Colorectal Cancer Agents
Stivarga (regorafenib)
Effective 06/01/2022

Plan	☐ MassHealth ☒ MassHealth UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☒ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☐ Medical Benefit (NLX)		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	**Specialty Medications**		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	Non-Specialty Medications		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	Medical Specialty Medications (NLX)		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
Exceptions	N/A		

Overview

Stivarga is a kinase inhibitor indicated for the treatment of patients with:

- Metastatic colorectal cancer (CRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an antiVEGF therapy, and, if RAS wild-type, an anti-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

No PA	Drugs that require PA
Gleevec® # (imatinib)	Stivarga® (regorafenib)

Coverage Guidelines

Authorization may be reviewed on a case by case basis for members new to AllWays Health Partners who are currently receiving treatment with the requested medication, excluding when the product is obtained as samples or via manufacturer's patient assistance programs

OR

Authorization may be granted if the member meets **ALL** following criteria and documentation has been submitted:

For Metastatic Colorectal Cancer

Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of metastatic colorectal cancer

2. Prescriber is an oncologist
3. Appropriate dose
4. Physician documented inadequate response or adverse reaction to **ONE** of the following regimens or a contraindication to **ALL** of the following regimens *(see appendix for components of commonly used regimens for Colorectal cancer):*
    a. CAPEOX
    b. FOLFIRI
    c. FOLFOX
    d. FOLFOXIRI
    e. irinotecan-based therapy
    f. oxaliplatin-based therapy
5. If KRAS/NRAS/BRAF wild-type cancer is present, physician documented inadequate response or adverse reaction to **ONE** or a contraindication to **BOTH** of the following:
    a. Erbitux® (cetuximab)
    b. Vectibix® (panitumumab)

For Gastrointestinal Stromal Tumor
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of gastrointestinal stromal tumor
2. Prescriber is an oncologist
3. Appropriate dose
4. Physician documented inadequate response, adverse reaction, or a contraindication to **BOTH** of the following:
    a. Gleevec® (imatinib)
    b. Sutent® (sunitinib)

For Hepatocellular Carcinoma
Prescriber provides documentation of **ALL** of the following:
1. Diagnosis of hepatocellular carcinoma
2. Prescriber is an oncologist
3. Appropriate dose
4. Member has Child-Pugh Class A
5. Physician documented inadequate response, adverse reaction or a contraindication to Nexavar® (sorafenib)

Continuation of Therapy
Reauthorization requires physician attestation of continuation of therapy and positive response to therapy.

Limitations
1. Initial approvals and reauthorizations will be granted for 6 months
2. The following quantity limits apply:

Stivarga (regorafenib) 40mg tablets	84 tablets per 28 days

*****Any requests for over the quantity limit must be reviewed against the Global Quantity Limit criteria.

Appendix

Appendix A: Components of Commonly Used Regimens for Treatment of Colorectal Cancer

Regimen Abbreviation	Drug Components
5-FU	fluorouracil
CAPEOX	capecitabine/oxaliplatin
FOLFIRI	leucovorin calcium (folinic acid)/fluorouracil/irinotecan
FOLFOX	leucovorin calcium (folinic acid)/fluorouracil/oxaliplatin
FOLFOXIRI	leucovorin calcium (folinic acid)/5-fluorouracil/oxaliplatin/irinotecan

Appendix B: Stivarga® (regorafenib) for the treatment of osteosarcoma

Stivarga® (regorafenib) is currently FDA-approved in adults for metastatic colorectal cancer, locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) and hepatocellular carcinoma (HCC). There are ongoing trials in ClinicalTrials.gov evaluating use of regorafenib in osteosarcoma in adults and children. NCT04055220, is evaluating safety and efficacy of regorafenib (120 mg QD for 21 days followed by seven days without treatment) as a maintenance therapy following first-line therapy in those ≥16 years of age with bone sarcomas. There is one referenced phase I study (https://pubmed.ncbi.nlm.nih.gov/34157616/), that found acceptable tolerability and preliminary antitumor activity in children at a dose of 82 mg/m2. Several phase II trials are currently under way looking at safety and efficacy of regorafenib in patients (adults and pediatric patients) with relapsed or refractory osteosarcoma (NCT04803877 and NCT02389244). Trial NCT04803877 is comparing the progression-free survival rate of those with regorafenib in combination with nivolumab to those who received regorafenib alone (historical control). Estimated primary completion dates are for 12/2022 and 9/2022 respectively.

Current conventional treatments for osteosarcoma combine chemotherapy and surgery. Per NCCN guidelines (Bone cancer V 2.2022), preferred regimens for osteosarcoma in the first-line setting included cisplatin and doxorubicin (category 1) or MAP (high-dose methotrexate, cisplatin, and doxorubicin) (category 1). Ifosfamide is listed as a potential other recommended regimen. For second-line therapy in the relapsed/refractory or metastatic disease setting, preferred regimens included high-dose ifosfamide +/- etoposide, sorafenib or regorafenib (category 1). There are many other recommended regimens and agents listed as useful in certain circumstances- please refer to full NCCN guideline.

If a request is received for regorafenib in osteosarcoma, the following approval criteria should be used: Prescriber provides documentation of **ALL** of the following:

1. Appropriate diagnosis
2. Prescriber is an oncologist
3. Inadequate response or adverse reaction to **ONE** of the following regimens or a contraindication to **BOTH** of the following regimens: (*Claims in POPS are NOT sufficient*)
   a. Cisplatin and doxorubicin
   b. High-dose methotrexate, cisplatin and doxorubicin
4. Appropriate dosing (adults: 160 mg QD 21 days on 7 days off; children 72 to 82 mg/m2/dose rounded to the nearest 20 mg, maximum dose of 120 mg)

References

1. Stivarga [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; June 2020.

Review History

10/9/2020: Created criteria to be in compliance with the Masshealth partial unified formulary requirements effective 1/1/21.

05/18/2022: Reviewed and Updated for May P&T. updated criteria name to Colorectal cancer. Added Reference Table for drugs. Appendix section added for off-label use of Stivarga (regorafenib) in the treatment of osteosarcoma. Effective 6/1/2022

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