Clinical Policy: Pazopanib (Votrient)

Reference Number: ERX.SPA.139
Effective Date: 03.01.14
Last Review Date: 08.21
Line of Business: Commercial, 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 adults with:
- Advanced renal cell carcinoma (RCC)
- 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ≥ 18 years;
4. Disease is advanced, relapsed, or stage IV;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 800 mg (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*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

B. Soft Tissue Sarcoma (must meet all)**:**
1. Diagnosis of STS and meets one of the following (a, b, or c):
   a. STS subtype is solitary fibrous tumor/hemangiopericytoma or alveolar soft part sarcoma;
   b. If GIST subtype, failure of one or more of the following agents unless contraindicated or clinically significant adverse effects are experienced: imatinib, Sutent®,Ayvakit™, Stivarga®;
      **Prior authorization is required for imatinib, Sutent, Ayvakit and Stivarga.*
   c. For all other STS subtypes, failure of prior chemotherapy unless contraindicated or clinically significant adverse effects are experienced;
2. Prescribed by or in consultation with an oncologist;

3. Disease is stage IV, unresectable, advanced, or recurrent with metastases;
4. Age ≥ 18 years;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 800 mg (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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

C. Uterine Sarcoma (off-label) (must meet all)**:**
1. Diagnosis of uterine sarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is recurrent or metastatic;
5. Failure of prior cytotoxic chemotherapy (hormonal therapies such as aromatase inhibitors are not considered cytotoxic);
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

D. Thyroid Carcinoma (off-label) (must meet all)**:**
1. Diagnosis of thyroid carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is unresectable, advanced, or metastatic;
5. If papillary, follicular, or Hurthle cell carcinoma, disease is progressive and/or symptomatic iodine-refractory;
6. Member meets one of the following (a or b);
   a. If papillary, follicular, or Hurthle cell carcinoma, failure of Lenvima® or Nexavar® unless clinically significant adverse effects are experienced or both are contraindicated;
   b. If medullary carcinoma, failure of Caprelsa® or Cabometyx® unless clinically significant adverse effects are experienced or both are contraindicated;

   **Prior authorization is required for Lenvima, Nexavar, Caprelsa, and Cabometyx*
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

E. NCCN-Recommended Off-Label Uses (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Ovarian cancer (including epithelial, fallopian tube and primary peritoneal cancer);
   b. Metastatic chondrosarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Used as single-agent therapy;

5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

F. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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 one of the following (a or b):*
   a. New dose does not exceed 800 mg (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*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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

A. 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 policy – ERX.PA.01 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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Soft Tissue Sarcoma		
Chemotherapy agents (examples): doxorubicin, dacarbazine, ifosfamide, mesna, epirubicin, gemcitabine, docetaxel (Taxotere®), vinorelbine, Lartruvo® (olaratumab)	STS (not GIST): regimens vary.	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
imatinib (Gleevec®)	GIST: 400 mg PO QD.	800 mg/day
Sutent® (sunitinib)	GIST: 50 mg PO QD 4 weeks on/2 weeks off.	87.5 mg/day
Stivarga® (regorafenib)	GIST: 160 mg PO QD 21 days on/7 days off.	160 mg/day
Ayvakit® (avapritinib)	GIST: 300 mg PO QD, until disease progression	300 mg/day
Uterine Sarcoma		
Cytotoxic chemotherapy agents (examples): doxorubicin, docetaxel, gemcitabine, Lartruvo® (olaratumab)	Regimens vary.	Varies
Thyroid Cancer		
Lenvima® (lenvatinib)	Papillary, follicular, or Hurthle cell carcinoma: 24 mg PO QD.	24 mg/day
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/Boxed Warnings
- Contraindication(s): none reported
- Boxed warning(s): hepatotoxicity

V. Dosage and Administration

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

VI. Product Availability
Tablet: 200 mg

VII. References
1. Votrient Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2020. Available at https://www.us.votrient.com. Accessed April 2, 2021.
2. Pazopanib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed April 2, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Split RCC and STS into two separate criteria sets. Added NCCN off label uses for STS. NCCN off label use for RCC is already aligned with the FDA indication. Added max dose criteria to continued therapy.	07.18.17	08.17
3Q 2018 annual review: 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 care and continuation of care statement added; references reviewed and updated.	05.08.18	08.18
3Q 2019 annual review: off-label ovarian cancer removed given 2B NCCN recommendation; solitary fibrous tumor/hemangiopericytoma and alveolar	05.14.19	08.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
soft part sarcoma added per NCCN; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.		
3Q 2020 annual review: for STS subtype GIST Ayvakit added per NCCN guidelines as a possible step through drug; for STS added criteria disease is stage IV, unresectable, advanced, or recurrent with metastases as per NCCN guidelines; for uterine carcinoma added criteria disease is recurrent or metastatic; for thyroid carcinoma added criteria disease is unresectable, advanced or metastatic; if papillary, follicular, or Hurthle cell carcinoma, disease is progressive and/or symptomatic iodine-refractory; off-label ovarian cancer added given 2A NCCN recommendation; references reviewed and updated.	05.04.20	08.20
RT4: updated indication to specify that FDA-approved indications are for adults.	08.31.20	
3Q 2021 annual review: added NCCN-recommended off-label uses for metastatic chondrosarcoma and use as single-agent therapy; references reviewed and updated.	04.02.21	08.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.