Clinical Policy Title:	pazopanib
Policy Number:	RxA.559
Drug(s) Applied:	Votrient®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2021
Line of Business Policy Applies to:	All lines of business

Background

Pazopanib (Votrient®) is a kinase inhibitor. It is indicated for the treatment of:

- 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pazopanib (Votrient®)	RCC, STS	800 mg orally once daily	800 mg/day
	Moderate Hepatic Impairment	200 mg orally once daily	

** Votrient® is not recommended in patients with severe hepatic impairment.

Dosage Forms

- Tablets: 200 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 (i.e., relapsed or stage IV [unresectable or metastatic]);
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*).

Approval Duration
Commercial: 6 months
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®, Stivarga®;
   *Prior authorization is required for imatinib, Sutent®, 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. Age ≥ 18 years;
4. 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*).

Approval Duration
Commercial: 6 months
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. Failure of prior cytotoxic chemotherapy (hormonal therapies such as aromatase inhibitors are not considered cytotoxic);
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*).

Approval Duration
Commercial: 6 months
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. Histology meets one of the following (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 required for Lenvima®, Nexavar®, and Cabometyx®.*

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*).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

E. Bone Cancer (off-label) (must meet all):
1. Diagnosis of bone cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member has chondrosarcoma;
5. Member meets one of the following (a or b):
   a. metastatic disease at presentation;
   b. systemic recurrence of high grade (grade II or III), clear cell, or extracompartmental chondrosarcoma;
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*).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications 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*).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GIST: gastrointestinal stromal tumor
RCC: renal cell carcinoma
STS: soft tissue sarcoma

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Soft Tissue Sarcoma		
Chemotherapy agents (examples): doxorubicin, dacarbazine, ifosfamide, mesna, epirubicin, gemcitabine, docetaxel , vinorelbine, Lartruvo®	STS (not GIST): regimens vary.	Varies
imatinib (Gleevec®)	GIST: 400 mg orally once daily	800 mg/day
sunitinib (Sutent®)	GIST: 50 mg orally once daily 4 weeks on/2 weeks off.	50 mg/day
Stivarga®	GIST: 160 mg orally once daily 21 days on/7 days off.	160 mg/day
Uterine Sarcoma		
Cytotoxic chemotherapy agents (examples): doxorubicin, docetaxel, gemcitabine	Regimens vary.	Varies
Ovarian, Fallopian Tube, Primary Peritoneal Cancer		
paclitaxel	Administered weekly per NCCN.	Varies
Platinum containing agents (examples): carboplatin, cisplatin	Regimens vary.	Varies
Thyroid Cancer		
Lenvima®	Papillary, follicular, or Hurthle cell carcinoma: 24 mg orally once daily.	24 mg/day
Nexavar®	Papillary, follicular, or Hurthle cell carcinoma: 400 mg orally twice daily.	800 mg/day
vandetanib (Caprelsa®)	Medullary carcinoma: 300 mg orally once daily	300 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Cabometyx®	Medullary carcinoma: 140 mg orally once daily	180 mg/day

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - Hepatotoxicity.

APPENDIX D: General Information

- The most common adverse reactions in patients with RCC (≥ 20%) are diarrhea, hypertension, hair color changes (depigmentation), nausea, anorexia, and vomiting.
- The most common adverse reactions in patients with STS (≥ 20%) are fatigue, diarrhea, nausea, decreased weight, hypertension, decreased appetite, vomiting, tumor pain, hair color changes, musculoskeletal pain, headache, dysgeusia, dyspnea and skin hypopigmentation.

References

1. Votrient Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2021. Available at: https://www.us.votrient.com . Accessed October 05, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/. Accessed October 05, 2021.
3. National Comprehensive Cancer Network. Kidney Cancer Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf . Accessed October 05, 2021.
4. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf . Accessed October 05, 2021.
5. National Comprehensive Cancer Network. Uterine Neoplasms Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf . Accessed October 05, 2021.
6. National Comprehensive Cancer Network. Thyroid Carcinoma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf . Accessed October 05, 2021.
7. National Comprehensive Cancer Network. Bone Cancer Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf . Accessed October 05, 2021.
8. National Comprehensive Cancer Network. Gastrointestinal Stromal Tumors (GIST) Version 1.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf . Accessed October 05, 2021.
9. National Comprehensive Cancer Network. Ovarian cancer Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf . Accessed October 05, 2021
10. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/. Accessed October 05, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date

Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title was updated as "pazopanib". 2. Line of business policy applies to all lines of business. 3. Initial approval criteria updated with "Ovarian cancer info. added". 4. Continued therapy approval criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance.." 5. Appendix D updated with common adverse effects. 6. References were reviewed and updated.	09/23/2020	12/07/2020
Policy was reviewed: 1. Dosing information table was updated by adding (Votrient® is not recommended in patients with severe hepatic impairment & by adding dose for hepatic impairment..). 2. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 3. Initial approval criteria 1.E," Ovarian cancer off label use" removed. It is 2B recommendation per NCCN. 4. Initial Approval criteria I.B.4 updated to include "Member has advanced or metastatic disease" 5. Initial Approval Criteria. I.D.2 updated to include criteria for differentiated thyroid carcinoma. 6. Initial approval criteria 1.D.4 updated to remove Capresla from prior authorization required. 7. Initial Approval criteria I.E.4 updated to include "Used as single-agent therapy for persistent disease or with recurrence" 8. Initial Approval criteria I.F added to include off label indication "Bone Cancer". 9. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name®	10/05/2021	12/07/2021

when the drug is available by brand only and generic name when the drug is available by generic only". 10. References were reviewed and updated.		