Vorifix

Voriconazole USP

COMPOSITION

Vorifix 50 Tablet: Each film coated tablet contains Voriconazole USP 50 mg.
Vorifix 200 Tablet: Each film coated tablet contains Voriconazole USP 200 mg.

PHARMACOLOGY

Voriconazole is an azole antifungal drug. The primary mode of action of it is the inhibition of fungal cytochrome P-450 mediated 14 alpha-lanosterol demethylations. This step is 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 wall and may be responsible for the antifungal activity of Voriconazole.

INDICATION

It is indicated for the below mentioned treatment of adults and paediatric patients 2 years of age and older with:

- Invasive aspergillosis.
- Candidemia in non-neutropenics and other deep tissue Candida infections.
- Esophageal candidiasis.
- Serious fungal infections caused by *Scedosporium apiospermum* and Fusarium species including *Fusarium solani*, in patient's intolerant of or refractory to other therapy.

DOSAGE AND ADMINISTRATION

Dosage in Adults (15 years and older)

	Patients 40 kg and above	Patients less than 40 kg
Loading dose (first 24 hours)	400 mg every 12 hours	200 mg every 12 hours
Maintenance dose (after first 24 hours)	200 mg twice daily	100 mg twice daily

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.
Dosage Adjustment (Adults): If patient's response to treatment is inadequate, the maintenance dose may be increased to 300 mg twice daily for oral administration. For patients less than 40 kg, this oral dose may be increased to 150 mg twice daily. If patient is unable to tolerate treatment at a higher dose, reduce the oral dose by 50 mg steps to the 200 mg twice daily (100 mg twice daily for patients less than 40 kg) maintenance dose.
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 (Child-Pugh A and B).
Renal Impairment: No dose adjustment is necessary for oral dosing for patients with mild to severe renal impairment.

Dosage for Children and Young Adolescents

Recommended dosing regimen for Children (2 to <12 years) and young adolescents with low body weight (12 to 14 years and <50 kg)-

Loading Dose Regimen (first 24 hours): Not recommended
Maintenance Dose (after first 24 hours): 9 mg/kg twice daily (a maximum dose of 350 mg twice daily)

Dosage Adjustment for Children and Young Adolescents:

If patient response to treatment is inadequate, the dose may be increased by 1 mg/kg steps (or by 50 mg steps if the maximum oral dose of 350 mg was used initially). If patient is unable to tolerate treatment, reduce the dose by 1 mg/kg steps (or by 50 mg steps if the maximum oral dose of 350 mg was used initially).
For paediatric patients aged 12 to 14 years weighing greater than or equal to 50 kg and those aged 15 years and older regardless of body weight use adult dosage.

Use in paediatric patients aged 2 to <12 years with hepatic or renal insufficiency has not been studied.

Prophylaxis in Adults and Children

Prophylaxis should be initiated on the day of transplant and may be administered for up to 100 days. It may only be continued up to 180 days after transplantation in case of continuing immunosuppression or graft versus host disease (GvHD).
Dosage as prophylaxis: The recommended dosing regimen for prophylaxis is the same as for treatment in the respective age groups.
Duration of Prophylaxis
Use of voriconazole in prophylaxis for greater than 180 days (6 months) requires careful assessment of the benefit-risk balance.

CONTRAINDICATION

It is contraindicated in the following states:

- Hypersensitivity to it or its excipients.
- Coadministration with Cisapride, Pimozide, Quinidine, Sirolimus or Ivabradine due to risk of serious adverse reactions.
- Coadministration with Rifampin, Carbamazepine, Long-acting Barbiturates, Efavirenz, Ritonavir, Rifabutin, Ergot Alkaloids and St. John's Wort due to risk of loss of efficacy.
- Coadministration with Naloxegol, Tolvaptan and Lurasidone due to risk of adverse reactions.
- Coadministration of it with Venetoclax at initiation and during the ramp-up phase in patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) due to increased risk of adverse reactions.

WARNING & PRECAUTION

Hepatic Toxicity: Serious hepatic reactions reported. Evaluate liver function tests at the start of and during its therapy.
Arrhythmias and QT Prolongation: Correct Potassium, Magnesium and Calcium prior to use; caution patients with proarrhythmic conditions.
Visual Disturbances (including optic neuritis and papilledema): Monitor visual function if treatment continues beyond 28 days.
Severe Cutaneous Adverse Reactions: Discontinue for exfoliative cutaneous reactions.
Photosensitivity: Avoid sunlight due to risk.
Adrenal Dysfunction: Carefully monitor patients receiving it and corticosteroids for adrenal dysfunction both during and after its treatment. Instruct patients to seek immediate medical care if they develop signs and symptoms of Cushing's syndrome or adrenal insufficiency.
Embryo-Fetal Toxicity: It can cause fetal harm when administered to a pregnant woman. Inform pregnant patients of the potential hazard to the fetus. Advise females of reproductive potential to use effective contraception during treatment with it.
Skeletal Adverse Reactions: Fluorosis and periostitis with long-term Voriconazole therapy. Discontinue if these adverse reactions occur.
Patients with Hereditary Galactose Intolerance, Lapp Lactase Deficiency or Glucose-Galactose Malabsorption: it should not be given to these patients because it contains lactose.

SIDE EFFECTS

Adult Patients: The most common side effects (incidence ≥2%) are visual disturbances, fever, nausea, rash, vomiting, chills, headache, abnormal liver function test, tachycardia and hallucinations.
Paediatric Patients: The most common side effects (incidence ≥5%) are visual disturbances, pyrexia, vomiting, epistaxis, nausea, rash, abdominal pain, diarrhea, hypertension, hypokalemia, cough, headache, thrombocytopenia, abnormal ALT, hypotension, peripheral edema, hyperglycemia, tachycardia, dyspnea, hypocalcemia, hypophosphatemia, abnormal LFT, mucosal inflammation, photophobia, abdominal distension, constipation, dizziness, hallucinations, hemoptysis, hypoalbuminemia, hypomagnesemia, renal impairment, upper respiratory tract infection.

USE IN PREGNANCY & LACTATION

Pregnancy: There are no available data on the use of it.
Lactation: No data are available regarding the presence of it in human milk, the effects on the breastfed infant or the effects on milk production.

USE IN CHILDREN & ADOLESCENTS

Safety and effectiveness in patients younger than 2 years have not been established.

DRUG INTERACTIONS

CYP3A4, CYP2C9, and CYP2C19 inhibitors and inducers: Adjust its dosage and monitor for adverse reactions or lack of efficacy.
Phenytoin or Efavirenz: With Coadministration, increase maintenance dosage of it.

OVERDOSAGE

Voriconazole is hemodialyzed with clearance of 121 mL/min. In an overdose, hemodialysis may assist in the removal of Voriconazole from the body. There is no known antidote to Voriconazole.

STORAGE

Store below 30°C temperature in a cool and dry place. Protect from light. Keep out of the reach of children.

HOW SUPPLIED

Vorifix 50 Tablet: Each box contains 10 tablets in Alu-Alu blister pack.
Vorifix 200 Tablet: Each box contains 10 tablets in Alu-Alu blister pack.

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NIPRO JMI Pharma

Manufactured by:
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