Votrient® (pazopanib)
(Oral)

Document Number: IC-0140

Last Review Date: 07/05/2023
Date of Origin: 01/01/2012
Dates Reviewed: 12/2012, 11/2013, 08/2014, 07/2015, 07/2016, 08/2017, 07/2018, 07/2019, 07/2020, 07/2021, 07/2022, 07/2023

I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Votrient 200 mg tablet: 4 tablets per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 800 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Baseline left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals during treatment in patients at risk of cardiac dysfunction, including prior anthracycline exposure; **AND**
- Patient has not had hemoptysis, cerebral hemorrhage, or clinically significant gastrointestinal hemorrhage within the prior 6 months; **AND**
- Patient has not had an arterial thromboembolic event within the previous 6 months; **AND**
- Patient will have an electrocardiogram (ECG) at baseline and will be assessed periodically during therapy; **AND**
- Patient must not have had a surgical procedure within the preceding 14 days or have a surgical wound that has not fully healed; **AND**
- Used as single-agent therapy, unless otherwise specified; **AND**
- Patient will avoid concomitant therapy all of the following:

- Coadministration with gastric acid-reducing agents (e.g., proton-pump inhibitors, H2 receptor antagonists, etc.) or if therapy is required, consider use of short-acting antacids at staggered administration times instead; **AND**
- Coadministration with strong CYP3A4 inhibitors (e.g., clarithromycin, itraconazole, indinavir, nefazodone, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
- Coadministration with strong CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
- Coadministration of strong P-glycoprotein (P-gp) or breast cancer resistance protein (BCRP) inhibitors (e.g., ketoconazole, imatinib, HIV protease inhibitors, etc.), or if therapy is required, an alternative product with no or minimal potential to inhibit P-gp or BCRP should be considered; **AND**
- Coadministration with drugs that prolong QT/QTc interval (e.g., amiodarone, sotalol, levofloxacin, venlafaxine, quetiapine, sumatriptan, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
- Coadministration simvastatin, or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

Renal Cell Carcinoma (RCC) † ‡ [1,2]

- Patient has advanced, relapsed, or stage IV disease † ‡; **OR**
- Patient has von Hippel-Lindau (VHL)-associated renal cell carcinoma ‡

Soft Tissue Sarcoma (STS) † ‡ Φ [1,2]

- Patient has advanced disease †; **AND**
  - Patient has received prior chemotherapy; **AND**
  - Patient does NOT have adipocytic disease; **OR**
- Used for one of the following:
  - Angiosarcoma
    - May also be in combination with gemcitabine
  - Retroperitoneal/Intra-Abdominal
    - Patient has non-adipocytic disease; **AND**
      - Used as first-line therapy for advanced, unresectable, or metastatic disease; **AND**
        - Used in patients who are not eligible for IV chemotherapy or who are not candidates for anthracyclines; **OR**
      - Used as palliative treatment; **AND**

- Used as alternative systemic therapy for unresectable or progressive disease after initial therapy for unresectable or stage IV disease; **OR**
- Used as subsequent lines of therapy for recurrent unresectable or recurrent stage IV disease

- Desmoid Tumors (Aggressive Fibromatosis)
  - Used in one of the following treatment settings:
    - Patient has ongoing progression with potential morbidity or significant symptoms in anatomic location where progression would not be morbid
    - Patient has documented progression in anatomic location where progression would be morbid
    - Patient has no documented progression in anatomic location where progression would be morbid but there are concerns for morbidity or significant symptoms; **AND**
      - Used as primary or subsequent treatment for intra-abdominal/retroperitoneal, abdominal wall, pelvic, trunk/extremity, or head/neck/intrathoracic tumors; **OR**
      - Used for treatment of gross residual disease (R2 resection) in abdominal wall, pelvic, trunk/extremity, or head/neck/intrathoracic tumors
- Rhabdomyosarcoma
  - Used for advanced or metastatic pleomorphic disease; **AND**
    - Used as first-line therapy in patients who are not eligible for IV chemotherapy or who are not candidates for anthracyclines; **OR**
    - Used palliatively as subsequent lines of therapy
- Extremity/Body Wall, Head/Neck
  - Patient has non-adipocytic disease; **AND**
    - Used as first-line therapy for advanced, metastatic, unresectable, or recurrent disease; **AND**
      - Used in patients who are not eligible for IV chemotherapy or who are not candidates for anthracyclines; **OR**
    - Used palliatively as subsequent lines of therapy for advanced or metastatic disease
- Alveolar Soft Part Sarcoma (ASPS)
- Solitary Fibrous Tumor
- Dermatofibrosarcoma Protuberans (DFSP) with Fibrosarcomatous Transformation
  - Used in patients who are not eligible for IV chemotherapy or who are not candidates for anthracycline-based regimens

Bone Cancer – Chondrosarcoma ‡ [2]

- Patient has metastatic and widespread disease; **AND**
  - Patient has metastatic disease at presentation; **OR**
  - Patient has systemic recurrence of high grade (grade II or III), clear cell, or extracompartmental disease

Gastrointestinal Stromal Tumors (GIST) ‡ [2,5]

- Patient has gross residual (R2 resection), unresectable primary, recurrent, or metastatic disease OR tumor rupture; **AND**
  - Used as first line therapy for succinate dehydrogenase (SDH)-deficient disease; **OR**
  - Used after progression on approved therapies including each of the following: imatinib, sunitinib, regorafenib, and ripretinib

Uterine Sarcoma ‡ [2]

- Patient has a diagnosis of adenosarcoma, endometrial stromal sarcoma (ESS), PEComa, undifferentiated uterine sarcoma (UUS), or uterine leiomyosarcoma (uLMS); **AND**
- Used as subsequent therapy for advanced, recurrent, metastatic, or inoperable disease

Thyroid Carcinoma ‡ [2]

- Patient has Medullary Carcinoma; **AND**
  - Patient has recurrent or persistent metastatic disease; **AND**
  - Disease is symptomatic or progressive; **AND**
    - Treatment with clinical trials, vandetanib, or cabozantinib are not available or appropriate; **OR**
    - Disease progressed on vandetanib or cabozantinib; **OR**
- Patient has Follicular, Oncocytic, or Papillary Carcinoma; **AND**
  - Patient has unresectable recurrent, persistent, metastatic disease; **AND**
  - Treatment with clinical trials or other systemic therapies are not available or appropriate; **AND**
  - Patient has progressive and/or symptomatic disease that is not amenable to radioactive iodine (RAI) therapy

† FDA-Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: hepatotoxicity (severe changes in liver function tests), QT prolongation and Torsades de Pointes, cardiac dysfunction (decreased LVEF, congestive heart failure, etc.), hemorrhagic events, arterial thromboembolic events, venous thrombotic events (venous thrombosis, pulmonary embolus, etc.), thrombotic microangiopathy, gastrointestinal perforation/fistula, severe proteinuria/nephrotic syndrome, interstitial lung disease (ILD)/pneumonitis, posterior reversible encephalopathy syndrome (PRES), hypertension, impaired wound healing, hypothyroidism, serious infections, tumor lysis syndrome (TLS), etc.

V. Dosage/Administration [1,4,6-12]

Indication	Dose
All Indications	800 mg daily without food (at least 1 hour before or 2 hours after a meal) until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS Code:

- J8999: Prescription drug, oral, chemotherapeutic, Not Otherwise Specified

NDC(s):

- Votrient 200 mg gray tablet – 00078-0670-xx
- Votrient 200 mg pink tablet – 00078-1077-xx

VII. References

1. Votrient [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; December 2021. Accessed June 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for pazopanib. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2023.
3. Sternberg CN, Szczylik C, Lee E, et al. A Randomized, Double-Blind Phase III Study of Pazopanib in Treatment-Naive and Cytokine-Pretreated Patients With Advanced Renal Cell Carcinoma (RCC). J Clin Oncol, 2009, 27(15s) [abstract 5021 from 2009 ASCO Annual Meeting].
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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. Epub 2009 May 18.

5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastrointestinal Stromal Tumors (GISTs) Version 1.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed June 2023.
6. van der Graaf WT, Blay JY, Chawla SP, et al; EORTC Soft Tissue and Bone Sarcoma Group; PALETTE study group. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2012 May 19;379(9829):1879-86. doi: 10.1016/S0140-6736(12)60651-5.
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10. Bible KC, Suman VJ, Molina JR, et al; Endocrine Malignancies Disease Oriented Group, Mayo Clinic Cancer Center, and the Mayo Phase 2 Consortium. A multicenter phase 2 trial of pazopanib in metastatic and progressive medullary thyroid carcinoma: MC057H. J Clin Endocrinol Metab. 2014 May;99(5):1687-93. doi: 10.1210/jc.2013-3713.
11. Rajendra R, Jones RL, Pollack SM. Targeted treatment for advanced soft tissue sarcoma: profile of pazopanib. Onco Targets Ther. 2013;6:217-22. doi: 10.2147/OTT.S32200.
12. Mir O, Cropet C, Toulmonde M, et al; PAZOGIST study group of the French Sarcoma Groupe-Groupe d'Etude des Tumeurs Osseuses (GSF-GETO). Pazopanib plus best supportive care versus best supportive care alone in advanced gastrointestinal stromal tumours resistant to imatinib and sunitinib (PAZOGIST): a randomised, multicentre, open-label phase 2 trial. Lancet Oncol. 2016 May;17(5):632-41. doi: 10.1016/S1470-2045(16)00075-9.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C22.3	Angiosarcoma of liver

ICD-10	ICD-10 Description
C40.00	Malignant neoplasm of scapula and long bones of unspecified upper limb
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.20	Malignant neoplasm of long bones of unspecified lower limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.30	Malignant neoplasm of short bones of unspecified lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.80	Malignant neoplasm of overlapping sites of bone and articular cartilage of unspecified limb
C48.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.90	Malignant neoplasm of unspecified bones and articular cartilage of unspecified limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
C44.90	Unspecified malignant neoplasm of skin, unspecified
C44.99	Other specified malignant neoplasm of skin, unspecified
C47.0	Malignant neoplasm of peripheral nerves of head, face and neck
C47.10	Malignant neoplasm of peripheral nerves of unspecified upper limb, including shoulder
C47.11	Malignant neoplasm of peripheral nerves of right upper limb, including shoulder
C47.12	Malignant neoplasm of peripheral nerves of left upper limb, including shoulder
C47.20	Malignant neoplasm of peripheral nerves of unspecified lower limb, including hip
C47.21	Malignant neoplasm of peripheral nerves of right lower limb, including hip
C47.22	Malignant neoplasm of peripheral nerves of left lower limb, including hip
C47.3	Malignant neoplasm of peripheral nerves of thorax

ICD-10	ICD-10 Description
C47.4	Malignant neoplasm of peripheral nerves of abdomen
C47.5	Malignant neoplasm of peripheral nerves of pelvis
C47.6	Malignant neoplasm of peripheral nerves of trunk, unspecified
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system
C47.9	Malignant neoplasm of peripheral nerves and autonomic nervous system, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.A0	Gastrointestinal stromal tumor, unspecified site
C49.A1	Gastrointestinal stromal tumor of esophagus
C49.A2	Gastrointestinal stromal tumor of stomach
C49.A3	Gastrointestinal stromal tumor of small intestine
C49.A4	Gastrointestinal stromal tumor of large intestine
C49.A5	Gastrointestinal stromal tumor of rectum
C49.A9	Gastrointestinal stromal tumor of other sites
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri

ICD-10	ICD-10 Description
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C73	Malignant neoplasm of thyroid gland
D48.1	Neoplasm of uncertain behavior of connective and other soft tissue
D48.3	Neoplasm of uncertain behavior of retroperitoneum
D48.4	Neoplasm of uncertain behavior of peritoneum
Q85.8	Other phakomatoses, not elsewhere classified
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.830	Personal history of malignant neoplasm of bone
Z85.831	Personal history of malignant neoplasm of soft tissue

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Article (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC