Voriconazole (vor-i-con-azole)

**Class**
Antifungal

**Pregnancy Category** D

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**Indications**

Severe systemic fungal infections including: candidiasis, esophageal candidiasis, cutaneous, deep tissue and skin infections, abdominal, kidney, bladder wall and wound infections, and aspergillosis.

**Action**

Inhibits fungal ergosterol synthesis leading to production of abnormal fungal plasma membranes. Therapeutic Effects: Antifungal activity.

**Pharmacokinetics**

- **Absorption:** Well absorbed following oral administration (96%); IV administration results in complete bioavailability.
- **Distribution:** Extensive tissue distribution.
- **Metabolism and Excretion:** Highly metabolized by the hepatic P450 enzymes variation in metabolism; metabolites are inactive.
- **Half-life:** 58%.

**Contraindications/Precautions**

- **Contraindicated in:** IV rapid end of infusion 12 hr, PO rapid 1–2 hr 12 hr.

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**Drug-Drug Interactions**

- **Drug Classes:** CYP2C19, CYP2C9, CYP3A4; Concurrent use of ritonavir, rifampin, rifabutin, St. John's wort, carbamazepine, and phenobarbital (CYP2C9, CYP2C19, and CYP3A4).
- **Contraindicated in:**
  - Concurrent use of ritonavir, rifampin, rifabutin, St. John's wort, carbamazepine, and phenobarbital.
  - Use Cautionally in: Adults (Child-Pugh Class A and B); maintenance dose reduction recommended; Renal impairment (CrCl < 30 mL/min); use only if justified by risk/benefit assessment (IV form should be avoided, use oral form only). Oral: Lactation: Use only if benefits justify risk, Prohib: Children < 12 yr (limited dosing information); suspension contains alcohol which may cause potentially fatal "panting syndrome" in neonates.

**Adverse Reactions/Side Effects**

- **CNS:** Nausea, vomiting, abdominal pain, diarrhea, nausea, pancreatitis, vomiting.
- **CV:** Changes in BP, peripheral edema, inotropic support.
- **GI:** Diarrhea, abdominal pain, diarrhea, nausea, pancreatitis, vomiting.
- ** Derm:** Stevens-Johnson syndrome, photodermatitis, rash, photosensitivity.
- **EENT:** Headache, hypotension, hypertension, MI, Ar, pneumonitis.

**DOSAGE & ADMINISTRATION**

- **Initiation Dose:** Maintenance dose reduction recommended; Renal impairment (CrCl < 30 mL/min); use only if justified by risk/benefit assessment (IV form should be avoided, use oral form only). Oral: Lactation: Use only if benefits justify risk, Prohib: Children < 12 yr (limited dosing information); suspension contains alcohol which may cause potentially fatal "panting syndrome" in neonates.

**Interactions**

- **Drug-Drug Interactions:** Voriconazole is a substrate and inhibitor of the CYP3A4, CYP2C9, and CYP2C19 enzyme systems. Voriconazole interacts with a wide range of other medications, resulting in increased plasma concentrations of the coadministered drugs. Concurrent use of voriconazole with other medications may result in increased plasma concentrations of these medications, increasing the risk of adverse effects. The interactions listed below are examples of how voriconazole can affect the metabolism of other medications, leading to increased plasma concentrations of these medications.

**Common Drug Interactions**

- **CYP3A4 Inhibitors:**
  - Fluconazole
  - Itraconazole
  - Ketoconazole
  - Posaconazole
- **CYP2C9 Inhibitors:**
  - Carbamazepine
  - Phenobarbital
- **CYP2C19 Inhibitors:**
  - Phenytoin
  - Carbamazepine
- **CYP2C9 and CYP2C19 Inhibitors:**
  - Rifampin
  - Rifabutin
- **CYP3A4 Inhibitors:**
  - Tamsulosin
  - Tacrolimus
  - Pimozide
  - Quinidine
  - Ergotamine
  - Dihydroergotamine
- **CYP2C19 Inhibitors:**
  - Efavirenz
  - Norethindone
  - Estriol
  - Ethinyl estradiol
  - Alprazolam
  - Methadone
  - Tolbutamide
  - Phenobarbital
  - Carbamazepine
  - Diclofenac
  - Cyclosporine
  - Sirolimus

**Pharmacodynamics**

- **Half-life:** 58%.
- **Dosage:** Oral 200 mg q 12 hr; IV 6 mg/kg over 1 hr (12 hr duration).
- **Maintenance:** Oral 200 mg q 12 hr; IV 12 mg/kg over 1 hr (48 hr duration).

**NURSE-FACED INTERVENTIONS**

- Monitor for signs of neurotoxicity, such as headache, dizziness, hallucinations, headache.
- Monitor for signs of GI upset, such as nausea, vomiting, diarrhea.
- Monitor for signs of hepatic toxicity, such as jaundice, liver enzyme elevations.
- Monitor for signs of renal toxicity, such as proteinuria, hematuria.
- Monitor for signs of cardiac toxicity, such as arrhythmias, electrolyte imbalances.
- Monitor for signs of respiratory toxicity, such as dyspnea, hypoxia.

**Patient/Family Teaching**

- Instruct the patient to take voriconazole exactly as prescribed, even if feeling better.
- Instruct the patient to report any signs of neurotoxicity, such as headache, dizziness, hallucinations, headache.
- Instruct the patient to report any signs of GI upset, such as nausea, vomiting, diarrhea.
- Instruct the patient to report any signs of hepatic toxicity, such as jaundice, liver enzyme elevations.
- Instruct the patient to report any signs of renal toxicity, such as proteinuria, hematuria.
- Instruct the patient to report any signs of cardiac toxicity, such as arrhythmias, electrolyte imbalances.
- Instruct the patient to report any signs of respiratory toxicity, such as dyspnea, hypoxia.

**Evaluation**

- **Knowledge:** Patient can describe the purpose of voriconazole and expected outcomes of therapy.
- **Adherence:** Patient takes voriconazole as prescribed.
- **Clinical:** Improvement in symptoms related to fungal infection.

**Storage**

- Store at room temperature, protected from light.

**Compatibility**


**Incompatibility**

- IV: Incompatible with: Calcium, H2-blockers, Protamine.
Route/Dosage

**IV (Adults and children >12 yr):** Loading dose—6 mg/kg every 12 hour for 2 doses, followed by maintenance dosing—10 mg/kg every 12 hours. IV then switched to oral dosing when possible. If intolerance occurs, dose may be decreased to 5 mg/kg every 12 hr. If phenytoin is coadministered, decrease maintenance dose to 2.5 mg/kg every 12 hr.

**IV (Children 2–11 yr):** Loading dose—6–8 mg/kg (maximum: 600 mg/12 hours) every 12 hours for 2 doses, followed by maintenance dosing—3–5 mg/kg every 12 hr. May be increased to 6 mg/kg every 12 hr if response is inadequate. If phenytoin is coadministered, decrease maintenance dose to 2.5 mg/kg every 12 hr.

**PO (Adults and children >12 yr):** Loading dose—200 mg every 12 hr for 2 doses, followed by maintenance dosing—200 mg every 12 hr. May be increased to 300 mg every 12 hr if response is inadequate. If phenytoin is coadministered, decrease maintenance dose to 5 mg/kg every 12 hr.

**PO (Children >12 yr and ≥25 kg):** Dosing—6 mg/kg every 12 hr. May be increased to 8 mg/kg every 12 hr if response is inadequate. If phenytoin is coadministered, decrease maintenance dose to 2.5 mg/kg every 12 hr.

**PO (Children 2–11 yr and <25 kg):** Loading dose—1.5 mg/kg every 12 hr, followed by maintenance dosing—2 mg/kg every 12 hr. May be increased to 3 mg/kg every 12 hr if response is inadequate. If phenytoin is coadministered, decrease maintenance dose to 5 mg/kg every 12 hr.

**PO (Children <12 yr):** Loading dose—100 mg every 12 hr for 14 days or 7 days following symptom resolution. Maintenance dosing—50 mg every 12 hr for 14 days or 7 days following symptom resolution.

**PO (Children ≤12 yr and ≤25 kg):** Loading dose—6 mg/kg every 12 hr for 2 doses, followed by maintenance dosing—3–5 mg/kg every 12 hr (maximum: 600 mg/12 hours) every 12 hours for 2 doses then Maintenance dosing—7 mg/kg (maximum: 200 mg) every 12 hrs.

**Hepatic Impairment**

**IV (Adults and children >12 yr):** Child-Pugh Class A and B—Use standard loading dose. **PO (Adults and children >12 yr):** Child-Pugh Class A—Use standard loading dose by 50%. Child-Pugh Class C—Not recommended.

**NURSING IMPLICATIONS**

**Assessment**

- Monitor for signs and symptoms of fungal infections prior to and during therapy.
- Obtain specimens for culture and histopathology prior to therapy to isolate and identify organism. Therapy may be started before results are received.
- Monitor visual function including visual acuity, visual field, and color perception in patients receiving more than 28 days of therapy. Vision usually returns to normal within 14 days after discontinuation of therapy.
- Monitor for allergic reactions during infusion of voriconazole (flushing, fever, sweating, tachycardia, chest tightness, dyspnea, tinnitus, nausea, pruritus, rash). Symptoms occur immediately upon start of infusion. May require discontinuation.
- Monitor patients with risk factors for acute pancreatitis (recent chemotherapy, hematopoietic stem cell transplantation [HSCT] for the signs of pancreatitis [abdominal pain, elevated amylase and lipase]).
- Assess for rash periodically during therapy. May cause Stevens-Johnson syndrome. Discontinue therapy if severe or if accompanied with fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, hepatitis and/or eosinophilia.

**Lab Test Considerations:** Monitor liver function tests prior to and during therapy. May cause severe hepatic injury. Discontinue therapy if clinical signs and symptoms of liver disease develop.

**Monitor renal function (serum creatinine)** during therapy. May cause severe nephrotoxicity. Discontinue therapy if levels are elevated.

**Monitor visual function including visual acuity, visual field, and color perception** during therapy.

**Potential Nursing Diagnoses**

- Infection (Infectious)
- Risk for infection (Indications)
- Implementation

- Use patient education oral medication. PO voriconazole must be used.
- Correct electrolyte disturbances (hypokalemia, hypomagnesemia, hypocalcemia) prior to initiation therapy.
- PO: Administer 1 hr before or 1 hr after meal.
- IV: Administer at a rate of 10 mg/mL in normal saline. Administer at a rate of 10 mg/mL in normal saline.

**Interim Infusion:** Reconstitute each 200 mg vial with 20 mL of sterile water for injection to achieve concentration of 10 mg/mL. Calculate volume of 20 mL.
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mg/mL solution required for patient dose. Dilute voriconazole 0.5–5 mg/mL solution into 0.9% NaCl, LR, D5W or D5/LR using aseptic technique. Withdraw and discard equal volume of diluent from infusion bag or bottle to be used. Withdraw required volume of voriconazole solution from vial(s) and add to appropriate volume of 0.9% NaCl, LR, D5W or D5/LR. Recommended solution stable for 24 hr if refrigerated. Discard partially used vials.

Concentration: Final concentration of infusion should be 0.5–5 mg/mL. Rate: Infuse over 1–2 hr at a rate not to exceed 3 mg/kg/hr.

Y-Site Compatibility: acyclovir, alemtuzumab, alfentanil, allopurinol, amifostine, amikacin, aminophylline, amiodarone, amphotericin B liposome, ampicillin, amoxicillin/sulbactam, aminoglycosides, aminoglycoside antibiotics, amphotericin B, azithromycin, aztreonam, bivalirudin, bleomycin, buprenorphine, butorphanol, bumetanide, buprenorphine, butorphanol, calcium acetate, calcium chloride, calcium gluconate, carboplatin, carmustine, carprofen, colchicine, colistimethate, doxorubicin, doxil, edaravone, eptifibatide, etoposide, etoposide phosphate, famotidine, fenoldopam, fentanyl, fluconazole, fludarabine, fluorouracil, foscarnet, fosphenytoin, furosemide, ganciclovir, gemcitabine, gentamicin, glycopyrrolate, granisetron, haloperidol, heparin, hydralazine, hydrocortisone, ifosfamide, imipenem/cilastatin, insulin, irinotecan, isoproterenol, ketorolac, labetalol, leucovorin, levofloxacin, lidocaine, linezolid, lorazepam, magnesium sulfate, mannitol, mesna, methylprednisolone, metoclopramide, metoprolol, metronidazole, midazolam, milrinone, mitomycin, morphine, mycophenolate, nafcillin, nalbuphine, naloxone, nicardipine, nimodipine, nitroglycerin, norepinephrine, octreotide, ondansetron, oxaliplatin, oxytocin, paclitaxel, pamidronate, pancuronium, pentamidine, pentazocine, pentobarbital, phenobarbital, phentolamine, phenylephrine, piperacillin/tazobactam, potassium acetate, potassium chloride, potassium phosphates, procainamide, propafenone, quinapril/hydrochlorothiazide, ranolazine, rosiglitazone, sodium acetate, sodium bicarbonate, sodium phosphate, streptokinase, succinylcholine, sulfonamides, succinylcholine, vancomycin, voriconazole, vorinostat, verapamil, vinblastine, vincristine, vinorelbine, zolmitriptan.

Y-Site Incompatibility: amphotericin B colloidal, amphotericin B lipid complex, besifloxacin, bivalirudin, chlorpromazine, cisplatin, cyclophosphamide, cyclosporine, cytarabine, daclizumab, daunorubicin, doxorubicin, dexamethasone, dexmedetomidine, doxercalciferol, doxoruadine, dopamine, doxorubicin, etoposide, famotidine, famotidine, fentanyl, fenoldopam, famotidine, fludarabine, fluorouracil, foscarnet, fosphenytoin, furosemide, ganciclovir, gemcitabine, gentamicin, glycopyrrolate, granisetron, haloperidol, heparin, hydralazine, hydrocortisone, ifosfamide, imipenem/cilastatin, insulin, irinotecan, isoproterenol, ketorolac, labetalol, leucovorin, levofloxacin, lidocaine, linezolid, lorazepam, magnesium sulfate, mannitol, mesna, methylprednisolone, metoclopramide, metoprolol, metronidazole, midazolam, milrinone, mitomycin, morphine, mycophenolate, nafcillin, nalbuphine, naloxone, nicardipine, nimodipine, nitroglycerin, norepinephrine, octreotide, ondansetron, oxaliplatin, oxytocin, paclitaxel, pamidronate, pancuronium, pentamidine, pentazocine, pentobarbital, phenobarbital, phentolamine, phenylephrine, piperacillin/tazobactam, potassium acetate, potassium chloride, potassium phosphates, procainamide, propafenone, quinapril/hydrochlorothiazide, ranolazine, rosiglitazone, sodium acetate, sodium bicarbonate, sodium phosphate, streptokinase, succinylcholine, sulfonamides, succinylcholine, vancomycin, voriconazole, vorinostat, verapamil, vinblastine, vincristine, vinorelbine, zolmitriptan.

Patient/Family Teaching

Advise patient to take voriconazole as directed, on an empty stomach.

Side effects: blurred vision, photophobia, and dizziness. Caution patient to avoid driving and other activities requiring alertness until response to medication is known. Also advise patient to avoid driving at night during voriconazole therapy.

Advises patient to avoid driving and other activities requiring alertness until response to medication is known. Also advise patients to avoid driving at night during voriconazole therapy.

Advises patient in patients taking 2 or more medications. Caution patient to notify health care professional if any new medications are taken.

Advise patient to notify health care professional if rash or signs and symptoms of allergic reaction occur.

Advises women of childbearing age to use contraception and notify health care professional if pregnancy is planned or suspected or if breast feeding. If pregnancy is detected, discontinue medication as soon as possible.

Evaluation/Desired Outcomes

Resolution of fungal infections.
Why was this drug prescribed for your patient?