pazopanib (pah-zoe-puh-nib)

**Votrient**

**Classification**
Therapeutic: antineoplastics
Pharmacologic: kinase inhibitors

**Pregnancy Category D**

**Indications**
Advanced renal cell carcinoma. Advanced soft tissue sarcoma in patients who have previously received chemotherapy.

**Action**
Acts as a tyrosine kinase inhibitor of several vascular endothelial growth factor (VEGF) receptors, platelet-derived growth factor receptor, fibroblast growth factor receptor, cytokine receptor, interleukin-2 receptor inducible T-cell kinase, leukocyte-specific protein tyrosine kinase, and transmembrane glycoprotein receptor tyrosine kinase. Overall effect is decreased angiogenesis in tumors.

**Therapeutic Effects:**
Decreased growth and spread of renal cell carcinoma. Improvement in progression-free survival.

**Pharmacokinetics**
**Absorption:** Well absorbed following oral administration; crushing tablet and ingesting food affects absorption.
**Distribution:** Unknown.
**Protein Binding:** 99%.
**Metabolism and Excretion:** Mostly metabolized by the liver (primarily by the CYP3A4 enzyme system, minor amounts by CYP1A2 and CYP2C8) followed by elimination in feces; 4% excreted by the kidneys.
**Half-life:** 30.9 hr.

**TIME/ACTION PROFILE (blood levels)**

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<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
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<td>PO</td>
<td>2–4 hr</td>
<td>24 hr</td>
<td>25/36</td>
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- = Cardiac dose needed
- = Generic Implication
- = OPSIG indicates life-threatening, underline indicates most frequent

**Contraindications/Precautions**
Contraindicated in: Severe hepatic impairment, history of hemothrombosis, cerebral or TIAs, bleeding during preceding 5 mo, Recent history of central thromboembolic events, including SE, amaurosis or ischemic stroke within preceding 5 mo, Concurrent use of strong CYP3A4 inhibitors (if concurrent use is necessary, dosage of pazopanib should be [ ] level due to drug-drug interaction). Concurrent use of drugs that have narrow therapeutic windows and that are metabolized by CYP3A4, CYP2D6, or CYP2C8 enzyme systems. OB: May cause fetal harm, avoid use during pregnancy; Lactation: Avoid use during breast feeding.

**Use Cautiously in:** Congenital prolonged (Qtc interval or concurrent medications causes that prolong Qtc interval, risk of potentially severe arrhythmias). Patients at risk for seizures or convulsions (consider alternate concurrent medication with little or no enzyme induction potential or avoid pazopanib). Moderate hepatic impairment (dose adjustment recommended). OB: May be more sensitive to drug effects, consider age-related changes in cardiac, renal, and hepatic function; concurrent disease states and drug therapy. OB: Women with childbearing potential; Lactation: Avoid use during breast feeding.

**Adverse Reactions/Side Effects**

**Interactions**
**Drug-Drug:** Concurrent use of strong CYP3A4 inhibitors, including ketoconazole, itraconazole and clarithromycin is recommended. Concurrent use of medications that prolong QT interval is recommended; concurrent use of strong CYP3A4 inhibitors (if concurrent use is necessary, dosage of pazopanib should be [ ] level due to drug-drug interaction). Concurrent use of drugs that have narrow therapeutic windows and that are metabolized by CYP3A4, CYP2D6, or CYP2C8 enzyme systems. OB: May cause fetal harm, avoid use during pregnancy; Lactation: Avoid use during breast feeding.
rent use of strong CYP3A4 inducers, including rifampin, may ↓ levels and effectiveness and should be avoided. Concurrent use with drugs with narrow therapeutic windows that are metabolized by CYP3A4, CYP2D6, or CYP2C9 will ↓ levels of such drugs and the risk of toxicity/adverse reactions is not recommended. Risk of hypertension with voriconazole.

Drug-Food: Grapefruit juice may ↑ levels, avoid concurrent use.

Route/Dosage
PO (Adults): 800 mg once daily. Concurrent use of strong CYP3A4 inhibitors — 400 mg once daily, further reductions may be necessary.

Hepatic Impairment
PO (Adults): Moderate hepatic impairment — 200 mg once daily.

Assessment
● Monitor BP during frequent therapy; may cause hypertension. BP should be well-controlled prior to initiating therapy. If persistent hypertension occurs despite antihypertensive therapy, reduce dose. If hypertension persists and is severe, discontinue therapy. Baseline and periodic evaluation of ESR is recommended in patients at risk of cardiac dysfunction.
● Obtain baseline ECG and monitor periodically during therapy. Maintain serum calcium, magnesium, and potassium within normal range during therapy.
● Monitor for signs and symptoms of GI perforation and fistula (abdominal pain; swelling in stomach area; vomiting blood; black sticky stools; GI bleeding) during therapy.

Lab Test Considerations: Monitor serum liver tests before initiation and weeks 3, 5, 7, 9, then at month 3 and month 6 if symptoms occur. Monitor periodically after month 6. If isolated ALT > 3 times the upper limit of normal, stop therapy until ALT returns to Grade 1 or baseline. If isolated ALT > 3 times the upper limit of normal, may continue with weekly monitoring of liver function until ALT returns to Grade 1 or baseline. If ALT > 3 times the upper limit of normal, permanently discontinue pazopanib. If ALT occurs concurrently with ↑ serum bilirubin — 2 times the upper limit of normal, discontinue pazopanib permanently. Monitor liver function tests until return to baseline. Patients with only mild indirect hyperbilirubinemia (Gilbert’s syndrome) and ALT > 3 times the upper limit of normal should be managed as per recommendations for ALT.

● Monitor thyroid function periodically during therapy. May cause hypothyroidism.

● Obtain baseline electrolytes and monitor periodically. May cause hypokalemia. Discontinue therapy if grade 3 potassium depletion develops.

● Monitor weight, sodium, potassium, creatinine, and phosphorus.

● May cause ↑ ALT and ↑ serum phosphorus, sodium, and magnesium. May cause ↑ T or ↑ serum phosphorus.

Potential Nursing Diagnoses
Deficit knowledge, related to medication regimen (Patient/Family Teaching)

Implementation
● PO: Administer at least 1 hr before or 2 hr after a meal. Swallow tablets whole; do not crush.

Patient/Family Teaching
● Instruct patient to take pazopanib on an empty stomach as directed. Take missed doses as soon as remembered; if less than 12 hr before next dose, omit dose. Advise patient to read the Medication Guide prior to taking pazopanib and with each Rx refill; new information may be available.

● Advise patient to avoid drinking grapefruit juice or eating grapefruit during therapy; may increase amounts of pazopanib absorbed.

● Advise patient to notify health care professional immediately of any signs and symptoms of liver problems (yellowing of skin or whites of eyes, unusual darkening of urine, unusual tiredness, pain in the right upper stomach area), heart failure (shortness of breath), heart attack or stroke (chest pain or pressure; pain in arms, back, neck or jaw; shortness of breath; numbness or weakness on one side of body; trouble talking; headache; dizziness), blood clots (new chest pain, trouble breathing or shortness of breath that starts suddenly; leg pain; swelling of arms and hands, or legs and feet; cool or pale arms or legs), bleeding problems (unusual bleeding, bruising, wounds that do not heal), GI perforation or fistula, reversible posterior leukoencephalopathy syndrome (headaches, seizures, lack of energy, confusion, high blood pressure, loss of speech, vision changes, nausea), hematuria, hypothyroidism, liver problems, peripheral edema, proteinuria, fatigue, headache, hypogonadism, increased transaminases, nausea, upper respiratory tract infection, weight loss, leukopenia, neutropenia, thrombocytopenia, lymphocytopenia.

● Advise patient to take pazopanib with or without food. Swell hollow tablets whole; do not crush or open. Swallow tablets whole; do not crush or open.
pazopanib

Blindness or changes in vision, and problems thinking; severe increase in blood pressure (severe chest pain, severe headache, blurred vision, confusion, nausea and vomiting, severe anxiety, shortness of breath, seizures, unconsciousness) or severe infections (fever, cold symptoms such as runny nose or sore throat that do not go away; flu symptoms such as cough, tiredness, and body aches; pain when urinating; cuts, scrapes or wounds that are red, warm, swollen or painful) occur.

Inform patient that diarrhea frequently occurs. Instruct patient on ways to manage diarrhea and to notify health care professional if moderate to severe diarrhea occurs.

Inform patient that loss of color (depigmentation) of skin or hair may occur during therapy. Explore methods of coping.

Instruct patient to notify health care professional of any impending surgery. Pazopanib must be stopped for at least 7 days prior to surgery due to the affects on healing.

Advise female patients to use effective contraception during therapy and to notify health care professional immediately if pregnancy is suspected.

Evaluation/Desired Outcomes

Decreased growth and spread of renal cell carcinoma.

Improvement in spread of sarcoma.

Why was this drug prescribed for your patient?