriconazole in prophylaxis for greater than 180 days (6 months) requires careful assessment of the benefit-risk balance. **The following instructions apply to both Treatment and Prophylaxis:** ***Dose adjustment:*** For prophylaxis use, dose adjustments are not recommended in the case of lack of efficacy or treatment-related adverse events. In the case of treatment-related adverse events, discontinuation of voriconazole and the use of alternative antifungal agents must be considered. ***Dose adjustments in case of co-administration:*** Phenytoin may be co-administered with voriconazole if the maintenance dose of voriconazole is increased from 200mg to 400mg orally, twice daily (100mg to 200mg orally, twice daily in patients less than 40kg). The combination of voriconazole with rifabutin should, if possible, be avoided. However, if the combination is strictly needed, the maintenance dose of voriconazole may be increased from 200mg to 350mg orally, twice daily (100mg to 200mg orally, twice daily in patients less than 40kg). Efavirenz may be co-administered with voriconazole if the maintenance dose of voriconazole is increased to 400mg every 12 hours and the efavirenz dose is reduced by 50%, i.e. to 300mg once daily. When treatment with voriconazole is stopped, the initial dose of efavirenz should be restored. ***Elderly:*** No dose adjustment is necessary for elderly patients. ***Renal impairment:*** The pharmacokinetics of orally administered voriconazole are not affected by renal impairment. Therefore, no adjustment is necessary for oral dosing for patients with mild to severe renal impairment. ***Hepatic impairment:*** It is recommended that the standard loading dose regimens be used but that the maintenance dose be halved in patients with mild to moderate hepatic cirrhosis receiving voriconazole. Voriconazole has been associated with elevations in liver function tests and clinical signs of liver damage, such as jaundice, and must only be used in patients with severe hepatic impairment if the benefit outweighs the potential risk. Patients with severe hepatic impairment must be carefully monitored for medicinal toxicity. ***Paediatric population:*** The safety and efficacy of voriconazole in children below 2 years have not been established. **Method of administration:** Voriconazole film-coated tablets are to be taken at least one hour before, or one hour following a meal.

CONTRAINDICATIONS: Hypersensitivity to the active substance. ● Co-administration with CYP3A4 substrates, terfenadine, astemizole, cisapride, pimozide, quinidine, or ivabradine since increased plasma concentrations of these medicinal products can lead to QTc prolongation and rare occurrences of torsades de pointes. ● Co-administration with rifampicin, carbamazepine, phenobarbital, and St. John's Wort since these medicinal products are likely to decrease plasma voriconazole concentrations significantly. ● Co-administration of standard doses of voriconazole with efavirenz doses of 400mg once daily or higher is contraindicated because efavirenz significantly decreases plasma voriconazole concentrations in healthy subjects at these doses. Voriconazole also significantly increases efavirenz plasma concentrations. ● Co-administration with high-dose ritonavir (400mg and above twice daily) because ritonavir significantly decreases plasma voriconazole concentrations in healthy subjects at this dose. ● Co-administration with ergot alkaloids (ergotamine, dihydroergotamine), which are CYP3A4 substrates, since increased plasma concentrations of these medicinal products can lead to ergotism. ● Coadministration with sirolimus since voriconazole is likely to increase plasma concentrations of sirolimus significantly. ● Co-administration of voriconazole with naloxegol, a CYP3A4 substrate, since increased plasma concentrations of naloxegol can precipitate opioid withdrawal symptoms. ● Co-administration of voriconazole with tolvaptan since strong CYP3A4 inhibitors such as voriconazole significantly increase plasma concentrations of tolvaptan. ● Co-administration of voriconazole with lurasidone since significant increases in lurasidone exposure have the potential for serious adverse reactions. ● Co-administration with venetoclax at initiation and during venetoclax dose titration phase since voriconazole is likely to significantly increase plasma concentrations of venetoclax and increase the risk of tumor lysis syndrome.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE: Hypersensitivity: Caution should be used in prescribing voriconazole to patients with hypersensitivity to other azoles. **Cardiovascular:** Voriconazole has been associated with QTc interval prolongation. There have been rare cases of torsades de pointes in patients taking voriconazole who had risk factors, such as a history of cardiotoxic chemotherapy, cardiomyopathy, hypokalaemia, and concomitant medicinal products that may have been contributory. Voriconazole should be administered with caution to patients with potentially proarrhythmic conditions, such as: ● Congenital or acquired QTc-prolongation. ● Cardiomyopathy, in particular when heart failure is present. ● Sinus bradycardia. ● Existing symptomatic arrhythmias. ● Concomitant medicinal product that is known to prolong QTc interval. Electrolyte disturbances such as hypokalaemia, hypomagnesemia, and hypocalcemia should be monitored and corrected, if necessary, prior to initiation and during voriconazole therapy. **Hepatic toxicity:** Treatment duration should be as short as possible; however, if based on the benefit-risk assessment the treatment is continued, monitoring frequency can be reduced to monthly if there are no changes in the liver function tests. If the liver function tests become markedly elevated, voriconazole should be discontinued. Monitoring of hepatic function should be carried out in both children and adults. **Serious dermatological adverse reactions:** ***Phototoxicity:*** Voriconazole has been associated with phototoxicity including reactions such as ephelides, lentigo, actinic keratosis, and pseudoporphyria. It is recommended that all patients, including children, avoid exposure to direct sunlight during voriconazole treatment and use measures such as protective clothing and sunscreen with a high sun protection factor (SPF). ***Squamous cell carcinoma of the skin (SCC):*** If phototoxic reactions occur, multidisciplinary advice should be sought, voriconazole discontinuation and use of alternative antifungal agents should be considered and the patient should be referred to a dermatologist. If voriconazole is continued, however, dermatologic evaluation should be performed on a systematic and regular basis, to allow early detection and management of premalignant lesions. Voriconazole should be discontinued if premalignant skin lesions or squamous cell carcinoma are identified. ***Severe cutaneous adverse reactions:*** Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with oeosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal with the use of voriconazole. If a patient develops a rash, he should be monitored closely and voriconazole discontinued if lesions progress. **Adrenal events:** On long-term treatment with voriconazole and corticosteroids (including inhaled corticosteroids e.g., budesonide and intranasal corticosteroids) should be carefully monitored for adrenal cortex dysfunction both during treatment and when voriconazole is discontinued. **Long-term treatment:** Long-term exposure (treatment or prophylaxis) greater than 180 days (6 months) requires careful assessment of the benefit-risk balance and physicians should therefore, consider the need to limit the exposure to voriconazole. If a patient develops skeletal pain and radiologic findings compatible with periostitis, voriconazole discontinuation should be considered after multidisciplinary advice. **Visual adverse reactions:** There have been reports of prolonged visual adverse reactions, including blurred vision, optic neuritis, and papilloedema. **Renal adverse reactions:** Acute renal failure has been observed in severely ill patients undergoing treatment with voriconazole. Patients being treated with voriconazole are likely to be treated concomitantly with nephrotoxic medicinal products and have concurrent conditions that may result in decreased renal function. **Monitoring of renal function:** Patients should be monitored for the development of abnormal renal function. This should include laboratory evaluation, particularly serum creatinine. **Monitoring of pancreatic function:** Patients, especially children, with risk factors for acute pancreatitis (e.g. recent chemotherapy, haematopoietic stem cell transplantation (HSCT)), should be monitored closely during voriconazole treatment. Monitoring of serum amylase or lipase may be considered in this clinical situation. **Paediatric population:** Safety and effectiveness in pediatric subjects below the age of two years have not been established. Voriconazole is indicated for

paediatric patients aged two years or older. Oral bioavailability may be limited in paediatric patients aged 2 to <12 years with malabsorption and very low body weight for age. In that case, intravenous voriconazole administration is recommended for age. In that case, intravenous voriconazole administration is recommended. ***Serious dermatological adverse reactions (including SCC):*** The frequency of phototoxicity reactions is higher in the paediatric population. As an evolution towards SCC has been reported, stringent measures for photoprotection are warranted in this population of patients. In children experiencing photoaging injuries such as lentigines or ephelides, sun avoidance, and dermatologic follow-up are recommended even after treatment discontinuation. **Prophylaxis:** In case of treatment-related adverse events (hepatotoxicity, severe skin reactions including phototoxicity and SCC, severe or prolonged visual disorders, and periostitis), discontinuation of voriconazole and use of alternative antifungal agents must be considered. **Phenytoin (CYP2C9 substrate and potent CYP450 inducer):** Careful monitoring of phenytoin levels is recommended when phenytoin is co-administration with voriconazole. Concomitant use of voriconazole and phenytoin should be avoided unless the benefit outweighs the risk. **Efavirenz (CYP450 inducer; CYP3A4 inhibitor and substrate):** When voriconazole is co-administration with efavirenz the dose of voriconazole should be increased to 400mg every 12 hours and the dose of efavirenz should be decreased to 300mg every 24 hours. **Rifabutin (Potent CYP450 inducer):** Careful monitoring of full blood counts and adverse reactions to rifabutin (e.g. uveitis) is recommended when rifabutin is co-administration with voriconazole. Concomitant use of voriconazole and rifabutin should be avoided unless the benefit outweighs the risk. **Ritonavir (potent CYP450 inducer; CYP3A4 inhibitor and substrate):** Co-administration of voriconazole and low dose ritonavir (100 mg twice daily) should be avoided unless an assessment of the benefit/risk to the patient justifies the use of voriconazole. **Everolimus (CYP3A4 substrate, P-gp substrate):** Co-administration of voriconazole with everolimus is not recommended because voriconazole is expected to significantly increase everolimus concentrations. **Naloxegol (CYP3A4 substrate):** Co-administration of voriconazole and naloxegol is not recommended because voriconazole is expected to significantly increase naloxegol concentrations. Methadone (CYP3A4 substrate) Frequent monitoring for adverse reactions and toxicity related to methadone, including QTc prolongation, is recommended when coadministered with voriconazole since methadone levels increased following co-administration of voriconazole. A dose reduction of methadone may be needed. **Short-acting opiates (CYP3A4 substrate):** Reduction in the dose of alfentanil, fentanyl, and other-short acting opiates similar in structure to alfentanil and metabolized by CYP3A4 (e.g. sufentanil) should be considered when co-administration with voriconazole. The half-life of alfentanil is prolonged in a four-fold manner when alfentanil is co-administration with voriconazole and concomitant use of voriconazole with fentanyl resulted in an increase in the mean $AUC_{0-\infty}$ of fentanyl, frequent monitoring for opiate-associated adverse reactions (including a longer respiratory monitoring period) may be necessary. **Long-acting opiates (CYP3A4 substrate):** Reduction in the dose of oxycodone and other long-acting opiates metabolized by CYP3A4 (e.g. hydrocodone) should be considered when coadministered with voriconazole. Frequent monitoring for opiate-associated adverse reactions may be necessary. **Fluconazole (CYP2C9, CYP2C19 and CYP3A4 inhibitor):** Co-administration of oral voriconazole and oral fluconazole resulted in a significant increase in C_{max} and AUCτ of voriconazole. The reduced dose and/or frequency of voriconazole and fluconazole that would eliminate this effect have not been established. Monitoring for voriconazole-associated adverse reactions is recommended if voriconazole is used sequentially after fluconazole. **Voriconazole film-coated tablets contain lactose:** Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take this medicinal product. **Information on sodium content:** This medicinal product contains less than 1mmol sodium (23mg) per film-coated tablet, that is to say essentially 'sodium-free'.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION: Effect of Other Drugs on Voriconazole Pharmacokinetics: ● ***Drugs that reduce Voriconazole Plasma Exposure (C_{max} and AUCτ after 200mg Q12h):*** Rifampin and rifabutin, efavirenz, high-dose ritonavir 400mg Q12h, low-dose ritonavir (100mg Q12h), carbamazepine (likely), long acting barbiturates (likely), phenytoin, St. John's Wort, fluconazole, metabolism of voriconazole to be Induced by efavirenz and Other NNRTIs. ● ***Drugs that increase Voriconazole Plasma Exposure (C_{max} and AUCτ after 200mg Q12h):*** Oral contraceptives containing ethinyl estradiol and norethindrone Fluconazole. **Effect of Voriconazole on Pharmacokinetics of Other Drugs:** ● Drugs that decrease Drug Plasma Exposure (C_{max} and AUCτ): Low-dose ritonavir (100mg Q12h). ● ***Drugs that increase Drug Plasma Exposure (C_{max} and AUCτ):*** Sirolimus, rifabutin, efavirenz, terfenadine, astemizole, cisapride, pimozide, quinidine, ergot alkaloids, cyclosporine, methadone, fentanyl, alfentanil, oxycodone, NSAIDs including, ibuprofen and diclofenac, tacrolimus, phenytoin, oral contraceptives containing ethinyl estradiol and norethindrone, warfarin, omeprazole, other NNRTIs, sulfonylurea oral Hypoglycemics, vinca alkaloids.

FERTILITY, PREGNANCY AND LACTATION: Fertility: Women of childbearing potential must always use effective contraception during treatment. **Pregnancy:** Voriconazole must not be used during pregnancy unless the benefit to the mother clearly outweighs the potential risk to the foetus. **Breast-feeding:** Breast-feeding must be stopped on initiation of treatment with voriconazole.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Voriconazole has a moderate influence on the ability to drive and use machines. It may cause transient and reversible changes to vision, including blurring, altered/enhanced visual perception, and/or photophobia. Patients must avoid potentially hazardous tasks, such as driving or operating machinery while experiencing these symptoms.

UNDESIRABLE EFFECTS: The most common adverse reactions are visual impairment, pyrexia, rash, vomiting, nausea, diarrhoea, headache, peripheral oedema, liver function test abnormal, respiratory distress, and abdominal pain. The frequency categories for adverse reactions are listed below:
Very common (≥1/10): Oedema peripheral, headache, visual impairment, respiratory distress, diarrhoea, vomiting, abdominal pain, nausea, liver function test abnormal, rash, pyrexia. **Common (≥1/100 to <1/10):** Sinusitis, agranulocytosis, pancytopenia, thrombocytopenia, leukopenia, anemia, hypoglycemia, hypokalaemia, hyponatremia, depression, hallucination, anxiety, insomnia, agitation, confusional state, convulsion, syncope, tremor, hypertonia, paraesthesia, somnolence, dizziness, retinal haemorrhage, arrhythmia supraventricular, tachycardia, bradycardia, hypotension, phlebitis, acute respiratory distress syndrome, pulmonary oedema, cheilitis, dyspepsia, constipation, gingivitis, jaundice, jaundice cholestatic, hepatitis, dermatitis exfoliative, alopecia, rash maculo-papular, pruritus, erythema, back pain, renal failure acute, haematuria, chest pain, face oedema, asthenia, chills, blood creatinine increased. **Uncommon (≥1/1,000 to <1/100):** Pseudomembranous colitis, bone marrow failure, lymphadenopathy, eosinophilia, hypersensitivity, adrenal insufficiency, hypothyroidism, brain oedema, encephalopathy, extrapyramidal disorder, neuropathy peripheral, ataxia, hypoaesthesia, dysgeusia, optic nerve disorder, papilloedema, oculogyric crisis, diplopia, scleritis, blepharitis, hypoacusis, vertigo, tinnitus, ventricular fibrillation, ventricular extrasystoles, ventricular tachycardia, electrocardiogram QT prolonged, supraventricular tachycardia, thrombophlebitis, lymphangitis, peritonitis, pancreatitis, swollen tongue, duodenitis, gastroenteritis, glossitis, hepatic failure, hepatomegaly, cholecystitis, cholelithiasis, Stevens-Johnson syndrome, phototoxicity, purpura, urticaria, dermatitis allergic, rash papular, rash macular, eczema, arthritis, renal tubular necrosis, proteinuria, nephritis, infusion site reaction, influenza like illness, blood urea increased, blood cholesterol increased. **Rare (≥1/10,000 to <1/1,000):** Disseminated intravascular coagulation, anaphylactoid reaction, hyperthyroidism, hepatic encephalopathy, Guillain-Barre syndrome, nystagmus, optic atrophy, corneal opacity, torsades de pointes, atrioventricular block complete, bundle branch block, nodal rhythm, toxic epidermal necrolysis, angioedema, actinic keratosis, pseudoporphyria, erythema multiforme, psoriasis, medicinal eruption, drug reaction with oeosinophillia and systemic symptoms (DRESS). **Not Known:** Squamous cell carcinoma, cutaneous lupus erythematosus, ephelides, lentigo, periostitis. **Dermatological reactions:** The majority of rashes are of mild to moderate severity, severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS) (uncommon), toxic epidermal necrolysis (TEN) (rare), drug reaction with eosinophillia and systemic symptoms (DRESS) (rare) and erythema multiforme (rare) during treatment with voriconazole. If a patient develops a rash, they should be monitored closely and voriconazole discontinued if lesions progress. Photosensitivity reactions such as ephelides, lentigo and actinic keratosis have occurred, especially during long-term therapy. **Liver function tests:** Liver function test abnormalities may be associated with higher plasma concentrations and/or doses. The majority of abnormal liver function tests either resolved during treatment without dose adjustment or following dose adjustment, including discontinuation of therapy. Voriconazole has been associated with cases of serious hepatic toxicity in patients with other serious underlying conditions. This includes cases of jaundice, hepatitis, and hepatic failure leading to death. **Post-marketing:** ● Includes febrile neutropenia and neutropenia. ● Immune thrombocytopenic purpura. ● Nuchal rigidity and tetany. ● Hypoxic-ischaemic encephalopathy and metabolic encephalopathy. ● Includes akathisia and parkinsonism. ● Prolonged optic neuritis has been reported post-marketing. ● Dyspnoea and dyspnoea exertional. ● Medicinal product-induced liver injury, hepatitis toxic, hepatocellular injury, and hepatotoxicity. ● Includes periorbital oedema, lip oedema, and oedema mouth.

OVERDOSE: There is no known antidote to voriconazole. In an overdose, haemodialysis may assist in the removal of voriconazole from the body. Voriconazole is haemodialysed with a clearance of 121mL/min.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES: Pharmacotherapeutic group: Antimycotics for systemic use, triazole derivatives. **ATC Code:** J02AC03. **Mechanism of action:** Voriconazole is a triazole antifungal agent. The primary mode of action of voriconazole is the inhibition of fungal cytochrome P450-mediated 14 alpha lanosterol demethylation, an essential step in fungal ergosterol biosynthesis. The accumulation of 14 alpha-methyl sterols correlates with the subsequent loss of ergosterol in the fungal cell membrane and may be responsible for the antifungal activity of voriconazole. Voriconazole has been shown to be more selective for fungal cytochrome P450 enzymes than for various mammalian cytochrome P450 enzyme systems.

PHARMACOKINETIC PROPERTIES: Absorption: Voriconazole is rapidly and almost completely absorbed following oral administration, with maximum plasma concentrations (C_{max}) achieved 1-2 hours after dosing. The absolute bioavailability of voriconazole after oral administration is estimated to be 96%. When multiple doses of voriconazole are administered with high-fat meals, C_{max} and AUCτ are reduced by 34% and 24%, respectively. The absorption of voriconazole is not affected by changes in gastric pH. **Distribution:** The volume of distribution at steady state for voriconazole is estimated to be 4.6L/kg, suggesting extensive distribution into tissues. Plasma protein binding is estimated to be 58%. **Biotransformation:** The CYP2C19 is significantly involved in the metabolism of voriconazole. This enzyme exhibits genetic polymorphism. The major metabolite of voriconazole is N-oxide, which accounts for 72% of the circulating metabolites in plasma. This metabolite has minimal antifungal activity and does not contribute to the overall efficacy of voriconazole. **Elimination:** Voriconazole is eliminated via hepatic metabolism with less than 2% of the dose excreted unchanged in the urine. **Pharmacokinetics in special patient groups:** ***Gender:*** No dose adjustment based on gender is necessary. ***Elderly:*** No dose adjustment is necessary for the elderly. ***Paediatric Population:*** Oral bioavailability may, however, be limited in paediatric patients with malabsorption and very low body weight for their age. In that case, intravenous voriconazole administration is recommended. ***Renal impairment:*** The pharmacokinetics of voriconazole were not significantly affected by renal impairment. ***Hepatic impairment:*** Protein binding of voriconazole was not affected by impaired hepatic function and no pharmacokinetic data are available for patients with severe hepatic cirrhosis.

SHELF LIFE

See expiry on the pack.

AVAILABILITY

VORY® 200mg tablet in a pack of 10's.

INSTRUCTIONS

Dosage: As directed by the physician.
To be sold on prescription of a registered medical practitioner only.
Keep out of reach of children.
Do not store over 30°C, and protect from heat and moisture.
Improper storage may deteriorate the medicine.

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
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وُری® ٹیبلٹ

(وُری کونازول)

ہدایات:

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

بچوں کی پہنچ سے دور رکھیں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،
گرمی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔