

## Clinical Policy: Pazopanib (Votrient)

Reference Number: CP.PHAR.81

Effective Date: 10/11

Last Review Date: 12/16

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for pazopanib (Votrient®).

### Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® that Votrient is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Renal Cell Carcinoma (must meet all):

1. Diagnosis of renal cell carcinoma (RCC);
2. RCC is advanced (i.e., progressive, recurrent, unresectable or metastatic);
3. Prescribed daily dose does not exceed 800 mg;
4. Member does not have any of the following medical conditions:
  - a. Hepatotoxicity as evidenced by total bilirubin >3 times the upper limit of normal (ULN) with any level of ALT;
  - b. In the past 6 months, hemoptysis, cerebral hemorrhage, clinically significant gastrointestinal hemorrhage, or an arterial thromboembolic event.

**Approval duration: 3 months**

##### B. Soft Tissue Sarcoma (must meet all):

1. Diagnosis of soft tissue sarcoma (STS);
2. Meets (a or b):
  - a. FDA approved use (i, ii and iii):
    - i. STS is advanced (i.e., progressive, recurrent, unresectable, metastatic);
    - ii. STS previously has been treated with chemotherapy;
    - iii. Member does not have either of the following STS subtypes:
      - a) Adipocytic/lipogenic STS;
      - b) Gastrointestinal stromal tumor (GIST) - unless meets the off-label NCCN GIST criteria below (section I.B.2.b.i);
  - b. Off-label NCCN recommended use (i or ii):
    - i. Votrient is prescribed as single agent therapy for progressive GIST that is no longer responsive to one or more of the following agents:
      - a) Imatinib (Gleevec);
      - b) Sunitinib (Sutent);
      - c) Regorafenib (Stivarga);
    - ii. Votrient is prescribed as single agent palliative therapy for any of the following STS subtypes:

- a) Angiosarcoma
  - b) Retroperitoneal/intra-abdominal STS of nonliposarcomal origin AND disease is unresectable or progressive;
  - c) Pleomorphic rhabdomyosarcoma;
  - d) Extremity/superficial trunk or head/neck STS of nonliposarcomal origin AND disease is stage IV (synchronous metastatic disease) or recurrent with disseminated metastases;
3. Member does not have any of the following medical conditions:
- a. Hepatotoxicity as evidenced by total bilirubin >3 x ULN with any level of ALT;
  - b. In the past 6 months, hemoptysis, cerebral hemorrhage, clinically significant gastrointestinal hemorrhage or an arterial thromboembolic event.

**Approval duration: 3 months**

**C. Other diagnoses/indications:** Refer to CP.PHAR.57 - Global Biopharm Policy.

1. The following NCCN recommended uses for Votrient, meeting NCCN categories 1, 2a or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
  - a. Dermatofibrosarcoma protuberans (DFSP);
  - b. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer;
  - c. Thyroid carcinoma: Specifically, follicular carcinoma, Hurthle cell carcinoma, medullary carcinoma, papillary carcinoma;
  - d. Uterine sarcoma.

**II. Continued Approval**

**A. All Indications** (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member has none of the following reasons to discontinue:
  - a. Disease progression or unacceptable toxicity;
  - b. Hemoptysis, cerebral hemorrhage, clinically significant gastrointestinal hemorrhage or an arterial thromboembolic event;
  - c. Hepatotoxicity:
    - i. Total bilirubin >3 x ULN with any level of ALT;
    - ii. ALT elevation >3 x ULN concurrently with bilirubin elevation >2 x ULN;
    - iii. ALT elevation >3 x ULN following reintroduction of Votrient after dose interruption or reduction due to hepatotoxicity;
  - d. Thrombotic microangiopathy, including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome;
  - e. Interstitial lung disease or pneumonitis;
  - f. Reversible posterior leukoencephalopathy syndrome;
  - g. Hypertensive crisis or severe/persistent hypertension despite anti-hypertensive therapy and Votrient dose reduction;
  - h. Wound dehiscence (wound rupture along surgical suture);
  - i. Repeat episodes of proteinuria (24-hour urine protein  $\geq$  3 grams) despite Votrient dose reduction.

**Approval duration: 6 months**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

**Background**

*Description/Mechanism of Action:*

Pazopanib is a multi-tyrosine kinase inhibitor of vascular endothelial growth factor receptor (VEGFR)-1, VEGFR-2, VEGFR-3, platelet-derived growth factor receptor (PDGFR)- $\alpha$  and - $\beta$ , fibroblast growth factor receptor (FGFR)-1 and -3, cytokine receptor (Kit), interleukin-2 receptor-inducible T-cell kinase (Itk), leukocyte-specific protein tyrosine kinase (Lck), and transmembrane glycoprotein receptor tyrosine kinase (cFms). In vitro, pazopanib inhibited ligand-induced autophosphorylation of VEGFR-2, Kit, and PDGFR- $\beta$  receptors. In vivo, pazopanib inhibited VEGF-induced VEGFR-2 phosphorylation in mouse lungs, angiogenesis in a mouse model, and the growth of some human tumor xenografts in mice.

*Formulations:*

Tablets of Votrient are for oral administration. Each 200-mg tablet of Votrient contains 216.7 mg of pazopanib hydrochloride, equivalent to 200 mg of pazopanib free base.

*FDA Approved Indications:*

Votrient is a kinase inhibitor/oral tablet formulation indicated for treatment of patients with:

- Advanced renal cell carcinoma;
- Advanced soft tissue sarcoma who have received prior chemotherapy.

Limitations of use:

- The efficacy of Votrient for the treatment of patients with adipocytic soft tissue sarcoma or gastrointestinal stromal tumors has not been demonstrated.

**Appendices**

**Appendix A: Abbreviation Key**

DESP: dermatofibrosarcoma protuberans

STS: soft tissue sarcoma

GIST: gastrointestinal stromal tumors

ULN: upper limit of normal

RCC: renal cell carcinoma

Reviews, Revisions, and Approvals	Date	Approval Date
No clinical changes	11/12	12/12
Converted embedded SGM document into Centene policy	08/13	
Added Table 1: Safety Concerns and Appendix C. Added safety concerns to algorithm	12/13	01/14
Added clinical trial data on efficacy to background Added dosing & dose modification information Added monotherapy & special population sections	12/14	01/15

Reviews, Revisions, and Approvals	Date	Approval Date
Removed Appendix on Malignant adipocyte soft tissue sarcoma subtypes Added Appendix B: Conditions that preclude initiation of Votrient Revised Appendix C: Discontinuation due to safety concerns Moved safety concerns to Appendix D Added Appendix E: Drug interactions Votrient algorithm changes: Added “Currently receiving other chemotherapy?”, combined total bilirubin criteria for initiation and continuation into Appendix B and C, added baseline LFT requirement for initiation		
Converted policy to new template. Criteria: added age restriction; added explanatory detail per NCCN guidelines around the term ‘advanced’ in the context of RCC and STS; added max dose and monotherapy criteria; changed initial approval period to 3 months; removed baseline LFT question (hepatotoxicity included in safety appendix). Safety appendices B, C, D and E combined into criteria points	12/15	01/16
Converted policy to new template. Removed prescriber and age requirements per template guidelines. In initial criteria, removed exclusions based on medical conditions if they were presented in the PI as discontinuation recommendations (they are maintained under continuation criteria). Added NCCN recommended uses.	11/16	1/17

**References**

1. Votrient Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at <https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/votrient.pdf>. Accessed November 16, 2016.
2. Pazopanib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at NCCN.org. Accessed November 16, 2016.
3. Kidney cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed November 16, 2016.
4. Soft tissue sarcoma (Version 2.2016). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed November 16, 2016.

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in

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**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members**, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs,

and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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