PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Stivarga Prior Authorization Policy
- Stivarga® (regorafenib tablets – Bayer HealthCare Pharmaceuticals, Inc.)

REVIEW DATE: 01/20/2021

OVERVIEW

Stivarga, a kinase inhibitor, is indicated for the treatment of patients with the following conditions:[1]

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.
2. **Gastrointestinal stromal tumor** (GIST), **locally advanced, unresectable or metastatic** in patients who have been previously treatment with imatinib mesylate (Gleevec®) and Sutent® (sunitinib malate capsules).
3. **Hepatocellular carcinoma** in patients who have been previously treated with Nexavar® (sorafenib tablets).

Guidelines

Stivarga is included in a number of National Comprehensive Cancer Network (NCCN) guidelines:

- **Bone cancer**: The NCCN guidelines (version 1.2021 – November 20, 2020) recommend Stivarga as a single agent for second-line therapy for relapsed/refractory or metastatic disease for patients with osteosarcoma (category 1), dedifferentiated chrondrosarcoma, and high-grade undifferentiated pleomorphic sarcoma (category 2B).[6,7]
- **Central nervous system cancers**: The NCCN guidelines on (version 3.2020 – September 11, 2020) recommend Stivarga as a single agent for the treatment of recurrent glioblastoma.[6,8]
- **Colon cancer and rectal cancer**: The NCCN guidelines on (version 1.2021 – December 22, 2020) and (version 1.2021 – December 22, 2020) 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.[2,3,6]
- **Gastrointestinal stromal tumors**: The NCCN guidelines (version 1.2021 – September 12, 2019) recommend Stivarga (category 1) as a single agent for treatment of unresectable, recurrent, or metastatic GIST disease with widespread, systemic progression after single-agent therapy with Gleevec and Sutent.[6,9] Stivarga in combination with Afinitor® (everolimus tablets) is recommended for unresectable, recurrent, or metastatic disease after failure on approved therapies.
- **Hepatobiliary cancers**: The NCCN clinical practice guidelines on (version 5.2020 – August 4, 2020) 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): 1) in patients who are not transplant candidates with unresectable disease, 2) in patients who are inoperable by performance status or comorbidity (local disease or local disease with minimal extrahepatic disease only), or in patients who have extensive liver tumor burden or metastatic disease.[5,6]
- **Soft tissue sarcoma**: The NCCN guidelines (version 1.2021 – October 30, 2020) recommend Stivarga (all category 2A) as single-agent subsequent therapy for patients with: 1) non-adipocytic extremity/body wall, head/neck sarcoma with advanced/metastatic disease with disseminated metastases, 2) non-adipocytic retroperitoneal/intra-abdominal sarcoma with recurrent unresectable

or stage IV disease, 3) advanced/metastatic pleomorphic rhabdomyosarcoma, 4) angiosarcoma, or 5) solitary fibrous tumor.[4,6]

Safety
Stivarga has Boxed Warnings concerning risks of hepatotoxicity.[1] Hepatic function should be monitored prior to and during treatment.

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 the following criteria:

FDA-Approved Indications

1. **Colon and Rectal Cancer.** Approve for 3 years if the patient meets all of the following criteria (A, B, C, D, and E):
   - **A)** Patient has advanced or metastatic disease; AND
   - **B)** Patient has been previously treated with a fluoropyrimidine (e.g., capecitabine, 5-fluorouracil [5-FU]); AND
   - **C)** Patient has been previously treated with oxaliplatin; AND
   - **D)** Patient has been previously treated with irinotecan; AND
   - **E)** If the patient's tumor or metastases are wild-type *RAS* (*KRAS* wild-type and/or *NRAS* wild-type) [that is, the tumors or metastases are *KRAS* and/or *NRAS* mutation negative], Erbitux (cetuximab injection for intravenous infusion) or Vectibix (panitumumab injection for intravenous infusion) has been tried.

2. **Gastrointestinal Stromal Tumor (GIST).** Approve for 3 years if the patient meets all of the following criteria (A, B, and C):
   - **A)** Patient has recurrent, metastatic, or unresectable disease; AND
   - **B)** Patient has been previously treated with imatinib ; AND
   - **C)** Patient has been previously treated with Sutent (sunitinib malate capsules).

3. **Hepatocellular Carcinoma.** Approve for 3 years if the patient has been previously treated with at least one tyrosine kinase inhibitor.
   Note: Tyrosine kinase inhibitors include Nexavar® (sorafenib tablets) and Lenvima® (lenvatinib capsules).

Other Uses with Supportive Evidence

4. **Glioblastoma.** Approve for 3 years if the patient has recurrent disease.

5. **Osteosarcoma.** Approve for 3 years if the patient meets both of the following criteria (A and B):
   - **A)** Patient has relapsed/refractory or metastatic disease; AND
   - **B)** Stivarga is used as subsequent therapy.

6. **Soft Tissue Sarcoma.** Approve for 3 years if the patient meets the following criteria (A and B):
   - **A)** Patient has advanced or metastatic disease; AND
   - **B)** Patient has one of the following (i, ii, iii, or iv):
     - **i.** Non-adipocytic extremity/body wall, head/neck, or retroperitoneal/intra-abdominal 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 HealthCare Pharmaceuticals Inc.; June 2018.
2. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (Version 1.2021 – December 22, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 14, 2021.
3. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (Version 1.2021 – December 22, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 14, 2021.
4. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (Version 1.2021 – October 30, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 15, 2021.
5. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (Version 5.2020 – August 4, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 15, 2021.
6. The NCCN Drugs and Biologics Compendium. © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 14, 2021. Search term: regorafenib.
7. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (Version 1.2021 – November 20, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 14, 2021.
8. The NCCN Central Nervous System Cancers Clinical Practice Guidelines in Oncology (Version 3.2020 – September 11, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 14, 2021.
9. The NCCN Gastrointestinal Stromal Tumors Clinical Practice Guidelines in Oncology (Version 1.2021 – October 30, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on: January 14, 2021.