

## PRIOR AUTHORIZATION POLICY

**POLICY:** Oncology – Stivarga Prior Authorization Policy

- Stivarga® (regorafenib tablets – Bayer)

**REVIEW DATE:** 02/09/2022; selected revision 06/22/2022 and 08/03/2022

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### OVERVIEW

Stivarga, a kinase inhibitor, is indicated for the following uses:<sup>1</sup>

- **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 mesylate and Sutent® (sunitinib capsules).
- **Hepatocellular carcinoma**, in patients who have been previously treated with Nexavar® (sorafenib tablets).

### Guidelines

Stivarga is discussed in National Comprehensive Cancer Network (NCCN) guidelines:<sup>2</sup>

- **Bone Cancer:** NCCN guidelines (version 2.2022 – October 8, 2021) recommend Stivarga as a single agent for second-line therapy for relapsed/refractory or metastatic disease for patients with osteosarcoma (category 1), dedifferentiated chondrosarcoma, and high-grade undifferentiated pleomorphic sarcoma (category 2B).<sup>3</sup>
- **Central Nervous System Cancers:** NCCN guidelines (version 2.2021 – September 8, 2021) recommend Stivarga as a single agent for the treatment of recurrent glioblastoma.<sup>4</sup>
- **Colon Cancer and Rectal Cancer:** NCCN guidelines (colon cancer [version 1.2022 – February 25, 2022] and rectal cancer [version 1.2022 – February 25, 2022]) 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. Stivarga may be given before or after Lonsurf.<sup>5,6</sup>
- **Gastrointestinal Stromal Tumors:** NCCN guidelines (version 1.2022 – January 21, 2022) recommend Stivarga (category 1) as a single agent for treatment of unresectable, recurrent, or metastatic disease with widespread, systemic progression after single-agent therapy with imatinib and Sutent.<sup>7</sup> Stivarga in combination with everolimus tablets is recommended 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.<sup>7</sup>
- **Hepatobiliary Cancers:** NCCN clinical practice guidelines (version 5.2021 – September 21, 2021) 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.<sup>8</sup> 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).<sup>8</sup>

- **Soft Tissue Sarcoma:** NCCN guidelines (version 3.2021 – January 26, 2022) recommend Stivarga (all category 2A) as a single-agent subsequent therapy for patients with non-adipocytic sarcoma with advanced/metastatic disease, advanced/metastatic pleomorphic rhabdomyosarcoma, angiosarcoma, or solitary fibrous tumor.<sup>9</sup>

## **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 and Rectal Cancer.** Approve for 1 year if the patient meets all of the following criteria (A, B, C, D, E, and F):
  - A) Patient is  $\geq 18$  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 flexure 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  $\geq 18$  years of age; AND
  - B) Patient has tried both of the following (i and ii):
    - i. Imatinib or Ayvakit (avapritinib tablets); AND
    - ii. Sutent (sunitinib malate capsules) or Sprycel (dasatinib tablets).
- 3. Hepatocellular Carcinoma.** Approve for 1 year if the patient meets the following criteria (A and B):
  - A) Patient is  $\geq 18$  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 intravenous infusion, Nexavar (sorafenib tablets), Lenvima (lenvatinib capsules), Opdivo (nivolumab intravenous infusion), oxaliplatin, fluorouracil.

### Other Uses with Supportive Evidence

4. **Glioblastoma.** Approve for 1 year if the patient meets the following criteria (A and B):
  - A) Patient is  $\geq 18$  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  $\geq 18$  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: cisplatin, 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  $\geq 18$  years of age; AND
  - B) Patient has advanced or metastatic disease; AND
  - C) Patient has one of the following (i, ii, iii, or iv):
    - i. Non-adipocytic sarcoma; OR
    - ii. Pleomorphic rhabdomyosarcoma; OR
    - iii. Angiosarcoma; OR
    - iv. Solitary fibrous tumor.

### 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. © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on February 4, 2022. Search term: regorafenib.
3. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – October 8, 2021). © 2021 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on February 4, 2022.
4. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (version 2.2021 – September 8, 2021). © 2021 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on February 4, 2022.
5. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 1.2022 – February 25, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on August 1, 2022.
6. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 1.2022 – February 25, 2022). © 2022 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on August 1, 2022.
7. The NCCN Gastrointestinal Stromal Tumors Clinical Practice Guidelines in Oncology (version 1.2022 – January 21, 2022). © 2021 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on: February 7, 2021.
8. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (version 5.2021 – September 21, 2021). © 2021 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on February 7, 2022.
9. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 3.2021 – January 26, 2022). © 2021 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on February 7, 2021.