

Stivarga® (regorafenib) (Oral)

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I. Length of Authorization

Coverage is provided for six months and may be renewed.

II. Dosing Limits

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

- 40 mg tablets: 84 tablets per 28 days

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

- 160 mg daily for 21 days per 28-day cycle

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

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

Universal Criteria ¹

- Patient will avoid concomitant therapy with all of the following:
 - Coadministration with strong CYP3A4 inducers (e.g., rifampin, phenytoin, carbamazepine, phenobarbital, St. John's Wort, etc.); **AND**
 - Coadministration with strong CYP3A4 inhibitors (e.g., clarithromycin, grapefruit juice, itraconazole, ketoconazole, nefazodone, posaconazole, telithromycin, and voriconazole, etc.); **AND**

Colorectal cancer † ^{1,5}

- Patient has advanced or metastatic disease; **AND**
- Patient has not previously been treated with regorafenib; **AND**
- Used as a single agent; **AND**

- Used as subsequent therapy for disease progression through all available regimens besides regorafenib or trifluridine/tipiracil

Gastrointestinal Stromal Tumors (GIST) † Φ

- Patient has locally advanced, unresectable, or metastatic disease; **AND**
 - Used as a single agent; **AND**
 - Patient was previously treated with single-agent imatinib and sunitinib; **OR**
 - Used in combination with everolimus as fourth-line therapy; **AND**
 - Patient has had disease progression after previous treatment with single-agent imatinib, sunitinib, and regorafenib

Hepatocellular Carcinoma (HCC) † Φ^{1,5,11}

- Used as a single agent; **AND**
- Patient is Child-Pugh Class A; **AND**
- Patient was previously treated with sorafenib

Soft Tissue Sarcoma ‡^{5,12}

- Used as a single-agent as subsequent therapy; **AND**
 - Patient has advanced or metastatic pleomorphic rhabdomyosarcoma; **OR**
 - Patient has non-adipocytic retroperitoneal/intraabdominal disease that is recurrent unresectable or stage IV; **OR**
 - Patient has non-adipocytic disease of the extremity/body wall/head/neck that is advanced or metastatic with disseminated metastases; **OR**
 - Patient has undifferentiated pleomorphic sarcoma (UPS); **OR**
 - Patient has angiosarcoma; **OR**
 - Patient has solitary fibrous tumor

Osteosarcoma ‡^{5,8}

- Used as a single agent; **AND**
- Used as second-line therapy for relapsed/refractory or metastatic disease; **AND**
- Patient does not have dedifferentiated chondrosarcoma or high-grade undifferentiated pleomorphic sarcoma (UPS)

Glioblastoma – Central Nervous System Cancer ‡^{5,9}

- Used as a single agent for recurrent disease

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

IV. Renewal Criteria^{1,5,8,9,11,12}

Coverage can be renewed based upon the following criteria:

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- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. 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 the following: severe hepatotoxicity, severe infections, hemorrhage, reversible posterior leukoencephalopathy syndrome (RPLS), gastrointestinal perforation or fistula, dermatologic toxicity, severe/uncontrolled hypertension, cardiac ischemia/infarction, impaired wound healing, etc.

V. Dosage/Administration ^{1,6,7,10,13}

| Indication | Dose |
|-----------------|---|
| All Indications | 160 mg (4 tablets) orally, once daily for the first 21 days of each 28-day cycle. Continue treatment until disease progression or unacceptable toxicity. |

VI. Billing Code/Availability Information

HCPCS code:

- J8999 – Prescription drug, oral, chemotherapeutic, nos

NDC:

- Stivarga 40 mg tablet: 50419-0171-xx

VII. References

1. Stivarga [package insert]. Whippany, NJ; Bayer HealthCare Pharmaceuticals Inc; June 2020. Accessed October 2020.
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3. Demetri GD, Reichardt P, Kang YK, et al. Efficacy and safety of regorafenib for advanced gastrointestinal stromal tumours after failure of imatinib and sunitinib (GRID): an international, multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet*. 2013 Jan 26;381(9863):295-302.
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12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma Version 2.2020. National Comprehensive Cancer Network, 2020. 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 October 2020.
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Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|--------|--|
| C17.0 | Malignant neoplasm duodenum |
| C17.1 | Malignant neoplasm jejunum |
| C17.2 | Malignant neoplasm ileum |
| C17.8 | Malignant neoplasm of overlapping sites of small intestines |
| C17.9 | Malignant neoplasm of small intestine, unspecified |
| C18.0 | Malignant neoplasm of cecum |
| C18.1 | Malignant neoplasm of appendix |
| C18.2 | Malignant neoplasm of ascending colon |
| C18.3 | Malignant neoplasm of hepatic flexure |
| C18.4 | Malignant neoplasm of transverse colon |
| C18.5 | Malignant neoplasm of splenic flexure |
| C18.6 | Malignant neoplasm of descending colon |
| C18.7 | Malignant neoplasm of sigmoid colon |
| C18.8 | Malignant neoplasm of overlapping sites of large intestines |
| C18.9 | Malignant neoplasm of colon, unspecified |
| C19 | Malignant neoplasm of rectosigmoid junction |
| C20 | Malignant neoplasm of rectum |
| C21.8 | Malignant neoplasm of overlapping sites of rectum, anus and anal canal |
| C22.0 | Liver cell carcinoma |
| C22.3 | Angiosarcoma of liver |
| C22.8 | Malignant neoplasm of liver, primary, unspecified as to type |
| C22.9 | Malignant neoplasm of liver, not specified as primary or secondary |
| 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 |

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| ICD-10 | ICD-10 Description |
|--------|--|
| 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 |
| C40.81 | 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 |
| 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 |
| C49.0 | 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 |
| C49.12 | Malignant neoplasm of connective and soft tissue of left lower limb |

| ICD-10 | ICD-10 Description |
|--------|---|
| 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 |
| C49.22 | Malignant neoplasm of connective and soft tissue of left lower limb |
| 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 |
| 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 |
| C49.4 | Malignant neoplasm of connective and soft tissue of abdomen |
| C49.8 | Malignant neoplasm of overlapping sites of connective and soft tissue |
| C49.9 | Malignant neoplasm of connective and soft tissue, unspecified |
| C71.0 | Malignant neoplasm of cerebrum, except lobes and ventricles |
| C71.1 | Malignant neoplasm of frontal lobe |
| C71.2 | Malignant neoplasm of temporal lobe |
| C71.3 | Malignant neoplasm of parietal lobe |
| C71.4 | Malignant neoplasm of occipital lobe |
| C71.5 | Malignant neoplasm of cerebral ventricle |
| C71.6 | Malignant neoplasm of cerebellum |
| C71.7 | Malignant neoplasm of brain stem |
| C71.8 | Malignant neoplasm of overlapping sites of brain |
| C71.9 | Malignant neoplasm of brain, unspecified |
| C72.0 | Malignant neoplasm of spinal cord |
| C72.9 | Malignant neoplasm of central nervous system, unspecified |
| C78.00 | Secondary malignant neoplasm of unspecified lung |
| C78.01 | Secondary malignant neoplasm of right lung |
| C78.02 | Secondary malignant neoplasm of left lung |

| ICD-10 | ICD-10 Description |
|---------|--|
| C78.6 | Secondary malignant neoplasm of retroperitoneum and peritoneum |
| C78.7 | Secondary malignant neoplasm of liver and intrahepatic bile duct |
| Z85.038 | Personal history of other malignant neoplasm of large intestine |
| Z85.068 | Personal history of other malignant neoplasm of small intestine |
| Z85.830 | Personal history of malignant neoplasm of bone |
| Z85.831 | Personal history of malignant neoplasm of soft tissue |
| Z85.841 | Personal history of malignant neoplasm of brain |

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 Articles (LCAs) and Local Coverage Determinations (LCDs) 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/LCA/LCD): 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 |
| 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 |