

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Stivarga Prior Authorization Policy

- Stivarga® (regorafenib tablets – Bayer)

REVIEW DATE: 03/06/2024

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 1.2024 – August 7, 2023) 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 Stivarga is also recommended under “Other Recommended Regimens” for second-line treatment (relapsed/refractory or metastatic disease) of Ewing sarcoma (category 2A).
- **Central Nervous System Cancers:** NCCN guidelines (version 1.2023 – March 24, 2023) recommend Stivarga as a single agent “Preferred Regimen” for the treatment of recurrent or progressive glioblastoma (category 2A).⁴
- **Colon Cancer and Rectal Cancer:** NCCN guidelines (colon cancer [version 1.2024 – January 29, 2024] and rectal cancer [version 1.2024 – January 29, 2024]) 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 1.2023 – March 13, 2023) recommend Stivarga as a “Preferred Regimen” in the third-line setting (category 1) for treatment of unresectable, progressive, or metastatic disease with after single-agent therapy with imatinib or sunitinib [both category 1].⁷ Ayvakit® (avapritinib tablets) is a “Preferred Regimen” in the first-line setting for GIST with *PDGFRA* exon 19 mutations that are insensitive to imatinib (including *PDGFRA D842V*). 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 “Useful in Certain Circumstances” for unresectable, succinate dehydrogenase-deficient disease (category 2A).⁷
- **Hepatocellular Carcinoma:** NCCN guidelines (version 2.2023 – September 14, 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

- **Soft Tissue Sarcoma:** NCCN guidelines (version 3.2023 – December 12, 2023) 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Stivarga is recommended in those who meet one of the following criteria:

FDA-Approved Indications

- 1. Colon, Rectal and Appendiceal Cancer.** Approve for 1 year if the patient meets all of the following (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 (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 (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 (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 (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 (A and B):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient has recurrent or progressive disease.

5. **Bone Cancer.** Approve for 1 year if the patient meets all of the following (A, B, C, and D):
 - 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; AND
Note: Examples of a systemic chemotherapy regimen contain one of more of the following: cisplatin, doxorubicin, methotrexate, ifosfamide, cyclophosphamide, etoposide, topotecan, irinotecan, vincristine, temozolomide.
 - D) Patient meets ONE of the following (i or ii):
 - i. Patient has Ewing sarcoma; OR
 - ii. Patient has osteosarcoma.

6. **Soft Tissue Sarcoma.** Approve for 1 year if the patient meets the following (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 RECOMMENDED FOR APPROVAL

Coverage of Stivarga is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Stivarga® tablets [prescribing information]. Whippany, NJ: Bayer; December 2020.
2. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 4, 2024. Search term: regorafenib.
3. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – August 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 4, 2024.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 1.2023 – March 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 4, 2024.
5. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – January 29, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 4, 2024.
6. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – January 29, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 4, 2024.
7. The NCCN Gastrointestinal Stromal Tumors Clinical Practice Guidelines in Oncology (version 1.2023 – March 13, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 4, 2024.
8. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 2.2023 – September 14, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 5, 2024.

9. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 3.2023 – December 12, 2023). © 2023 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 5, 2024.