

Prior Authorization DRUG Guidelines

Votrient™ (pazopanib)

Effective Date: 7/24/12

Date Developed: 7/17/12 by Albert Reeves MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19

(Archived 1/22/19)

Votrient is an Antineoplastic Agent, Tyrosine Kinase Inhibitor; Vascular Endothelial Growth Factor (VEGF) Inhibitor.

Pre-Authorization Criteria:

VCHCP will authorize Votrient for FDA approved treatment of advanced renal cell cancer (RCC); and treatment of advanced soft tissue sarcoma (STS) in patients previously treated with chemotherapy.

Off-label use: treatment of thyroid cancer (advanced, differentiated). Note: off label uses are not covered except under certain strict circumstances. See the VCHCP policy on Coverage of Prescription Medication for Off-Label Use.

VCHCP requires that Votrient be prescribed by an Oncologist or Endocrinologist.

Dosing:

Renal cell cancer (RCC): Oral: 800 mg once daily (Sternberg, 2010)

Soft tissue sarcoma (STS), advanced refractory: Oral: 800 mg once daily (Van Der Graaf, 2011)

Thyroid cancer, advanced differentiated (unlabeled use): Oral: 800 mg once daily until disease progression or unacceptable toxicity (Bible, 2010)

Dosage Forms: U.S.

Tablet, oral: Votrient™: 200 mg

Warnings/Precautions

Boxed warnings:

- Hepatotoxicity: See “Concerns related to adverse effects” below.

Concerns related to adverse effects:

- Gastrointestinal perforation/fistula: Perforation and fistula (including fatal) have been reported; monitor for symptoms of gastrointestinal perforation and fistula.
- Heart failure: May cause new-onset or worsening of existing heart failure.
- Hemorrhage: Hemorrhagic events (including fatal) have been reported. Use is not recommended in patients with a history of hemoptysis, cerebral hemorrhage or clinically significant gastrointestinal hemorrhage within 6 months.
- Hepatotoxicity: **[U.S. Boxed Warning]: Severe and fatal hepatotoxicity (transaminase and bilirubin elevations) has been reported with use. Monitor hepatic function. May require dosage interruption, reduction, or discontinuation.**
- Hypertension: May cause and/or worsen hypertension; hypertensive crisis has been observed.
- Infections: Serious, including fatal, infections have been reported; monitor for signs and symptoms of infection. Temporarily or permanently discontinue therapy for serious infections as clinically indicated.
- Proteinuria: Has been reported with use.
- QT_c prolongation: QT_c prolongation, including torsade de pointes, has been observed.
- Reversible posterior leukoencephalopathy syndrome (RPLS): Has been reported (rarely); may be fatal.
- Thromboembolic events: Venous and arterial thromboembolism have been reported.
- Thyroid disorders: Hypothyroidism has been reported with use; monitor thyroid function tests.
- Wound healing complications: Vascular endothelial growth factor (VEGF) receptor inhibitors are associated with impaired wound healing.

Disease-related concerns:

Renal impairment: Patients with mild-to-moderate renal impairment ($Cl_{cr} \geq 30$ mL/minute) were included in trials. There are no pharmacokinetic data in patients with severe renal impairment undergoing dialysis (peritoneal and hemodialysis, however, renal impairment is not expected to significantly influence pazopanib pharmacokinetics or exposure.

REFERENCES:

1. Appleby L, Morrissey S, Bellmunt J, et al, "Management of Treatment-Related Toxicity With Targeted Therapies for Renal Cell Carcinoma: Evidence-Based Practice and Best Practices," *Hematol Oncol Clin North Am*, 2011, 25(4):893-915. [PubMed [21763973](#)]
2. Bible KC, Suman VJ, Molina JR, et al, "Efficacy of Pazopanib in Progressive, Radioiodine-Refractory, Metastatic Differentiated Thyroid Cancers: Results of a Phase 2 Consortium Study," *Lancet Oncol*, 2010, 11(10):962-72. [PubMed [20851682](#)]
3. Cella D, Pickard AS, Duh MS, et al, "Health-Related Quality of Life in Patients With Advanced Renal Cell Carcinoma Receiving Pazopanib or Placebo in a Randomised Phase III Trial," *Eur J Cancer*, 2012, 48(3):311-23. [PubMed [21689927](#)]
4. Hawkins RE, Hong SJ, Ulys A, et al, "An Open-Label Extension Study to Evaluate Safety and Efficacy of Pazopanib in Patients With Advanced Renal Cell Carcinoma (RCC)," *J Clin Oncol*, 2009, 27(15s):5110 [abstract 5110 from 2009 ASCO Annual Meeting].

5. Heath EI, Chiorean EG, Sweeney CJ, et al, "A Phase I Study of the Pharmacokinetic and Safety Profiles of Oral Pazopanib With a High-Fat or Low-Fat Meal in Patients With Advanced Solid Tumors," *Clin Pharmacol Ther*, 2010, 88(6):818-23. [PubMed [20980999](#)]
 6. Hurwitz HI, Dowlati A, Saini S, et al, "Phase I Trial of Pazopanib in Patients With Advanced Cancer," *Clin Cancer Res*, 2009, 15(12):4220-7. [PubMed [19509175](#)]
 7. Hutson TE, Davis ID, Machiels JP, et al, "Efficacy and Safety of Pazopanib in Patients With Metastatic Renal Cell Carcinoma," *J Clin Oncol*, 2010, 28(3):475-80. [PubMed [20008644](#)]
 8. Schutz FA, Je Y, Richards CJ, et al, "Meta-Analysis of Randomized Controlled Trials for the Incidence and Risk of Treatment-Related Mortality in Patients With Cancer Treated With Vascular Endothelial Growth Factor Tyrosine Kinase Inhibitors," *J Clin Oncol*, 2012, 30(8):871-7. [PubMed [22312105](#)]
 9. Shibata S, Longmate J, Chung VM, et al, "A Phase I and Pharmacokinetic Single Agent Study of Pazopanib (P) in Patients (Pts) With Advanced Malignancies and Varying Degrees of Liver Dysfunction (LD)," *J Clin Oncol*, 2010, 28(Suppl 15):2571 [abstract 2571 from 2010 ASCO Annual Meeting].
 10. Sleijfer S, Ray-Coquard I, Papai Z, et al, "Pazopanib, a Multikinase Angiogenesis Inhibitor, in Patients With Relapsed or Refractory Advanced Soft Tissue Sarcoma: A Phase II Study from the European Organisation for Research and Treatment of Cancer-Soft Tissue and Bone Sarcoma Group (EORTC Study 62043)," *J Clin Oncol*, 2009, 27(19):3126-32. [PubMed [19451427](#)]
 11. Sternberg CN, Davis ID, Mardiak J, et al, "Pazopanib in Locally Advanced or Metastatic Renal Cell Carcinoma: Results of a Randomized Phase III Trial," *J Clin Oncol*, 2010, 28(6):1061-8. [PubMed [20100962](#)]
- Sternberg CN, Szczylik C, Lee E, et al, "A Randomized, Double-Blind Phase III Study of Pazopanib in Treatment-Naïve and Cytokine-Pretreated Patients With Advanced Renal Cell Carcinoma (RCC)," *J Clin Oncol*, 2009, 27(15s):5021 [abstract 5021 from 2009 ASCO Annual Meeting].
12. Van Der Graaf WT, Blay J, Chawla SP, et al, "PALETTE: A Randomized, Double-Blind, Phase III Trial of Pazopanib Versus Placebo in Patients (pts) With Soft-Tissue Sarcoma (STS) Whose Disease has Progressed During or Following Prior Chemotherapy -- An EORTC STBSG Global Network Study (EORTC 62072)," *J Clin Oncol*, 2011, 29(Suppl 18):LBA10002 [abstract LBA10002 from 2011 ASCO Annual Meeting].
 13. Xu CF, Reck BH, Xue Z, et al, "Pazopanib-Induced Hyperbilirubinemia is Associated With Gilbert's Syndrome UGT1A1 Polymorphism," *Br J Cancer*, 2010, 102(9):1371-7. [PubMed [20389299](#)]

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