

Clinical Policy: Pazopanib (Votrient)

Reference Number: CP.PHAR.81

Effective Date: 10.01.11

Last Review Date: 08.18

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

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

Description

Pazopanib (Votrient[®]) is a kinase inhibitor.

FDA Approved Indication(s)

Votrient is indicated:

- For the treatment of advanced renal cell carcinoma (RCC)
- For the treatment of advanced soft tissue sarcoma (STS) in patients who have received prior chemotherapy.

Limitation(s) of use: The efficacy of Votrient for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors (GIST) has not been demonstrated.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval 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 RCC;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Disease is advanced (i.e., relapsed or stage IV [unresectable or metastatic]);
5. Dose does not exceed 800 mg per day (4 tablets per day).

Approval duration:

Medicaid/HIM – 6 months

Commercial – Length of Benefit

B. Soft Tissue Sarcoma (must meet all):

1. Diagnosis of STS;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Confirmation of STS histologic subtype:

- a. If GIST subtype, failure of one or more of the following agents unless contraindicated or clinically significant adverse effects are experienced: imatinib, Sutent[®], Stivarga[®];
**Prior authorization may be required for these agents.*
- b. For all other STS subtypes, failure of prior chemotherapy unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):
 - a. Dose does not exceed 800 mg per day (4 tablets per day);
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Medicaid/HIM – 6 months

Commercial – Length of Benefit

C. Uterine Sarcoma (off-label) (must meet all):

1. Diagnosis of uterine sarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Failure of prior cytotoxic chemotherapy (hormonal therapies such as aromatase inhibitors are not considered cytotoxic);
5. Request meets any of the following (a or b):
 - a. Dose does not exceed 800 mg per day (4 tablets per day);
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Medicaid/HIM – 6 months

Commercial – Length of Benefit

D. Ovarian, Fallopian Tube, Primary Peritoneal Cancer (off-label) (must meet all):

1. Diagnosis of ovarian, fallopian tube or primary peritoneal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Histology confirmed as one of the following: serous, endometrioid, carcinosarcoma, clear cell, or mucinous;
5. Prescribed in combination with paclitaxel;
6. Failure of platinum-containing chemotherapy (e.g., carboplatin, cisplatin);
7. Request meets any of the following (a or b):
 - a. Dose does not exceed 800 mg per day (4 tablets per day);
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Medicaid/HIM – 6 months

Commercial – Length of Benefit

E. Thyroid Carcinoma (off-label) (must meet all):

1. Diagnosis of thyroid carcinoma;

2. Prescribed by or in consultation with an oncologist;
 3. Age \geq 18 years;
 4. Histology (a or b):
 - a. If papillary, follicular, or Hurthle cell carcinoma, failure of Lenvima[®] or Nexavar[®] unless contraindicated or clinically significant adverse effects are experienced;*
 - b. If medullary carcinoma, failure of Caprelsa[®] or Cabometyx[®] unless contraindicated or clinically significant adverse effects are experienced;
- *Prior authorization is or may be required for Lenvima, Nexavar, Caprelsa, Cabometyx*
5. Request meets any of the following (a or b):
 - a. Dose does not exceed 800 mg per day (4 tablets per day);
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Medicaid/HIM – 6 months

Commercial – Length of Benefit

F. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Votrient for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets any of the following (a or b):
 - a. New dose does not exceed 800 mg per day (4 tablets per day);
 - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:

Medicaid/ HIM – 12 months

Commercial – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration RCC: renal cell carcinoma
GIST: gastrointestinal stromal tumor STS: soft tissue sarcoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<i>Soft Tissue Sarcoma</i>		
Chemotherapy agents (examples): doxorubicin, dacarbazine, ifosfamide, mesna, epirubicin, gemcitabine, docetaxel (Taxotere®), vinorelbine, Lartruvo® (olaratumab)	STS (not GIST): regimens vary.	Varies
imatinib (Gleevec®)	GIST: 400 mg PO QD	800 mg/day
Sutent (sunitinib)	GIST: 50 mg PO QD 4 weeks on/2 weeks off.	50 mg/day
Stivarga (regorafenib)	GIST: 160 mg PO QD 21 days on/7 days off.	160 mg/day
<i>Uterine Sarcoma</i>		
Cytotoxic chemotherapy agents (examples): doxorubicin, docetaxel, gemcitabine, Lartruvo® (olaratumab)	Regimens vary.	Varies
<i>Ovarian, Fallopian Tube, Primary Peritoneal Cancer</i>		
paclitaxel	Administered weekly per NCCN.	Varies
Platinum containing agents - (examples): carboplatin, cisplatin	Regimens vary.	Varies
<i>Thyroid Cancer</i>		
Lenvima (lenvatinib)	Papillary, follicular, or Hurthle cell carcinoma: 24 mg PO QD.	24 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Nexavar (sorafenib)	Papillary, follicular, or Hurthle cell carcinoma: 400 mg PO BID.	800 mg/day
Caprelsa (vandetanib)	Medullary carcinoma: 300 mg PO QD.	300 mg/day
Cabometyx (cabozantinib)	Medullary carcinoma: 140 mg PO QD.	180 mg/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications

Not applicable

Appendix D: Black Box Warning

- Votrient has a black box warning for hepatotoxicity. Severe and fatal hepatotoxicity has been observed in clinical trials. It is not recommended to initiate Votrient in patients with pre-existing severe hepatic impairment (total bilirubin > 3 times the upper limit of normal).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RCC, STS	800 mg PO QD	800 mg/day

VI. Product Availability

Tablets: 200 mg

VII. References

1. Votrient Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2017. Available at <https://www.us.votrient.com>. Accessed April 2018.
2. Pazopanib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed April 2018.
3. Kidney cancer (Version 4.2018). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed April 2018.
4. Soft tissue sarcoma (Version 2.2018). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed April 2018.
5. Uterine neoplasms (Version 1.2018). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed April 2018.
6. Ovarian cancer (Version 2.2018). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed April 2018.
7. Thyroid carcinoma (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed April 2018.
8. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed April 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>Added clinical trial data on efficacy to background Added dosing & dose modification information Added monotherapy & special population sections 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</p>	12.14	01.15
<p>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</p>	12.15	01.16
<p>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.</p>	11.16	01.17
<p>Converted policy to new template. Added age limit as safety and efficacy have not been established in pediatric populations. Removed the following safety criteria: hepatotoxicity (although it is a BBW, the action to mitigate risk is limited to withholding the drug); hemoptysis, cerebral hemorrhage, clinically significant gastrointestinal hemorrhage, or an arterial thromboembolic event in the past 6 months (they are not absolute contraindications or BBW); and all reasons to discontinue per new safety strategy. Added requirement for positive response to therapy. Added max dose criteria for STS and continued therapy. Increased approval durations from 3/6 months to 6/12 months.</p>	07.18.17	11.17
<p>3Q 2018 annual review: policies combined for Commercial (new), HIM (new), and Medicaid lines of business; off-label uses added for uterine, ovarian and thyroid cancer; NCCN and FDA-approved uses summarized for improved clarity (STS: palliative therapy collapsed under the requirement for prior therapy); specialist involvement in</p>	05.08.18	08.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
care and continuation of care statement added; references reviewed and updated.		

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 developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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