Voriconazole
for Oral Suspension
200 mg/5 ml
28-20245
21022-7

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VORICONAZOLE FOR ORAL SUSPENSION safely and effectively. See full prescribing information for VORICONAZOLE FOR ORAL SUSPENSION.

VORICONAZOLE for oral suspension
Initial U.S. Approval: 2002

RECENT MAJOR CHANGES

Warnings and Precautions, Photosensitivity (5.8) 10/2022

INDICATIONS AND USAGE

Voriconazole for oral suspension is an azole antifungal indicated for the treatment of adults and pediatric patients 2 years of age and older with:

- Invasive aspergillosis (1.1)
- Candidemia in non-neutropenic patients and other deep tissue Candida infections (1.2)
- Esophageal candidiasis (1.3)
- Refractory fungal infections caused by *Scedosporium apiospermum* and *Fusarium* species including *Fusarium solani*, in patients intolerant of, or refractory to, other therapies (1.4)

DOSAGE AND ADMINISTRATION

- **Dosage in Adults (2.3)**

Infection	Loading Dose	Maintenance Dose	
	Intravenous infusion	Intravenous infusion	Oral
Invasive Aspergillosis	6 mg/kg every 12 hours for the first 24 hours	4 mg/kg every 12 hours	200 mg every 12 hours
Candidemia in nonneutropenic and other deep tissue Candida infections	6 mg/kg every 12 hours for the first 24 hours	3 to 4 mg/kg every 12 hours	200 mg every 12 hours
Esophageal Candidiasis	Not Evaluated	4 mg/kg every 12 hours	200 mg every 12 hours
Scedosporium and Fusarium	6 mg/kg every 12 hours for the first 24 hours	4 mg/kg every 12 hours	200 mg every 12 hours

- Patients weighing less than 40 kg, oral maintenance dose 100 mg every 12 hours (2.3)
- Hepatic impairment: Cirrhosis Child-Pugh Class B patients with evidence of liver disease with prolonged Child-Pugh Class A and B (2.3)
- *Renal impairment:* Avoid intravenous administration in adult patients with moderate to severe impairment (creatinine clearance < 50 mL/min) (2.8)
- **Dosage in Pediatric Patients 2 years of age and older (2.4)**
- For pediatric patients 2 to less than 12 years of age and 12 to 14 years of age weighing less than 50 kg use Table below.

Infection	Loading Dose	Maintenance Dose	
	Intravenous infusion	Intravenous infusion	Oral
Invasive Aspergillosis	9 mg/kg every 12 hours for the first 24 hours	8 mg/kg every 12 hours after the first 24 hours	9 mg/kg every 12 hours (maximum dose of 350 mg every 12 hours)
Candidemia in nonneutropenic and other deep tissue Candida infections	9 mg/kg every 12 hours for the first 24 hours	7 mg/kg every 12 hours	9 mg/kg every 12 hours (maximum dose of 350 mg every 12 hours)
Scedosporium and Fusarium	9 mg/kg every 12 hours for the first 24 hours	8 mg/kg every 12 hours	9 mg/kg every 12 hours (maximum dose of 350 mg every 12 hours)
Esophageal Candidiasis	Not Evaluated	Not Evaluated	9 mg/kg every 12 hours (maximum dose of 350 mg every 12 hours)

- For pediatric 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. (2.4)
- Dosage adjustment of voriconazole in pediatric patients with renal or hepatic impairment has not been established (2.5, 2.8)
- See full prescribing information for instructions on reconstitution of voriconazole oral suspension and important administration instructions (2.1, 2.6, 2.7)

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Invasive Aspergillosis

Voriconazole for oral suspension is indicated in adults and pediatric patients 2 years of age and older for the treatment of invasive aspergillosis (AI). In clinical trials, the majority of isolates recovered were *Aspergillus fumigatus*. There was a small number of cases of culture-proven disease due to species of *Aspergillus* other than *A. fumigatus* (see *Clinical Studies 7.1 of and Microbiology 12.4*).

1.2 Candidemia in Non-neutropenic Patients and Other Deep Tissue Candida Infections

Voriconazole for oral suspension is indicated in adults and pediatric patients 2 years of age and older for the treatment of candidemia in non-neutropenic patients and the following Candida infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall, and wounds (see *Clinical Studies 7.2, 7.6 and Microbiology 12.4*).

1.3 Esophageal Candidiasis

Voriconazole for oral suspension is indicated for the treatment of serious fungal infections caused by *Scedosporium apiospermum* (asexual form of *Pseudallescheria boydii*) and *Fusarium* species, including *Fusarium solani*, in adults and pediatric patients 2 years of age and older intolerant of, or refractory to, other therapies (see *Clinical Studies 7.4 and Microbiology 12.4*).

1.5 Usage

Specimens for fungal cultures and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organisms. Therapy may be instituted before results of the cultures and other laboratory studies are known. However, once these results become available, antifungal therapy should be adjusted accordingly.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions for Use in All Patients

Intravenous administration of voriconazole should be given at a rate not to exceed 3 mg/kg/hour over a 3 hour period.

2.2 Recommended Dosing Regimen in Adults

Invasive aspergillosis and serious fungal infections due to *Fusarium* spp. and *Scedosporium apiospermum*

See Table 1. Therapy must be initiated with the specified loading dose regimen of intravenous voriconazole on Day 1 followed by the recommended maintenance dose (RMD) regimen. Intravenous treatment should be continued for at least 7 days. Once the patient has clinically improved and can tolerate oral medication, oral voriconazole may be administered. The total duration of treatment should be based on the patient's overall clinical response. Administration of 200 mg oral tablets or a voriconazole suspension similar to 2 mg/kg intravenous dose, or 200 mg oral dose (tablet or suspension) are equivalent (see *Clinical Pharmacology 12.3*).

Candidemia in non-neutropenic patients and other deep tissue Candida infections

See Table 1. Patients should be treated for at least 14 days following resolution of symptoms or following laboratory test positive cultures, whichever is longer.

Esophageal Candidiasis

See Table 1. Patients should be treated for a minimum of 14 days and for at least 7 days following resolution of symptoms.

Table 1: Recommended Dosing Regimen (Adults)

Infection	Loading Dose	Maintenance Dose	
	Intravenous infusion	Intravenous infusion	Oral[a]
Invasive Aspergillosis[b]	6 mg/kg every 12 hours for the first 24 hours	4 mg/kg every 12 hours	200 mg every 12 hours
Candidemia in nonneutropenic patients and other deep tissue Candida infections	6 mg/kg every 12 hours for the first 24 hours	3 to 4 mg/kg every 12 hours	200 mg every 12 hours
Esophageal Candidiasis	Not Evaluated[c]	Not Evaluated	200 mg every 12 hours
Scedosporium and Fusarium	6 mg/kg every 12 hours for the first 24 hours	4 mg/kg every 12 hours	200 mg every 12 hours

[a] Intravenous dosage when voriconazole oral suspension is co-administered with phenytoin or efavirenz: (7) Decreasing the maintenance dose to 2 mg/kg intravenous every 12 hours in healthy volunteer studies, the 200 mg oral every 12 hours dose provided an exposure (AUC) similar to a 2 mg/kg intravenous infusion every 12 hours dose, the 300 mg oral every 12 hours dose provided an exposure (AUC) similar to the 3 mg/kg intravenous every 12 hours dose (12.3).

[b] Adult patients who weigh less than 40 kg should receive half of the oral maintenance dose.

[c] Data from a study in 24 immunocompromised adult patients with esophageal candidiasis treated for 10 days (range 1 to 21 days) of oral voriconazole therapy was 10 days (range 2 to 22 days) (14.3).

In clinical trials, patients with candidemia received 2 mg/kg intravenous infusion every 12 hours as primary therapy, while patients with other deep tissue Candida infections received 3 mg/kg every 12 hours as salvage therapy. Appropriate dose should be based on the severity and nature of the infection.

Oral dosing recommended in patients with CC.

Method for Adjusting the Dosing Regimen in Adults

If patient's response is inadequate, the oral maintenance dose may be increased from 200 mg every 12 hours (similar to 3 mg/kg intravenous every 12 hours) to 300 mg every 12 hours (similar to 4 mg/kg intravenous every 12 hours). For adult patients weighing less than 40 kg, the oral maintenance dose may be increased from 100 mg every 12 hours to 150 mg every 12 hours. If patient is unable to tolerate 200 mg orally every 12 hours, reduce the oral maintenance dose to 100 mg every 12 hours (or 150 mg every 12 hours if patient weighs less than 40 kg) or administer intravenously.

If patient is unable to tolerate 4 mg/kg intravenously every 12 hours, reduce the intravenous maintenance dose to 3 mg/kg every 12 hours.

2.4 Recommended Dosing Regimen in Pediatric Patients

Intravenous dosing regimen for pediatric patients 2 to less than 12 years of age and 12 to 14 years of age with body weight less than 50 kg is shown in Table 2. For pediatric patients 12 to 14 years of age with a body weight greater than or equal to 50 kg and those 15 years of age and above regardless of body weight, administer the adult dosing regimen (see Table 1 and Section 2.2).

Table 2: Recommended Dosing Regimen for Pediatric Patients 2 to less than 12 years of age and 12 to 14 years of age with body weight less than 50 kg

	Loading Dose	Maintenance Dose	
	Intravenous infusion	Intravenous infusion	Oral
Invasive Aspergillosis[a]	9 mg/kg every 12 hours for the first 24 hours	8 mg/kg every 12 hours after the first 24 hours	9 mg/kg every 12 hours (maximum dose of 350 mg every 12 hours)
Candidemia in nonneutropenic and other deep tissue Candida infections	9 mg/kg every 12 hours for the first 24 hours	7 mg/kg every 12 hours	9 mg/kg every 12 hours (maximum dose of 350 mg every 12 hours)
Scedosporium and Fusarium	9 mg/kg every 12 hours for the first 24 hours	8 mg/kg every 12 hours	9 mg/kg every 12 hours (maximum dose of 350 mg every 12 hours)
Esophageal Candidiasis[b]	Not Evaluated	9 mg/kg every 12 hours	9 mg/kg every 12 hours (maximum dose of 350 mg every 12 hours)

[a] Based on a population pharmacokinetic analysis in 112 immunocompromised pediatric patients aged 2 to less than 12 years of age and immunocompromised adolescent patients aged 12 to 14 years of age (12.3).

[b] No Phase 3 trial data are available in pediatric patients with CC treated with voriconazole. The treatment for at least 8 weeks and up to a maximum of 12 weeks. Patients who have achieved a complete response within the first 4 weeks of therapy may be considered for an abbreviated course of therapy.

Study treatment for primary or salvage invasive candidiasis and candidemia (CC) in CC consisted of intravenous voriconazole, with an option to switch to oral therapy after at least 5 days of IV therapy, based on subject's meeting switch criteria. For subjects with primary or salvage CC, voriconazole was administered for a median of 15 days (range 1 to 122 days) and 14 days (range 1 to 122 days) respectively. Subjects with primary or salvage CC were treated for at least 7 days after the resolution of clinical signs and symptoms. A treatment of 42 days of treatment was permitted.

Intent therapy with an intravenous infusion regimen. Consider oral regimen only after there is a significant clinical improvement. Note that an 4 mg/kg intravenous dose will provide voriconazole exposure approximately 1.4 times higher than a 3 mg/kg dose.

The oral dose recommendation for children is based on studies in which voriconazole was administered as the powder for oral suspension formulation, pediatric bioavailability was lower than that observed with the film-coated tablet formulation. Although the oral bioavailability of the film-coated tablet formulation in adult patients is 2 to 12 times with malabsorption and very low body weight for age, in that case, intravenous voriconazole administration is recommended.

Method for Adjusting the Dosing Regimen in Pediatric Patients

Pediatric Patients 2 to less than 12 years of age and 12 to 14 years of age with body weight less than 50 kg

If patient's response is inadequate, the oral maintenance dose may be increased from 9 mg/kg every 12 hours, the maintenance dose may be increased to 9 mg/kg every 8 hours. If patient response is inadequate with the patient's clinic to tolerate the oral maintenance dose, the dose may be increased to 7 mg/kg every 12 hours. If patients are unable to tolerate the oral maintenance dose, reduce the dose to 7 mg/kg every 12 hours. If patients are unable to tolerate the oral maintenance dose, reduce the dose to 7 mg/kg every 12 hours.

Pediatric patients 12 to 14 years of age weighing greater than or equal to 50 kg and 15 years of age and older regardless of body weight:

Use the optimal method for titrating dosage recommended in Adults Dosage Dose Adjustment (Section 2.2).

2.5 Dosage Modifications in Patients With Hepatic Impairment

Mild Cirrhosis

The maintenance dose of voriconazole for oral suspension should be reduced in adult patients with mild to moderate hepatic impairment. Child-Pugh Class A and B. There are no PK data to allow for dosage adjustment recommendations in patients with severe hepatic impairment Child-Pugh Class C.

Duration of therapy should be based on the severity of the patient's underlying disease, recovery from immunosuppression, and clinical response.

Adult patients with baseline liver function tests (ALT, AST) of up to 5 times the upper limit of normal (ULN) were included in the clinical program. Dose adjustments are not recommended for patients with baseline ALT and AST of up to 5 times the ULN. Caution is recommended when prescribing to these patients.

It is recommended that the recommended voriconazole for oral suspension loading dose regimen be used, but that the maintenance dose be halved in adult patients with mild to moderate hepatic cirrhosis (Child-Pugh Class A and B) and that patients be closely monitored for signs of toxicity.

Voriconazole for oral suspension has not been studied in adult patients with severe hepatic cirrhosis (Child-Pugh Class C) or in patients with chronic hepatitis B or chronic hepatitis C disease. Voriconazole for oral suspension has been associated with abnormal liver function tests and with clinical signs of liver damage, such as jaundice. Voriconazole for oral suspension should only be used in patients with severe hepatic impairment if the benefit outweighs the potential risk. Patients with hepatic impairment may be at higher risk for adverse reactions.

Pediatric Patients

Dosage adjustment of voriconazole for oral suspension in pediatric patients with hepatic impairment has not been established (see *Use in Specific Populations 8.6*).

2.6 Dosage Modifications in Patients With Renal Impairment

Renal Impairment

The pharmacokinetics of orally administered voriconazole for oral suspension are not significantly affected by renal impairment. Therefore, no adjustment is necessary for patients dosing in patients with mild to severe renal impairment (see *Clinical Pharmacology 12.3*).

In patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min) who are receiving intravenous infusion of voriconazole, accumulation of the intravenous vehicle, SBECD, occurs. Oral voriconazole should be administered to these patients, unless an assessment of the benefit/risk of intravenous voriconazole administration is considered to outweigh the potential risks associated with the accumulation of the vehicle.

Intravenous voriconazole should be given in hemodialysis patients only if the benefit outweighs the potential risk. Hemodialysis and the intravenous vehicle, SBECD, are dialyzed. A 4 hour hemodialysis session does not remove a sufficient amount of voriconazole to warrant dose adjustment (see *Clinical Pharmacology 12.3*).

Pediatric Patients

Dosage adjustment of voriconazole for oral suspension in pediatric patients with renal impairment has not been established (see *Use in Specific Populations 8.6*).

2.7 Dosage Adjustment When Co-Administered With Phenytoin or Efavirenz

The maintenance dose of voriconazole should be increased when co-administered with phenytoin or efavirenz. Use the optimal method for titrating dosage recommended in Adults Dosage Dose Adjustment (Section 2.2).

2.8 Preparation and Administration of Voriconazole Oral Suspension

Reconstitution

Tap the bottle to release the powder. Add 46 mL of water to the bottle. Shake the closed bottle vigorously for about 1 minute. Remove child-resistant cap and push bottle adapter into the neck of the bottle. Replace the cap. Write the date of preparation of the reconstituted suspension on the bottle label as the suspension is stable for only 14 days. Shake the reconstituted suspension for 15 seconds before each use.

Instructions for use

Shake the closed bottle of reconstituted suspension for approximately 15 seconds before each use. The reconstituted oral suspension should only be administered using the oral dispenser supplied with each pack.

- *For Oral Suspension:* 40 mg/ml, (200 mg/5 ml), white to off white color.

4 CONTRAINDICATIONS

- Hypersensitivity to voriconazole or its excipients (4).
- Coadministration with pimozide, quinidine, sirolimus or ivabradine due to risk of severe adverse reactions (4, 7).
- Coadministration with rifampin, carbamazepine, long acting barbiturates, efavirenz, rimonavir, ritonavir, rapid acting oral ergot alkaloids, and St. John's Wort due to risk of loss of efficacy (4, 7).
- Coadministration with sulmazapil, terfenadine, and lovastatin due to risk of adverse reactions (4, 7).
- Coadministration with rifampin, carbamazepine and efavirenz in patients with 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 (4, 7).

5 WARNINGS AND PRECAUTIONS

Hepatic Toxicity: Serious hepatic reactions reported. Evaluate liver function tests at start of and during voriconazole therapy (5.1).

Arrhythmias and QT Prolongation: Correct potassium, magnesium and calcium prior to use; caution patients with proarrhythmic conditions (5.2).

Visual Disturbances: Including severe and prolonged blindness. Monitor ophthalmic examinations if visual disturbances occur (5.3).

Severe Cutaneous Adverse Reaction: Discontinue for exfoliative cutaneous reactions (5.3).

Photosensitivity: Avoid exposure to direct sunlight (5.5).

Adrenal Dysfunction: Carefully monitor patients receiving voriconazole and corticosteroids (all routes of administration) for adrenal dysfunction both during and after voriconazole treatment. Instruct patients to seek immediate medical care if they develop signs and symptoms of Cushing's syndrome or adrenal insufficiency (5.7).

Embryo-Fetal Toxicity: Voriconazole can cause fetal harm when administered to a pregnant woman. Inform pregnant patients of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with voriconazole (see *Use in Specific Populations 8.1, 8.3*).

Diabetic Adverse Reaction: Pancreatitis and hypoglycemia with long term voriconazole therapy. Discontinue if these adverse reactions occur (5.10).

Clinically Significant Drug Interactions: Review patient's concomitant medications (5.12, 7).

6 ADVERSE REACTIONS

Adult Patients: The most common adverse reactions (> 2%) were visual disturbances, pyrexia, vomiting, nausea, rash, vomiting, chills, headache, diarrhea, abdominal pain, and peripheral edema (6.1).

Pediatric Patients: The most common adverse reactions (≥ 5%) were visual disturbances, pyrexia, vomiting, epistaxis, nausea, chills, abdominal pain, diarrhea, hypertension, hypokalemia, cough, headache, thrombocytopenia, ALT elevated, hypotension, peripheral edema, hypoglycemia, tachycardia, dyspnea, hypocalcemia, hypokalemia, GGT elevated, neutropenia, bilirubin elevated, alkaline phosphatase elevated, AST elevated, hypotension, peripheral edema, hypertension, rash, and renal dysfunction (see *Clinical Studies 7.6*).

To report SUSPECTED ADVERSE REACTIONS, contact **Camber Pharma Inc. at 1-888-495-1088 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

DRUG INTERACTIONS

CYP3A4, CYP2C19, and CYP2C9 inhibitors and inducers: Adjust voriconazole dosage and monitor for adverse reactions or lack of efficacy (7).

Oral contraceptives (combined oral contraceptives containing a form of estrogen and a form of progestin): Adjust dosage of both drugs and monitor for adverse reactions (7, 8).

Phenytoin or Efavirenz: With co-administration, increase maintenance oral and intravenous dosage of voriconazole (2.2, 2.7, 7).

- *Pediatrics:* Safety and effectiveness in pediatric younger than 2 years has not been established (8.4).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

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7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

13 NONCLINICAL TOXICOLOGY

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

Incompatibilities

Voriconazole for oral suspension and the 40 mg/ml, reconstituted oral suspension should not be mixed with any other medication or additional flavoring agent. It is not intended that the suspension be further diluted for administration.

3 DOSAGE FORMS AND STRENGTHS

Powder for Oral Suspension

Voriconazole for oral suspension is supplied as a white to off white powder in 100 mL high density polyethylene (HDPE) bottles. Following reconstitution, the resulting suspension contains approximately 5 mL of voriconazole for oral suspension 40 mg/mL, 5 ml of the oral suspension contains 40 mg of voriconazole (200 mg of voriconazole per 5 ml).

4 CONTRAINDICATIONS

- Voriconazole for oral suspension is contraindicated in patients with known hypersensitivity to voriconazole or its excipients. There is no cross-hypersensitivity between voriconazole and other antifungal drugs. Consider that azole antifungals should be used when prescribing voriconazole for oral suspension.
- Coadministration of pimozide, quinidine or ivabradine with voriconazole is contraindicated because increased plasma concentrations of these medications may lead to severe adverse reactions including cardiac events (see *Drug Interactions 7*).
- Coadministration of voriconazole with sirolimus is contraindicated because voriconazole significantly increases sirolimus concentrations (see *Drug Interactions 7*) and *Clinical Pharmacology 12.3*).
- Coadministration of voriconazole with efavirenz is contraindicated in low-dose efavirenz (400 mg daily) given with voriconazole because voriconazole significantly decreases plasma concentrations of efavirenz in healthy subjects at these doses. Voriconazole also significantly increases efavirenz plasma concentrations (see *Drug Interactions 7*) and *Clinical Pharmacology 12.3*).
- Coadministration of voriconazole with rifampin is contraindicated because rifampin is contraindicated because rimonavir (400 mg every 12 hours) significantly decreases plasma voriconazole concentrations. Coadministration of voriconazole and low-dose ritonavir (100 mg every 12 hours) significantly decreases the pharmacokinetic assessment of the bioeffectivity in the patient profile the use of voriconazole (see *Drug Interactions 7*) and *Clinical Pharmacology 12.3*).
- Coadministration of voriconazole with rifabutin is contraindicated since voriconazole significantly increases rifabutin plasma concentrations and rifabutin significantly decreases voriconazole plasma concentrations (see *Drug Interactions 7*) and *Clinical Pharmacology 12.3*).
- Coadministration of voriconazole with rifampin, carbamazepine, long acting barbiturates, and St. John's Wort is contraindicated because these drugs are likely to decrease plasma voriconazole concentrations significantly (see *Drug Interactions 7*) and *Clinical Pharmacology 12.3*).
- Coadministration of voriconazole with sulmazapil, terfenadine, and lovastatin is contraindicated because these medications may increase plasma concentrations (see *Drug Interactions 7*) and *Clinical Pharmacology 12.3*).
- Coadministration of voriconazole with ivabradine is contraindicated since it may result in significant increases in ivabradine exposure and the occurrence of cardiac adverse events (see *Drug Interactions 7*).

5 WARNINGS AND PRECAUTIONS

5.1 Hepatic Toxicity

In clinical trials, there have been uncommon cases of serious hepatic reactions during treatment with voriconazole (including clinical hepatitis, cholestasis and fulminant hepatic failure, including fatalities). Instances of hepatic reactions were noted to occur primarily in patients with serious underlying medical conditions (predominantly hematological malignancy). Hepatic reactions, including hepatitis and jaundice, have occurred among patients without apparent risk factors or underlying diseases during treatment with voriconazole for oral suspension. Hepatic reactions have been reported to be higher frequency of have occurred among patients with severe underlying medical conditions when voriconazole for oral suspension was administered in the pediatric population (see *Adverse Reactions 6*). Hepatic function should be monitored in both adult and pediatric patients.

Measure serum transaminases and bilirubin at the initiation of voriconazole therapy and monitor at least weekly for the first month of treatment. Monitoring frequency can be reduced to monthly during continued use if no clinically significant changes are noted. If liver function tests become markedly abnormal, voriconazole administration should be discontinued unless the medical judgment of the benefit to the patient outweighs the risk. Consider the benefit of the treatment for the patient (see Contraindications and *Administration 2.8* and *Adverse Reactions 6.1, 6.2*).

5.2 Arrhythmias and QT Prolongation

Some azoles, including voriconazole, have been associated with prolongation of the QT interval on the electrocardiogram. During clinical development and postmarketing surveillance, there have been rare cases of arrhythmias, including ventricular arrhythmias such as torsade de pointes, cardiac arrest and sudden deaths in patients taking voriconazole. These cases usually involved seriously ill patients with multiple predisposing factors such as history of cardiotoxic chemotherapy, cardiomyopathy, hypokalemia and concomitant medications that may have been contributory.

Use voriconazole for oral suspension with caution in patients with potentially proarrhythmic conditions, such as:

- Congenital or acquired QT prolongation
- Cardiomyopathy, in particular when heart failure is present
- Sinus bradycardia
- Existing symptomatic arrhythmias
- Concomitant medical product that is known to prolong QT interval (see Contraindications 4), *Drug Interactions 7.5*, and *Clinical Pharmacology 12.2*)

Rigorous attempts to correct potassium, magnesium and calcium should be made before starting and during voriconazole therapy (see *Clinical Pharmacology 12.2*).

5.4 Visual Disturbances

Serious and prolonged visual function is not known if treatment continues beyond 28 days. There have been postmarketing reports of prolonged visual adverse reactions, including optic neuritis and papilledema. Most of these events occurred in patients receiving systemic antifungals, visual field, and color perception should be monitored (see *Adverse Reactions 6.2*).

5.5 Severe Cutaneous Adverse Reactions

Severe cutaneous adverse reactions (SCAR), such as Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in patients taking voriconazole.

Consider the occurrence of photosensitivity related lesions, dermatological evaluation should be performed on a systematic and regular basis to allow early detection and management of potential SCAR. Advise patients to avoid exposure to direct sunlight. Discontinue voriconazole if SCAR occur. There are reoccurrence lesions reported among voriconazole therapy in patients with photosensitivity skin reactions. If a patient develops a skin lesion consistent with photosensitivity skin lesions, squamous cell carcinoma or melanoma, voriconazole should be discontinued. In addition, voriconazole has been associated with photosensitivity related events including photokeratitis, erythema, and photosensitivity dermatitis. Photosensitivity related events in children appear to be at a higher risk than in adults with voriconazole and may be associated with developing SCC in children. Consider the benefit-risk of voriconazole in children and adolescents and consider discontinuation of voriconazole if SCAR occur.

5.6 Pharmacovigilance

Voriconazole has been associated with severe reactions. Patients, including pediatric patients, should avoid exposure to direct sunlight during voriconazole treatment and should use measures such as protective clothing and sunscreen with high sun protection factor (SPF). If photosensitive reactions occur, the patient should be referred to a dermatologist and voriconazole discontinued should be considered. Long-term voriconazole is continued despite the occurrence of photosensitivity related lesions, dermatological evaluation should be performed on a systematic and regular basis to allow early detection and management of potential SCAR. Advise patients to avoid exposure to direct sunlight. Discontinue voriconazole if SCAR occur. There are reoccurrence lesions reported among voriconazole therapy in patients with photosensitivity skin reactions. If a patient develops a skin lesion consistent with photosensitivity skin lesions, squamous cell carcinoma or melanoma, voriconazole should be discontinued. In addition, voriconazole has been associated with photosensitivity related events including photokeratitis, erythema, and photosensitivity dermatitis. Photosensitivity related events in children appear to be at a higher risk than in adults with voriconazole and may be associated with developing SCC in children. Consider the benefit-risk of voriconazole in children and adolescents and consider discontinuation of voriconazole if SCAR occur.

5.7 Adrenal Insufficiency

The frequency of photosensitivity reactions is higher in the pediatric population. Because exposures will overstress have been reported in patients who experience photosensitivity reactions, stringent measures for photoprotection are warranted in children. In children experiencing photosensitivity reactions such as lentigines or ephelides, sun exposure and sunscreen use. Consider the benefit-risk of voriconazole in children and adolescents.

5.8 Embryo-Fetal Toxicity

Voriconazole can cause fetal harm when administered to a pregnant woman.

In animals, voriconazole administration was associated with fetal malformations, embryotoxicity, increased gestational length, dystocia and stillbirths at systemic exposures lower than those in humans.

Voriconazole is contraindicated during pregnancy, or if the patient is pregnant while taking voriconazole, inform the patient of the potential hazard to the fetus. Advise females of reproductive potential to use effective contraception during treatment with voriconazole (see *Use in Specific Populations 8.1, 8.3*).

5.9 Laboratory Tests

Electrolyte disturbances such as hypokalemia, hypomagnesemia and hypocalcemia should be corrected prior to initiation of and during voriconazole therapy.

Patient management should include laboratory evaluation of renal and hepatic function (particularly liver function tests [LFTs]).

5.10 Pancreatitis

Pancreatitis has been observed in patients undergoing treatment with voriconazole (see *Adverse Reactions 6.1, 6.2*) Patients with risk factors for pancreatitis, such as recent chemotherapy, hematopoietic stem cell transplantation (HSCT) should be monitored for the development of pancreatitis during voriconazole treatment.

5.11 Diabetic Adverse Reactions

Pancreas and pancreatitis have been reported during long term voriconazole therapy. If a patient develops abdominal pain and nauseous, hypoglycemia and hypokalemia, discontinue voriconazole and monitor for signs of pancreatitis.

5.12 Clinically Significant Drug Interactions

See Table 10 for a listing of drugs that may significantly alter voriconazole concentrations. Also, see Table 11 for a listing of drugs that may interact with voriconazole resulting in altered pharmacodynamics. Consider the benefit-risk of the other drug (see Contraindications 4) and Drug Interactions 7).

6 ADVERSE REACTIONS

The following serious reactions are described elsewhere in the labeling:

Hepatic Toxicity (see *Warnings and Precautions 5.1*)

Serious Cutaneous Adverse Reaction (see *Warnings and Precautions 5.3*)

Visual Disturbances (see *Warnings and Precautions 5.4*)

Severe Cutaneous Adverse Reactions (see *Warnings and Precautions 5.5*)

Photosensitivity (see *Warnings and Precautions 5.6*)

Fetal Toxicity (see *Warnings and Precautions 5.8*)

6.1 Clinical Trials Experience

Because clinical trials are conducted in a variety of settings, the observed adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience in Adults

Overview

The most frequently reported adverse reactions (see Table 4) in the adult pharmacokinetic trials were visual disturbances (10.7%), fever (6.7%), nausea (6.4%), vomiting (6.4%), rash (5.9%), diarrhea (5.2%), headache (5.2%), liver function test increased (2.7%), hypokalemia (2.4%), hallucinations (2.4%). The adverse reactions which most often led to discontinuation of voriconazole treatment were drug-related liver function tests, rash, and visual disturbances (see *Warnings and Precautions 5.1, 5.4 and Adverse Reactions 6.1*).

The data described in Table 4 reflect exposure to voriconazole in 1055 patients in nine therapeutic studies. This represents a heterogeneous population, including patients treated for invasive fungal infections (IFI) and those with other medical conditions. Most of the adverse reactions in Table 4 were observed in the patients treated for IFI and patients receiving voriconazole for prophylaxis of IFI. The patient population was 55% male, 45% female, 76% Caucasian, 14% Black, 3% Hispanic, 2% Asian, and 5% other. The patient population was 2% aged 12-17 years, 2% aged 18-64 years, and 96% aged ≥65 years. Patients received a wide variety of concomitant medications while receiving voriconazole. Of the patients who received voriconazole, 27% were treated for more than 12 weeks, 16% for more than 24 weeks, 10% for more than 36 weeks, and 5% for more than 48 weeks. The most common underlying diseases were hematopoietic stem cell transplantation (HSCT) allogeneic (26.4%), hematopoietic stem cell transplantation (HSCT) autologous (14.5%), and acute myelogenous leukemia (AML) (12.4%).

Table 4: Adverse Reactions Rate ≥ 2% in Voriconazole or Adverse Reactions of Concern in Therapeutic Studies Population, Studies 307/802 + 600 Combined, or Study 309, Possibly Related to Therapy or Causality Unknown

	Therapeutic Studies[a]	Studies 307/802 and 600 (Fixed therapy)		Study 309 (oral therapy)	
	Voriconazole N = 1,055	Voriconazole N = 546	Amphotericin B[b] N = 165	Voriconazole N = 288	Fluconazole[c] N = 131
	N (%)	N (%)	N (%)	N (%)	N (%)
Special Senses[d,e,f]					
Abnormal vision	310 (10.7)	83 (15.5)	1 (0.5)	0	31 (15.5)
Photophobia	37 (2.2)	6 (1.1)	0	1 (0.3)	5 (2.5)
Chromatopsia	20 (1.2)	2 (0.4)	0	2 (1.0)	0
Body as a Whole					
Fever	84 (6.7)	8 (1.7)	25 (13.5)	5 (1.8)	0
Chills	87 (5.0)	1 (0.2)	36 (19.6)	8 (6.1)	1 (0.5)
Headache	40 (2.0)	9 (1.9)	8 (4.3)	1 (0.8)	0 (0.5)
Cardiovascular System					
Tachycardia	34 (2.4)	6 (1.3)	1 (2.7)	0	0
Digestive System					
Nausea	89 (6.4)	16 (3.8)	29 (15.7)	2 (1.5)	2 (1.8)
Vomiting	72 (4.4)	15 (3.2)	18 (8.7)	1 (0.8)	2 (1.8)
Liver function tests abnormal	46 (2.7)	15 (3.2)	4 (2.2)	1 (0.8)	4 (3.0)
Cholestatic jaundice	17 (1.0)	8 (1.5)	0	1 (0.8)	2 (1.5)
Metabolic and Nutritional Systems					
Hypokalemia[g]	18 (2.6)	19 (4.1)	4 (2.2)	3 (2.3)	10 (6.0)
Hepatic enzymes increased	30 (1.8)	11 (2.4)	5 (2.7)	1 (0.8)	3 (1.8)
Edema	21 (1.8)	8 (1.8)	0	1 (0.8)	8 (4.8)
SGPT increased	25 (1.8)	8 (1.8)	1 (0.5)	2 (1.5)	6 (3.8)
Hypokalemia	22 (1.8)	3 (0.6)	26 (16.9)	10 (12.5)	0
Bilirubinemia	15 (0.9)	5 (1.1)	3 (1.8)	2 (1.5)	1 (0.5)
Creatinine increased	4 (0.2)	0	10 (21.3)	10 (1.8)	1 (0.5)

Drug/Drug Class (Mechanism of interaction by Voriconazole)	Drug Plasma Exposure (C_{max} and AUC)	Recommendations for Drug Dosage Adjustment/Comments
NSAIDs ******* including Ibuprofen and diclofenac (CYP2C9 Inhibition)	Increased	Frequent monitoring for adverse reactions and toxicity related to NSAIDs; dose reduction of NSAIDs may be needed.
Tacrolimus* (CYP3A4 Inhibition)	Significantly Increased	When initiating therapy with voriconazole in patients already receiving tacrolimus, reduce the tacrolimus dose to one third of the baseline dose and monitor tacrolimus blood levels. Increased tacrolimus levels have been associated with nephrotoxicity. When voriconazole is discontinued, tacrolimus concentrations must be frequently monitored for at least two weeks thereafter.
Phenytoin* (CYP2C9 Inhibition)	Significantly Increased	Frequent monitoring of phenytoin plasma concentrations and frequent monitoring of adverse effects related to phenytoin.
Oral Contraceptives containing Ethinylestradiol and Levonorgestrel (CYP3A4 Inhibition)*	Increased	Monitoring for adverse reactions related to oral contraceptives is recommended.
Prednisolone and other corticosteroids (CYP3A4 Inhibition)	*In Vitro Studies Showed No Significant Effects of Voriconazole on Prednisolone Exposure.* Not Studied *In vitro* or *In vivo* for Other Corticosteroids, but Drug Exposure Likely to be Increased	No dosage adjustment for prednisolone when coadministered with voriconazole. Refer to *Prednisolone Pharmacology (12.3)* Monitor for potential altered duration for other corticosteroids is administered with voriconazole. Refer to *Drug Interactions, Pharmacology (12.3), Other Warnings and Dosage & Administration (2.8)*
Warfarin* (CYP2C9 Inhibition) Other Oral Coumarin Anticoagulants (CYP2C9/3A4 Inhibition)	Prothrombin Time Significantly Increased Not Studied *In vitro* or *In Vivo* for other Oral Coumarin Anticoagulants, but Drug Plasma Exposure Likely to be Increased	If patients receiving coumarin preparations are treated concomitantly with voriconazole, the prothrombin time or other appropriate coagulation tests should be monitored at close intervals and the dosage of anticoagulants adjusted accordingly.
Ivacaftor (CYP3A4 Inhibition)	Not Studied *In Vivo* or *In Vitro*, but Drug Plasma Exposure Likely to be Increased which may increase the Adverse Reactions	Dose reduction of ivacaftor is recommended. Refer to the prescribing information for ivacaftor.
Sulfonylurea (CYP2C9 Inhibition)	Not Studied *In Vivo* or *In Vitro*, but Drug Plasma Exposure Likely to be Increased which may Increase the Sulfonylurea Effect of Hypoglycemia	Frequent monitoring for adverse reactions. Dose reduction of sulfonylurea is recommended. Refer to the prescribing information for sulfonylurea.
Omeprazole* (CYP2C19/3A4 Inhibition)	Significantly Increased	When initiating therapy with voriconazole in patients receiving doses of omeprazole of 40 mg or greater, reduce the omeprazole dose by half. Increased omeprazole or proton pump inhibitors that use CYP2C19 substrates may also be inhibited by voriconazole which may lead to increased plasma concentrations of other proton pump inhibitors.
Other NSI Immune Inhibitors (CYP3A4 Inhibition)	*In Vitro Studies Showed No Significant Effects on Sirolimus Exposure.* *In Vitro Studies Demonstrated Potential for Voriconazole to Inhibit Metabolism Decreased Sirolimus Exposure.*	No dosage adjustment for sirolimus when coadministered with voriconazole. Frequent monitoring for adverse reactions and toxicity related to other NSI immune inhibitors.
Other MMTN ******* (CYP3A4 Inhibition)	*In Vitro Studies Showed No Significant Effects on Midazolam Exposure.* *In Vitro Studies Demonstrated Potential for Voriconazole to Inhibit Metabolism of Other MMTN Decreased Plasma Exposure.*	Frequent monitoring for adverse reactions and toxicity related to MMTN.
Tacrolimus (CYP3A4 Inhibition)	Although Not Studied, Tacrolimus exposure Increase Toxicity Concentrations and Increase the Risk of Nephrotoxicity	Frequent monitoring for signs and symptoms of preoptimize creatinine in hepatectomies.
Midazolam (CYP3A4 Inhibition) Other benzodiazepines including triazolam and alprazolam	Significantly Increased *In Vitro Studies Demonstrated Potential for Voriconazole to Inhibit Metabolism Decreased Plasma Exposure*	Increased plasma concentrations increase the risk of adverse reactions and toxicities related to benzodiazepines. Refer to drug specific labeling for details.
HMG-CoA Reductase Inhibitors (Statins) (CYP3A4 Inhibition)	*In Vitro Studies Demonstrated Potential for Voriconazole to Inhibit Metabolism Decreased Plasma Exposure*	Frequent monitoring for adverse reactions and toxicity related to statins. Increased statin concentrations in plasma have been associated with rhabdomyolysis. Temporarily suspend dosing of the statin drug may be needed.
Dihydropyridine Calcium Channel Blockers (CYP3A4 Inhibition)	*In Vitro Studies Demonstrated Potential for Voriconazole to Inhibit Metabolism Decreased Plasma Exposure*	Frequent monitoring for adverse reactions and toxicity related to calcium channel blockers. Adjustment of calcium channel blocker dosage may be needed.
Sulfonylurea Oral Hypoglycemics (CYP2C9 Inhibition)	Not Studied *In Vivo* or *In Vitro*, but Drug Plasma Exposure Likely to be Increased	Frequent monitoring for adverse reactions for signs and symptoms of hypoglycemia. Adjustment of oral hypoglycemic drug dosage may be needed.
Vinca Alkaloids (CYP3A4 Inhibition)	Not Studied *In Vivo* or *In Vitro*, but Drug Plasma Exposure Likely to be Increased	Frequent monitoring for adverse reactions and toxicity (i.e., neurotoxicity) related to vinca alkaloids. Reduce vinca alkaloids, including vincristine, for patients receiving a vinca alkaloid who have an alternative antifungal treatment options.
Tacrolimus (CYP3A4 Inhibition)	Not Studied *In Vivo* or *In Vitro*, but Drug Plasma Exposure Likely to be Increased	Concentration administration of voriconazole and vincristine is not recommended.

* Results based on *in vivo* clinical studies generally following repeat oral dosing with 200 mg BID voriconazole to healthy subjects
** Results based on *in vivo* clinical studies generally following repeat oral dosing with 400 mg every 12 hours for 7 days, 200 mg every 12 hours for at least 2 days voriconazole to healthy subjects
*** Results based on *in vivo* clinical studies generally following repeat oral dosing with 400 mg every 12 hours for 7 day, then 200 mg every 12 hours for 4 days voriconazole to subjects receiving voriconazole maintenance dose (200 to 300 mg every 24 hours)
NSI = Non-Steroidal Anti-Inflammatory Drug
MMTN = Non-Benzodiazepine Tranquilizer/Anxiolytic

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Voriconazole can cause fetal harm when administered to a pregnant woman. There are no available data on the use of voriconazole in pregnant women. In animal reproduction studies, oral voriconazole was associated with embryotoxicity and fetal malformations in rats and fetal toxicity in rabbits (skeletal hydrocephalus/hydrocephalus were observed in rat pups exposed to voriconazole during ontogenesis) at and above 10 mg/kg (0.2 times the RMD of 200 mg BID based on a 60 kg patient). Oral administration of voriconazole to rats during ontogenesis (gestation day 17 through lactation day 21) resulted in adverse effects on survival (at the oral maternal administration dose were observed at doses as low as 10 mg/kg (0.2 times the RMD based on body surface area comparison) during ontogenesis. Rats exposed to voriconazole from implantation to weaning experienced increased perinatal length and duration, which were associated with increased perinatal pup mortality at the 10 mg/kg/day dose (the RMD is 200 mg BID for a 60 kg patient). Voriconazole has been shown to penetrate the placenta and to be present in the blood of the umbilical vein at birth in patients treated with voriconazole for the fetal risk. See Warnings and Precautions (5.2).

If this medicine is used during pregnancy, or if the patient becomes pregnant while taking this medicine, the potential risks to the fetus should be explained to the patient. Based on animal data and the mechanism of action, the potential risks to the fetus include skeletal and visceral malformations and fetal death. Women of childbearing potential should avoid exposure during pregnancy. Rats exposed to voriconazole from implantation to weaning experienced increased perinatal length and duration, which were associated with increased perinatal pup mortality at the 10 mg/kg/day dose (the RMD is 200 mg BID for a 60 kg patient). Voriconazole has been shown to penetrate the placenta and to be present in the blood of the umbilical vein at birth in patients treated with voriconazole for the fetal risk. See Warnings and Precautions (5.2).

Data

Human Data

Voriconazole was administered orally to pregnant rats during organogenesis (gestation days 6 to 17) at 10, 20, and 40 mg/kg/day. Voriconazole was administered orally to pregnant rabbits during organogenesis (gestation days 6 to 18) at 10, 20, and 40 mg/kg/day. The lowest dose tested in rabbits (10 mg/kg) is recommended human RMD based on body surface area comparisons, and both species at 40 mg/kg, approximate to the RMD based on body surface area comparisons. Reduced ossification of sacral and caudal vertebrae, skull, pelvis, and hyoid bones, supernumerary ribs, anomalies of the sternebrae, and dilatation of the ventricular pelvis were also observed in rat fetuses at 40 mg/kg/day or greater. There was no evidence of teratogenicity in rabbits at doses up to 40 mg/kg/day.

Voriconazole was administered orally to pregnant rats during the period of organogenesis (gestation days 7 to 18) at 10, 40, and 160 mg/kg/day. Voriconazole was associated with increased post implantation fetal loss and reduced fetal weight at 160 mg/kg/day (approximately 2 times the RMD based on body weight gain and food consumption) at 160 mg/kg/day (6 times the RMD based on body surface area comparisons). Fetal skeletal variations (increase in the incidence of cervical ribs and wavy ossified sternebrae) were observed at 160 mg/kg/day.

In a pre- and postnatal toxicity study in rats, voriconazole was administered orally to female rats from implantation through the end of lactation at 5, 20, and 40 mg/kg/day. Increased stillbirths and decreased survival of the pups were observed at 40 mg/kg/day. Skeletal anomalies which entailed increase in maternal mortality and decrease in perinatal survival of F1 pups at 10 mg/kg/day, approximately 0.2 times the RMD.

8.2 Lactation

Risk Summary

No data are available regarding the presence of voriconazole in human milk, the effects of voriconazole on the breastfed infant, or the effects on milk production. Because many drugs are excreted in human milk, breastfeeding should be considered along with the mother's clinical need for voriconazole and any potential adverse effects on the breastfed child from voriconazole or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Contraception

Advise females of reproductive potential to use effective contraception during treatment with voriconazole. The coadministration of voriconazole with hormonal contraceptives (e.g. Ortho Novum 1350 mcg ethinyl estradiol/1 mcg norethindrone), results in pharmacokinetic interactions between the two drugs, but it unlikely to reduce the contraceptive effect. Monitoring for adverse reactions associated with oral contraceptives and voriconazole is recommended. See Drug Interactions (7) and Pharmacokinetics (12.3).

8.4 Pediatric Use

The safety and effectiveness of voriconazole have been established in pediatric patients 2 years of age and older based on evidence from adequate and well-controlled studies in adult and pediatric patients (see additional information in pharmacokinetics and safety subsections below). Voriconazole is contraindicated in less than 12 lb (5kg) and aged 12 to less than 18 lb (7lb) from two, non-comparative Phase 3 pediatric studies and eight adult therapeutic trials supporting safety. Information for voriconazole use in the pediatric population (*See Adverse Reactions (6.2), Pharmacokinetics (12.3) and Clinical Studies (14)*).

Safety and effectiveness in pediatric patients below the age of 2 years has not been established. Therefore, voriconazole is not recommended for pediatric patients less than 2 years of age.

A higher frequency of liver enzyme elevations was observed in the pediatric patients (*See Dosage and Administration (2.8), Warnings and Precautions (5.7) and Adverse Reactions (6.1)*).

The frequency of photosensitivity reactions is higher in the pediatric population. Squamous cell carcinoma has been reported in pediatric oncology patients receiving long-term treatment with voriconazole for photoprotection are warranted. Sun avoidance and dermatologic follow-up are recommended in pediatric patients experiencing phototoxicity, such as blistering or sunburn, even after treatment discontinuation (*See Warnings and Precautions (5.8)*).

Voriconazole has not been studied in pediatric patients with hepatic or renal impairment (*See Dosage and Administration (2.2, 2.8)*). Hepatic function and serum creatinine levels should be closely monitored in pediatric patients (*See Dosage and Administration (2.8) and Warnings and Precautions (5.2, 5.10)*).

8.5 Geriatric Use

In the voriconazole therapeutic trials of voriconazole, 9.2% of patients were ≥ 65 years of age and 1.8% of patients were ≥ 75 years of age. In a study in healthy subjects, the systemic exposure (AUC) and peak plasma concentrations (C_{max}) were increased in elderly males compared to young males. Pharmacokinetic data obtained from 552 patients from 10 voriconazole therapeutic trials showed that voriconazole plasma concentrations in the elderly patients were approximately 80% to 90% higher than those in younger adult patients when either 200 mg or 400 mg voriconazole was administered. The overall safety profile of the elderly patients was similar to that of the young on dosage adjustment is recommended (*See Clinical Pharmacology (12.3)*).

10 OVERDOSAGE

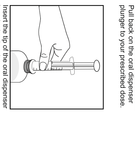
In clinical trials, there were three cases of accidental overdose. All occurred in pediatric patients who received up to five times the recommended intravenous dose for a period of 1 day. The adverse events reported were consistent with the safety profile.

There is no known antidote to voriconazole.

Voriconazole is hemodialyzed with clearance of 121 mL/min. The intravenous vehicle, SBECD, is hemodialyzed with clearance of 55 mL/min. In an overdose, hemodialysis may assist in the removal of unabsorbed SBECD from the body.

11 DESCRIPTION

Voriconazole is an orally and enteral agent is available as a powder for oral suspension. The structural formula is:



Voriconazole is designated chemically as 4-Pyrimidinecarbonitrile, α-(2-4-difluorophenyl)-5-fluoro-5-ethyl- α-(1H-1,2,4-triazol-1-ylmethyl)-, (α, R), (2S)-, (2,5,6,8,9,11,12,14,15,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000,1001,1002,1003,1004,1005,1006,1007,1008,1009,1010,1011,1012,1013,1014,1015,1016,1017,1018,1019,1020,1021,1022,1023,1024,1025,1026,1027,1028,1029,1030,1031,1032,1033,1034,1035,1036,1037,1038,1039,1040,1041,1042,1043,1044,1045,1046,1047,1048,1049,1050,1051,1052,1053,1054,1055,1056,1057,1058,1059,1060,1061,1062,1063,1064,1065,1066,1067,1068,1069,1070,1071,1072,1073,1074,1075,1076,1077,1078,1079,1080,1081,1082,1083,1084,1085,1086,1087,1088,1089,1090,1091,1092,1093,1094,1095,1096,1097,1098,1099,1100,1101,1102,1103,1104,1105,1106,1107,1108,1109,1110,1111,1112,1113,1114,1115,1116,1117,1118,1119,1120,1121,1122,1123,1124,1125,1126,1127,1128,1129,1130,1131,1132,1133,1134,1135,1136,1137,1138,1139,1140,1141,1142,1143,1144,1145,1146,1147,1148,1149,1150,1151,1152,1153,1154,1155,1156,1157,1158,1159,1160,1161,1162,1163,1164,1165,1166,1167,1168,1169,1170,1171,1172,1173,1174,1175,1176,1177,1178,1179,1180,1181,1182,1183,1184,1185,1186,1187,1188,1189,1190,1191,1192,1193,1194,1195,1196,1197,1198,1199,1200,1201,1202,1203,1204,1205,1206,1207,1208,1209,1210,1211,1212,1213,1214,1215,1216,1217,1218,1219,1220,1221,1222,1223,1224,122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