PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Stivarga Prior Authorization Policy
- Stivarga® (regorafenib tablets – Bayer)

REVIEW DATE: 03/08/2023

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Stivarga, a kinase inhibitor, is indicated for the following uses:[1]

- **Colorectal cancer**, metastatic, in patients who have been previously treated with
  fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-vascular endothelial growth factor (VEGF) therapy, and, if *RAS* wild-type, an anti-epidermal growth factor receptor (EGFR) therapy.
- **Gastrointestinal stromal tumor**, locally advanced, unresectable, or metastatic in patients who have been previously treated with imatinib and sunitinib.
- **Hepatocellular carcinoma**, in patients who have been previously treated with sorafenib.

Guidelines

Stivarga is discussed in National Comprehensive Cancer Network (NCCN) guidelines:[2]

- **Bone Cancer**: NCCN guidelines (version 2.2023 – September 28, 2022) recommend Stivarga as a single agent "Preferred Regimen" for second-line therapy for relapsed/refractory or metastatic disease for patients with osteosarcoma (category 1).[3]

- **Central Nervous System Cancers**: NCCN guidelines (version 2.2022 – September 29, 2022) recommend Stivarga as a single agent "Preferred Regimen" for the treatment of recurrent glioblastoma (category 2A).[4]
- **Colon Cancer and Rectal Cancer**: NCCN guidelines (colon cancer [version 3.2022 – January 25, 2023] and rectal cancer [version 4.2022 – January 25, 2023]) recommend Stivarga as subsequent therapy as a single agent for advanced or metastatic disease not previously treated with Stivarga in patients who have progressed through all available regimens except Stivarga or Lonsurf® (trifluridine and tipiracil tablets) with or without bevacizumab.[5,6] Stivarga may be given before or after Lonsurf. Appendiceal adenocarcinoma are treated similarly to colon cancer.
- **Gastrointestinal Stromal Tumors**: NCCN guidelines (version 2.2022 – September 1, 2022) recommend Stivarga as a "Preferred Regimen" for treatment of unresectable, recurrent, or metastatic disease with widespread, systemic progression after single-agent therapy with imatinib and sunitinib or Sprycel (dasatinib tablets) [category 1].[7] Stivarga in combination with everolimus tablets is recommended as "Useful in Certain Circumstances" for unresectable, recurrent, or metastatic disease after failure on approved therapies. Stivarga is also recommended as a special consideration for unresectable, succinate dehydrogenase-deficient disease.[7]
- **Hepatobiliary Cancers**: NCCN guidelines (version 5.2022 – January 13, 2023) recommend Stivarga for subsequent treatment as a single agent for patients with hepatocellular carcinoma (adenocarcinoma) [Child-Pugh Class A only] and disease progression for the following uses (all are category 1): in patients who are not transplant candidates with unresectable disease; in patients who have liver-confined disease, inoperable by performance status or comorbidity or with minimal or uncertain extrahepatic disease; or in patients who have extensive liver tumor burden or metastatic disease.[8] Stivarga is also recommended as subsequent treatment as a single agent for progression on or after systemic treatment for unresectable or metastatic disease (category 2B).[8]
- **Soft Tissue Sarcoma**: NCCN guidelines (version 2.2022 – May 17, 2022) recommend Stivarga as a single-agent subsequent therapy for patients with non-adipocytic sarcoma with advanced/metastatic disease, advanced/metastatic pleomorphic rhabdomyosarcoma, or angiosarcoma (all category 2A).[9]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Stivarga. All approvals are provided for the duration noted below.

- **Stivarga® (regorafenib tablets (Bayer)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Colon, Rectal and Appendiceal Cancer.** Approve for 1 year if the patient meets all of the following criteria (A, B, C, D, E, and F):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced or metastatic disease; AND
   - **C)** Patient has been previously treated with a fluoropyrimidine (e.g., capecitabine, 5-fluorouracil [5-FU]); AND
   - **D)** Patient has been previously treated with oxaliplatin; AND
   - **E)** Patient has been previously treated with irinotecan; AND
   - **F)** Patient meets one of the following criteria (i or ii):
     - **i.** Patient's tumor or metastases are wild-type *RAS* (*KRAS* wild-type and *NRAS* wild-type) and the patient meets one of the following criteria (a or b):
       Note: This includes tumors or metastases that are *KRAS* and *NRAS* mutation-negative.
       - **a)** The patient has tried Erbitux (cetuximab intravenous infusion) or Vectibix (panitumumab intravenous infusion); OR
       - **b)** The patient's tumor did not originate on the left side of the colon (from the splenic fixture to rectum); OR
     - **ii.** The patient's tumor has or metastases have a *RAS* mutation (either *KRAS* mutation or *NRAS* mutation).

2. **Gastrointestinal Stromal Tumor.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has tried both of the following (i and ii):
     - **i.** Imatinib or Ayvakit (avapritinib tablets); AND
     - **ii.** Sunitinib or Sprycel (dasatinib tablets).

3. **Hepatocellular Carcinoma.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has been previously treated with one systemic regimen.
     Note: Examples of a systemic regimen include: Tecentriq (atezolizumab intravenous infusion), bevacizumab, sorafenib, Lenvima (lenvatinib capsules), Opdivo (nivolumab intravenous infusion), Imjudo (tremelimumab-actl intravenous infusion), Imfinzi (durvalumab intravenous infusion).

Other Uses with Supportive Evidence

4. **Glioblastoma.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has recurrent disease.

5. **Osteosarcoma.** Approve for 1 year if the patient meets all of the following criteria (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has relapsed/refractory or metastatic disease; AND
   C) Patient has tried one systemic chemotherapy regimen.
   Note: Examples of a systemic chemotherapy regimen contain one of more of the following products: cisplastin, doxorubicin, methotrexate, or ifosfamide.

6. **Soft Tissue Sarcoma.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has advanced or metastatic disease; AND
   C) Patient has one of the following (i, ii, or iii):
      i. Non-adipocytic sarcoma; OR
      ii. Pleomorphic rhabdomyosarcoma; OR
      iii. Angiosarcoma.

CONDITIONS NOT COVERED

- **Stivarga® (regorafenib tablets (Bayer)**

is(are) considered experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Stivarga® tablets [prescribing information]. Whippany, NJ: Bayer; December 2020.
2. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 5, 2023. Search term: regorafenib.
3. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2023 – September 28, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 5, 2023.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2022 – September 29, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 6, 2023.
5. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 3.2022 – January 25, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 6, 2023.
6. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 4.2022 – January 25, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 6, 2023.
7. The NCCN Gastrointestinal Stromal Tumors Clinical Practice Guidelines in Oncology (version 2.2022 – September 1, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 5, 2023.
8. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (version 5.2022 – January 13, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 6, 2023.
9. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 2.2022 – May 17, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 5, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Gastrointestinal Stromal Tumor:** Sprycel (dasatinib tablets) was added as an option to Sutent (sunitinib malate capsules) as a medication tried. **Hepatocellular Carcinoma:** The requirement that the patient has been previously treated with one tyrosine kinase inhibitor was reworded to "one systemic regimen" and a Note was added with examples of a systemic regimen. **Osteosarcoma:** The requirement that Stivarga is used as subsequent therapy was changed to "patient has tried one systemic regimen" and a Note was added with examples of a systemic regimen. **Soft Tissue Sarcoma:** The type of soft tissue sarcoma, **"**Non-adipocytic extremity/body wall, head/neck, or retroperitoneal/intra-abdominal sarcoma" was reworded to "non-adipocytic sarcoma."	02/09/2022
Selected Revision	**Colon and Rectal Cancer:** The duration of approval was changed from 3 years to 1 year. **Gastrointestinal Stromal Tumor:** The duration of approval was changed from 3 years to 1 year. **Hepatocellular Carcinoma:** The duration of approval was changed from 3 years to 1 year. **Glioblastoma:** The duration of approval was changed from 3 years to 1 year. **Osteosarcoma:** The duration of approval was changed from 3 years to 1 year. **Soft Tissue Sarcoma:** The duration of approval was changed from 3 years to 1 year.	06/22/2022
Selected Revision	**Colon and Rectal Cancer:** The definition of RAS wild-type was updated to remove the word "or" from "KRAS wild-type and NRAS wild-type" and "KRAS and NRAS mutation negative." The statement, "This includes tumors or metastases that are KRAS and NRAS mutation negative" was removed from the criteria and added as a note. The following qualifier, "the patient's tumor did not originate on the left side of the colon (from the splenic fixture to rectum)" was added as an option when the patient's tumor or metastases is RAS wild-type. A criterion was added when the patient's tumor or metastases has a RAS mutation (either KRAS mutation or NRAS mutation).	08/03/2022
Annual Revision	**Colon, Rectal, and Appendiceal Cancer:** Appendiceal cancer was added to this condition of approval. **Soft Tissue Sarcoma:** Solitary fibrous tumor was removed from the list of soft tissue sarcomas.	03/08/2023