

## Votrient<sup>®</sup> (pazopanib) (Oral)

Document Number: IC-0140

Last Review Date: 07/01/2021

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

### I. Length of Authorization

Coverage will be provided for six 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 <sup>1,2</sup>

Coverage is provided in the following conditions:

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

#### Universal Criteria <sup>1</sup>

- 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**
- Used as single-agent therapy; **AND**
- Patient will avoid concomitant therapy all of the following:
  - Coadministration with acid-reducing agents (e.g., proton-pump inhibitors, H2 receptor antagonists, etc.) or if therapy is required, consider short-acting antacids instead; **AND**

- Coadministration with strong CYP3A4 inhibitors (e.g., clarithromycin, itraconazole, indinavir, nefazodone, etc.), 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 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 †<sup>1,2</sup>**

- Patient has advanced disease †; **OR**
- Patient has relapsed or stage IV disease; **AND**
  - Used as first line or subsequent therapy for clear cell histology; **OR**
  - Used as systemic therapy for non-clear cell histology

### **Soft Tissue Sarcoma † ‡ ◊<sup>1,2</sup>**

- Patient has advanced disease †; **AND**
  - Patient must have received prior chemotherapy; **AND**
  - Patient does NOT have adipocytic disease; **OR**
- Used for one of the following:
  - Angiosarcoma
  - Retroperitoneal/Intra-abdominal
    - Patient has advanced, unresectable, or metastatic disease; **AND**
      - Used in patients not eligible for intravenous (IV) chemotherapy as first-line or post-operative treatment; **OR**
    - Patient has recurrent unresectable or metastatic disease; **AND**
      - Used palliatively as subsequent lines of therapy in patients with non-adipocytic disease
  - Desmoid Tumors (Aggressive Fibromatosis)
    - Timeframe for a treatment response is more critical; **AND**
    - Used as primary treatment or for treatment of gross residual disease (R2 resection) in abdominal wall tumors; **AND**

- Patient has ongoing progression with potential morbidity or significant symptoms in anatomic location where progression would not be morbid; **OR**
- Patient has documented progression in anatomic location where progression would be morbid; **OR**
- Patient has no documented progression in anatomic location where progression would be morbid but there are concerns for morbidity or significant symptoms
- Rhabdomyosarcoma
  - Used for advanced or metastatic pleomorphic disease
- Extremity/Body Wall, Head/Neck
  - Patient has advanced, metastatic, unresectable, or recurrent disease; **AND**
    - Used as first-line treatment in patients not eligible for intravenous (IV) chemotherapy; **OR**
  - Patient has advanced or metastatic disease; **AND**
    - Used palliatively as subsequent lines of therapy in patients with non-adipocytic disease
- Alveolar Soft Part Sarcoma (ASPS)
- Solitary Fibrous Tumor

### **Chondrosarcoma ‡<sup>2</sup>**

- 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) <sup>2,5</sup>**

- Patient has unresectable, recurrent, or metastatic disease; **AND**
- Disease has progressed after single-agent treatment with each of the following: imatinib, sunitinib, regorafenib, and ripretinib

### **Uterine Sarcoma ‡<sup>2</sup>**

- Patient has a diagnosis of high-grade endometrial stromal sarcoma (ESS), undifferentiated uterine sarcoma (UUS), or uterine leiomyosarcoma (uLMS); **AND**
- Patient has recurrent or metastatic disease that has progressed following prior cytotoxic chemotherapy

### **Thyroid Carcinoma ‡<sup>2</sup>**

- 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, Hürthle cell, or Papillary carcinoma; **AND**
  - Patient has unresectable locoregional recurrent or persistent disease OR 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 susceptible to radioactive iodine (RAI) therapy

† FDA-labeled indication(s); ‡ Compendia recommended indication(s); ◊ Orphan Drug

#### IV. Renewal Criteria <sup>1</sup>

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, reversible posterior leukoencephalopathy syndrome (RPLS), hypertension, impaired wound healing, hypothyroidism, infection, tumor lysis syndrome (TLS), etc.

#### V. Dosage/Administration <sup>1,4,6-11</sup>

Indication	Dose
All Indications	800mg 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

HCPSC Code:

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

## NDC:

- Votrient 200 mg tablet – 00078-0670-xx

## VII. References

1. Votrient [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; August 2020. Accessed June 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for pazopanib. National Comprehensive Cancer Network, 2021. 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 2021.
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].
4. Sleijfer S, Ray-Coquard I, Papai Z, et al. Pazopanib, a multikinase angiogenesis inhibitor, in patients with relapsed or refractory advanced soft tissue sarcoma: a phase II study from 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 1.2021. National Comprehensive Cancer Network, 2021. 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 2021.
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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9. Bible KC, Suman VJ, Molina JR, et al; Endocrine Malignancies Disease Oriented Group; Mayo Clinic Cancer Center; Mayo Phase 2 Consortium. Efficacy of pazopanib in progressive, radioiodine-refractory, metastatic differentiated thyroid cancers: results of a

phase 2 consortium study. *Lancet Oncol.* 2010 Oct;11(10):962-72. doi: 10.1016/S1470-2045(10)70203-5.

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.

## Appendix 1 – Covered Diagnosis Codes

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



ICD-10	ICD-10 Description
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
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

ICD-10	ICD-10 Description
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
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
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: <http://www.cms.gov/medicare-coverage-database/search/advanced-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.



### Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
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
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