Clinical Policy: Regorafenib (Stivarga)

Reference Number: PA.CP.PHAR.107
Effective Date: 01/18
Last Review Date: 04/18 Revision Log

Coding Implications

Description
Regorafenib (Stivarga®) is a kinase/VEGFR inhibitor.

FDA Approved Indications
Stivarga is indicated for treatment of patients with:

- Metastatic colorectal cancer (CRC) 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-endothelial growth factor (EGFR) therapy.
- Locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.
- Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Stivarga is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Colorectal Cancer (must meet all)**:**
1. Diagnosis of CRC;
2. Previously treated with systemic chemotherapy;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Dose does not exceed 160 mg/day.

Approval duration: 6 months

B. Gastrointestinal Stromal Tumor (must meet all)**:**
1. Diagnosis of GIST;
2. Previously treated with imatinib (Gleevec®)* or sunitinib (Sutent®)* unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is (or may be) required*
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Dose does not exceed 160 mg/.

Approval duration: 6 months

C. Hepatocellular Carcinoma (must meet all)**:**
1. Diagnosis of HCC;

2. Previously treated with sorafenib (Nexavar®)* unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is (or may be) required*
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Dose does not exceed 160 mg/day.

Approval duration: 6 months

D. Other diagnoses/indications: Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Approval

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or documentation supports that member is currently receiving Stivarga for CRC, GIST or HCC; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (e.g., no disease progression, no significant toxicity);
3. Dose does not exceed 160 mg/day.

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BID: twice daily
CRC: colorectal cancer
EGFR: epidermal growth factor receptor
GIST: gastrointestinal stromal tumor
HCC: hepatocellular carcinoma
PO: by mouth
VEGF: vascular endothelial growth factor
VEGFR: vascular endothelial growth factor receptor

Appendix B: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Colorectal Cancer (CRC)		
5-FU (fluorouracil)†	Varies upon protocol and patient tolerance	
Avastin® (bevacizumab)	Varies upon protocol and patient tolerance	
Camptosar® (irinotecan)	Varies upon protocol and patient tolerance	
Cyramza® (ramucirumab)	Varies upon protocol and patient tolerance	
Eloxatin® (oxaliplatin)	Varies upon protocol and patient tolerance	
Erbitux® (cetuximab)	Varies upon protocol and patient tolerance	
Lonsurf® (trifluridine and tipiracil)	35 mg/m^2/dose by mouth (PO) twice daily (BID) on Days 1 through 5 and Days 8 through 12 of each 28-day cycle.	70 mg/m^2/day
Vectibix® (panitumumab)	Varies upon protocol and patient tolerance	
Xeloda® (capecitabine)†	1250 mg/m^2 PO BID for 2 weeks followed by a 1-week rest period given as 3-week cycles.	2500/m^2/day
Zaltrap® (ziv-aflibercept)	Varies upon protocol and patient tolerance	
FOLFOX*	Varies upon protocol and patient tolerance	
CAPEOX*	Varies upon protocol and patient tolerance	
FOLFIRI*	Varies upon protocol and patient tolerance	
FOLFOXIRI*	Varies upon protocol and patient tolerance	
IROX*	Varies upon protocol and patient tolerance	
Gastrointestinal Stromal Tumor (GIST)		
Gleevec® (imatinib)	400 mg PO daily up to 400 mg PO BID	800 mg/day
Sutent® (sunitinib)	50 mg PO daily for 4 weeks followed by 2 weeks off	87.5 mg/day
Hepatocellular Carcinoma (HCC)		
Nexavar® (sorafenib)	400 mg PO BID	800 mg/day

**FOLFOX: oxaliplatin, leucovorin, fluorouracil (5-FU); CAPEOX: oxaliplatin, capecitabine (Xeloda); FOLFIRI: irinotecan, leucovorin, 5-FU; FOLFOXIRI: irinotecan, oxaliplatin, leucovorin, 5-FU; IROX: oxaliplatin, irinotecan*

†Examples of fluoropyrimidines include fluorouracil (5-FU) and capecitabine (Xeloda).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CRC	160 mg PO daily for the first 21 days of each 28-day cycle	160 mg/day
GIST		
HCC		

VI. Product Availability

Stivarga oral tablets: 40 mg

VII. References

1. Stivarga Prescribing Information. Whippany, NJ: Bayer HealthCare Pharmaceuticals. Inc.; April 2017. Available at http://labeling.bayerhealthcare.com/html/products/pi/Stivarga_PI.pdf. Accessed February 2018.
2. Regorafenib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed February 2018.
3. Colon cancer (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed February 2018.
4. Rectal cancer (Version 3.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed February 2018.
5. Soft tissue sarcoma (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed February 2018.
6. Hepatobiliary cancers (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed February 2018.

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: no significant changes; age added; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; references reviewed and updated.	02.13.18	04.18

04.18