Stivarga® (regorafenib)
(Oral)

Document Number: IC-0160

Last Review Date: 10/30/2023
Date of Origin: 02/07/2013
Dates Reviewed: 03/2013, 02/2014, 12/2014, 10/2015, 10/2016, 05/2017, 10/2017, 10/2018, 11/2019, 11/2020, 11/2021, 11/2022, 11/2023

I. Length of Authorization

Coverage is provided for 6 months and may be renewed.

II. Dosing Limits

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

- Stivarga 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 must not have had a surgical procedure within the preceding 2 weeks or have a surgical wound that has not fully healed; **AND**
- 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 (CRC) † ‡ [1,5]

- Used as a single agent; **AND**
- Patient has advanced or metastatic disease; **AND**

- Patient has not previously been treated with regorafenib; **AND**
- Used as subsequent therapy for disease progression through all available regimens besides regorafenib or trifluridine/tipiracil with or without bevacizumab; **AND**
  - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease**; **OR**
  - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease** AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy**

***Note: Only applies to advanced disease*

Appendiceal Adenocarcinoma – Colon Cancer ‡ [5]

- Used as a single agent; **AND**
- Patient has advanced or metastatic disease; **AND**
- Patient has not previously been treated with regorafenib; **AND**
- Used as subsequent therapy for disease progression through all available regimens besides regorafenib or trifluridine/tipiracil with or without bevacizumab; **AND**
  - Patient has mismatch repair proficient/microsatellite-stable (pMMR/MSS) disease; **OR**
  - Patient has mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) disease AND is not a candidate for or has progressed on checkpoint inhibitor immunotherapy

Gastrointestinal Stromal Tumors (GIST) † ‡ Φ [1,5]

- Used as a single agent; **AND**
  - Patient was previously treated with imatinib AND either sunitinib or ripretinib; **AND**
    - Patient has locally advanced, unresectable, recurrent/metastatic, gross residual (R2 resection) disease or tumor rupture; **OR**
  - Patient has succinate dehydrogenase (SDH)-deficient tumors ‡; **AND**
    - Used as first-line therapy; **AND**
    - Patient has gross residual disease (R2 resection), unresectable primary disease, recurrent/metastatic disease or tumor rupture; **OR**
- Used in combination with everolimus ‡; **AND**
  - Patient has gross residual (R2 resection), unresectable primary, recurrent/metastatic disease or tumor rupture; **AND**
  - Used after progression on approved therapies*; **AND**

** imatinib, sunitinib, regorafenib, and ripretinib*

Hepatocellular Carcinoma (HCC) † ‡ Φ [1,5,11]

- Used as a single agent; **AND**
- Patient has Child-Pugh Class A hepatic impairment; **AND**

- Used as subsequent therapy for progressive disease; **AND**
  - Patient was previously treated with sorafenib †; **OR**
  - Patient has unresectable disease and is not a candidate for transplant ‡; **OR**
  - Patient has liver-confined disease that is inoperable by performance status, comorbidity or with minimal or uncertain extrahepatic disease ‡ ; **OR**
  - Patient has metastatic disease or extensive liver tumor burden ‡

Soft Tissue Sarcoma ‡ [5,12]

- Used as a single agent; **AND**
  - Used as subsequent treatment for one of the following:
    - Advanced or metastatic pleomorphic rhabdomyosarcoma; **OR**
    - Non-adipocytic retroperitoneal/intra-abdominal disease; **AND**
      - Used as alternative systemic therapy for unresectable or progressive disease after initial therapy for unresectable or stage IV disease; **OR**
      - Patient has recurrent unresectable or recurrent stage IV disease; **OR**
    - Non-adipocytic extremity/body wall/head/neck disease that is advanced/metastatic with disseminated metastases; **OR**
  - Patient has angiosarcoma

Bone Cancer ‡ [5,8]

- Used as second-line therapy as a single agent; **AND**
  - Patient has Ewing Sarcoma; **AND**
    - Patient does not have mesenchymal chondrosarcoma; **AND**
      - Patient has progressive disease following primary treatment; **OR**
      - Patient has relapsed or metastatic disease; **OR**
  - Patient has Osteosarcoma; **AND**
    - Patient has relapsed/refractory or metastatic disease; **AND**
    - Patient does not have dedifferentiated chondrosarcoma or high-grade undifferentiated pleomorphic sarcoma (UPS)

Glioblastoma – Central Nervous System (CNS) Cancer ‡ [5,9]

- Used as a single agent for recurrent or progressive disease

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

IV. Renewal Criteria [1,5,8,9,11,12]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the 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: 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	Administer 160 mg (four 40 mg 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 tablets: 50419-0171-xx

VII. References

1. Stivarga [package insert]. Whippany, NJ; Bayer HealthCare Pharmaceuticals Inc.; December 2020. Accessed October 2023.
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5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) regorafenib. National Comprehensive Cancer Network, 2023. The NCCN

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9. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers, 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 September 2023.
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12. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma, Version 2.2023. 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 September 2023.
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14. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastrointestinal Stromal Tumors, 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 September 2023.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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

ICD-10	ICD-10 Description
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
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

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

ICD-10	ICD-10 Description
C78.02	Secondary malignant neoplasm of left lung
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
Z85.830	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: 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/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