MEDICAL MUTUAL®

Drug Policy

Policy:	Stivarga (regorafenib)	Annual Review Date: 02/18/2021 Last Revised Date: 02/18/2021

OVERVIEW

Stivarga, a kinase inhibitor, is FDA approved for the treatment of patients with the following conditions: 1) Metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, and, if *KRAS* wild-type, an anti-epidermal growth factor receptor (EGFR) therapy; 2) Locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treatment with Gleevec (imatinib mesylate tablets) and Sutent (sunitinib malate capsules); 3) Hepatocellular carcinoma (HCC) who have been previously treated with Nexavar (sorafenib tablets). Stivarga is a small molecule inhibitor of multiple membrane-bound and intracellular kinases involved in normal cellular functions and in pathologic processes such as oncogenesis, tumor angiogenesis, and maintenance of the tumor microenvironment. Stivarga treatment should continue until disease progression or unacceptable toxicity.

POLICY STATEMENT

This policy involves the use of Stivarga. Prior authorization is recommended for pharmacy benefit coverage of Stivarga. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Stivarga as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Stivarga be prescribed by or in consultation with a physician who specializes in the condition being treated. In order to be considered for coverage, Stivarga must be prescribed by or in consultation with a hematologist or oncologist. All approvals for initial therapy are provided for the initial approval duration noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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

1. **Metastatic or Unresectable Advanced Colon Cancer**
   Criteria. *Patient must meet the following criteria*
   - **A.** First progression (KRAS/NRAS mutation only) or second progression and patient was previously treated with fluorouracil, leucovorin, oxaliplatin, and irinotecan regimen; OR
   - **B.** Second progression and patient was previously treated with irinotecan and oxaliplatin; OR

C. Patient has progressed through all available regimens

2. Metastatic or Unresectable Advanced Rectal Cancer
Criteria. *Patient must meet the following criteria*

A. First progression (KRAS/NRAS mutation only) or second progression and patient was previously treated with fluorouracil, leucovorin, oxaliplatin, and irinotecan regimen; OR
B. Second progression and patient was previously treated with irinotecan and oxaliplatin; OR
C. Patient has progressed through all available regimens, including trifluride and tipiracil

3. Metastatic and/or Unresectable Gastrointestinal Stromal Tumor (GIST)
Criteria. *Patient must meet the following criteria*

A. The patient meets one of the following:
  a. The patient has previously tried Gleevec AND Sutent; OR
  b. Stivarga will be used in combination with everolimus after progression on Stivarga as single-agent therapy

4. Hepatocellular Carcinoma
Criteria. *Patient must meet the following criteria*

A. Patient has previously tried Nexavar (sorafenib); AND
B. The patient has Child-Pugh Class A only; AND
C. Stivarga will be used as a single agent; AND
D. Patient meets ONE of the following:
  a. Patient is a nontransplant candidate with unresectable disease; OR
  b. Patient is inoperable by performance status or comorbidity (local disease or local disease with minimal extrahepatic disease only); OR
  c. Patient has extensive liver tumor burden or metastatic disease

5. Soft Tissue Sarcoma of Extremity/Superficial Trunk, Head/Neck, and/or Retroperitoneal/Intra-Abdominal
Criteria. *Patient must meet the following criteria*

A. Stivarga will be used as single-agent palliative therapy; AND
B. The patient has non-adipocytic sarcoma with stage IV or recurrent disease with disseminated metastases

6. Rhabdomyosarcoma
Criteria. *Approve if Stivarga is requested as single-agent palliative therapy for pleomorphic rhabdomyosarcoma.*

7. Osteosarcoma
Criteria. *Approve if Stivarga is requested as a single-agent for relapsed/refractory or metastatic disease.*

8. **Patients with another indication that is not listed but is cited in the National Comprehensive Cancer Network (NCCN) guidelines as a category 1, 2A, or 2B recommendation**
   Criteria. *Prescriber will provide specific diagnosis for documentation.*

9. **Patient has been started on Stivarga**
   Criteria. *Approve for an indication or condition addressed as an approval in this document.*

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Stivarga has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Stivarga® tablets [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; April 2017.
2. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (Version 1.2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 11,2020.
3. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (Version 1.2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed September 8, 2016.
4. The NCCN Soft Tissue Sarcoma Practice Guidelines in Oncology (Version 6.2019). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed October 8, 2015.
5. Eisen T, Joensuu H, Nathan PD, et al. Regorafenib for patients with previously untreated metastatic or unresectable renal-cell carcinoma: a single-group phase 2 trial. *Lancet Oncol.* 2012;13:1055-1062.

6. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (Version 4.2019). National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on 11 February 2020.
7. Regorafenib. In: DRUGDEX (online database). Truven Health Analytics; Greenwood Village, CO. Last updated 15 January 2019. Accessed on 19 February 2019.
8. The NCCN Drugs and Biologics Compendium. © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on 20 February 2020. Search term: regorafenib
9. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (Version 1.2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 11,2020.