Vorizol-200 Injection

DRUG INTERNATIONAL LTD.

Composition : Each vial contains Voriconazole USP 200mg sterile lyophilized powder.

Pharmacology : Voriconazole is a broad spectrum, triazole systemic antifungal agent. The primary mode of action of voriconazole is the inhibition of fungal cytochrome P-450-mediated 14 alpha-lanosterol demethylation, an essential step in fungal ergosterol biosynthesis.

Indications : It is indicated for the treatment of adults and pediatric 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 patients intolerant of, or refractory to, other therapy.

Dosage and Administration :

Infection	Adults		Pediatric patients 2 to less than 12 years of age and 12 to 14 years of age weighing less than 50kg	
	Loading dose	Maintenance Dose	Loading dose	Maintenance Dose
	Intravenous Infusion	Intravenous Infusion	Intravenous Infusion	Intravenous Infusion
Invasive Aspergillosis	6 mg/kg every 12 hours for the first 24 hours	4 mg/kg every 12 hours	9 mg/kg every 12 hours for the first 24 hours	8 mg/kg every 12 hours after the first 24hours
Candidemia in nonneutropenics and other deep tissue Candida infections		3-4 mg/kg every 12 hours		
Scedosporiosis and Fusariosis		4 mg/kg every 12 hours		
Esophageal Candidiasis	Not Evaluated	Not Evaluated	Not Evaluated	4 mg/kg every 12hours

For pediatric patients aged 12 to 14 years weighing greater than or equal to 50kg and those aged 15 years and older regardless of body weight use adult dosage. Or, as directed by the registered physician.

Reconstitution : Voriconazole injection requires reconstitution and dilution prior to administration as intravenous infusion. The powder is reconstituted with 19 ml of water for injection to obtain an extractable volume of 20ml of clear concentrate containing 10mg/ml of voriconazole. Shake the vial until all the powder is dissolved. This medicinal product is for single use only and any unused solution should be discarded.

Dilution : It must be infused over 1 to 3 hours, at a concentration of 5 mg/ml or less. Therefore, the required volume of the 10 mg/ml Voriconazole concentrate should be further diluted as follow: • Calculate the volume of 10 mg/ml Voriconazole concentrate required based on the patient's weight. • In order to allow the required volume of Voriconazole concentrate to be added, withdraw and discard at least an equal volume of diluent from the infusion bag or bottle to be used. The volume of diluent remaining in the bag or bottle should be such that when the 10 mg/ml concentrate is added, the final concentration is not less than 0.5 mg/ml nor greater than 5mg/ml. • Using a suitable size syringe and aseptic technique, withdraw the required volume of Voriconazole concentrate from the appropriate number of vials and add to the infusion bag or bottle. Discard partially used vials.

The final Voriconazole solution must be infused over 1 to 3 hours at a maximum rate of 3mg/kg per hour.

Contraindications : It is contraindicated in patients having hypersensitivity to the drug or other azoles.

Precautions : It should be given with caution in hepatic toxicity, arrhythmias and QT prolongation, infusion related reactions (including anaphylaxis), visual disturbances (including optic neuritis and papilledema), serious exfoliative cutaneous reactions, photosensitivity, skeletal adverse reactions.

Side Effects : Most common adverse reactions : visual disturbances, fever, nausea, rash, vomiting, chills, headache, liver function test abnormal, tachycardia and hallucinations.

Use in Pregnancy and Lactation : There are no adequate data on the use of Voriconazole in pregnant women available. Voriconazole must not be used during pregnancy unless the benefit to the mother clearly outweighs the potential risk to the foetus. The excretion of Voriconazole into breast milk has not been investigated.

Use in Child : Safety and effectiveness in pediatric patients below the age of 2 years has not been established.

Drug Interactions : CYP3A4, CYP2C9, and CYP2C19 inhibitors and inducers: Voriconazole may increase the concentrations and activity of drugs that are CYP3A4, CYP2C9 and CYP2C19 substrates. Reduce dosage of these other drugs and monitor for adverse reactions. Phenytoin or Efavirenz: With co-administration, increase maintenance oral and intravenous dosage of Voriconazole.

Overdose : There is no known antidote to voriconazole. In an overdose, hemodialysis may assist in the removal of voriconazole from the body.

Storage : Powder vials should be stored below 30°C in a dry place. Protect from light and moisture. Keep all medicines out of reach of children. The reconstituted solution should be used immediately. If not used immediately, store under refrigerator (2° to 8° C) temperatures for 24 hours maximum.

Packing : Vorizol-200 Injection (IV): Each combipack contains 1 vial of Voriconazole USP 200mg sterile lyophilized powder, with two ampoules of 10ml Water for Injection BP.