ROCKY MOUNTAIN HEALTH PLANS®
We understand Colorado. We understand you.

UNIFORM PHARMACY PRIOR AUTHORIZATION REQUEST FORM

CONTAINS CONFIDENTIAL PATIENT INFORMATION

Complete this form in its entirety and send to Rocky Mountain Health Plans at 858-357-2538

☐ **Urgent**[1] ☐ **Non-Urgent**

Requested Drug Name: Stivarga® (regorafenib)

Patient Information:	**Prescribing Provider Information:**
Patient Name:	Prescriber Name:
Member/Subscriber Number:	Prescriber Fax:
Policy/Group Number:	Prescriber Phone:
Patient Date of Birth (MM/DD/YYYY):	Prescriber Pager:
Patient Address:	Prescriber Address:
Patient Phone:	Prescriber Office Contact:
Patient Email Address:	Prescriber NPI:
	Prescriber DEA:
Prescription Date:	Prescriber Tax ID:
	Specialty/Facility Name (If applicable):
	Prescriber Email Address:

Prior Authorization Request for Drug Benefit: ☐ New Request ☐ Reauthorization

Patient Diagnosis and ICD Diagnostic Code(s):

Drug(s) Requested (with J-Code, if applicable):

Strength/Route/Frequency:

Unit/Volume of Named Drug(s):

Start Date and Length of Therapy:

Location of Treatment: (e.g. provider office, facility, home health, etc.) including name, Type 2 NPI (if applicable), address and tax ID:

Clinical Criteria for Approval, Including other Pertinent Information to Support the Request, other Medications Tried, Their Name(s), Duration, and Patient Response:

Stivarga® (regorafenib)

Diagnosis (documentation supportive of diagnosis is required)

☐ Metastatic colorectal cancer (mCRC)
☐ Locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST)
☐ Other (please state): _____

☐ **Diagnosis for mCRC ONLY:**

☐ Previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if KRAS wild type, an anti-EGFR therapy (*Documentation of prior treatments and documentation of KRAS mutation status required if no prior anti-EGFR therapy*).

☐ **Acknowledge the following:**

- **Difference in median OS (1º endpoint): 1.4 months** (6.4 months for Stivarga® vs. 5 months for placebo; p=0.0102)
- **Difference in median PFS time: 0.3 months** (2 months for Stivarga® vs. 1.7 months for placebo; p<0.0001)
- **Overall response rate: 1%** (95% CI, 0.3% to 2.3%) **for Stivarga® vs. 0.4% (95% CI, 0% to 2.2%) for placebo**

☐ **Diagnosis for GIST only *(Documentation of prior treatments required):***

☐ Previously treated with Gleevec (imatinib) with either intolerance or disease progression **AND**
☐ Previously treated with Sutent (sunitinib) with disease progression

Physician Specialty

☐ Oncologist
☐ Other (please state): _____

☐ For use in clinical trial? (If yes, provide trial name and registration number):

Drug Name (Brand Name and Scientific Name)/Strength:

Dose:	Route:	Frequency:
Quantity:	Number of Refills:	

Product will be delivered to: ☐ Patient's Home ☐ Physician Office Other:

Prescriber or Authorized Signature: Date:

Dispensing Pharmacy Name and Phone Number:

☐ **Approved** ☐ **Denied**

If denied, provide reason for denial, and include other potential alternative medications, if applicable, that are found in the formulary of the carrier:

1. A request for prior authorization that if determined in the time allowed for non-urgent requests could seriously jeopardize the life or health of the covered person or the ability of the covered person to regain maximum function, or subject the person to severe pain that cannot be adequately managed without the drug benefit contained in the prior authorization request

Stivarga® (regorafenib)

CLASSIFICATION

- Antineoplastic
- Multi-Kinase Inhibitor

DESCRIPTION

- Regorafenib is a small molecule inhibitor of various membrane-bound and intracellular kinases involved in cellular functions and pathological processes, including oncogenesis, tumor angiogenesis, and maintenance of the tumor microenvironment. Regorafenib or its major human active metabolites M-2 and M-5 have shown in-vitro inhibition of RET, VEGFR1, VEGFR2, VEGFR3, KIT, PDGFR-alpha, PDGFR-beta, FGFR1, FGFR2, TIE2, DDR2, Trk2A, Eph2A, RAF-1, BRAF, BRAF(V600E), SAPK2, PTK5, and Abl. In vivo animal studies, including models for human colorectal carcinoma have demonstrated antiangiogenic activity, anti-metastatic activity, and inhibition of tumor growth
- Regorafenib is indicated for the treatment of patients with **metastatic colorectal cancer (mCRC)** who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and if KRAS wild type, an anti-EGFR therapy.
- In a multicenter, randomized, double-blind, placebo-controlled study (n=760), treatment with Stivarga® resulted in prolonged overall survival (OS) compared with placebo in adults with previously treated metastatic colorectal cancer. All patients had received prior fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy and bevacizumab, and all but 1 patient with KRAS mutation-negative tumors had received panitumumab or cetuximab. All patients received best supportive care and were randomized to receive either Stivarga 160 mg orally once daily (n=505) or placebo (n=255) for days 1 through 21 of each 28-day cycle, until disease progression or unacceptable toxicity.
- **Results:** The difference in median OS (primary endpoint) was 1.4 months (6.4 months for Stivarga® vs. 5 months for placebo; p=0.0102). The difference in median progression-free survival (PFS) time was 0.3 months (2 months for Stivarga® vs. 1.7 months for placebo; p<0.0001). The overall response rate was 1% (95% CI, 0.3% to 2.3%) in the Stivarga® arm and 0.4% (95% CI, 0% to 2.2%) in the placebo arm.
- Adverse reactions for regorafenib that occurred ≥30% in the clinical trials include asthenia/fatigue (65%), decreased appetite and food intake (47%), hand-foot skin reaction(HFSR) [palmar-plantar erythrodysesthesia (PPE)] (45%), diarrhea (43%), mucositis (33%), weight loss (32%), infection (31%), hypertension (30%), and dysphonia (30%).
- Regorafenib is also indicated in adults for the treatment **of locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST)** after treatment with imatinib and sunitinib.
- Efficacy of regorafenib for GIST was demonstrated in an international, randomized, double-blind, placebo-controlled, phase 3, GIST- Regorafenib In progressive Disease trial (GRID; n=199). Patients with histologically confirmed GIST, at least 1 measurable lesion on CT or MRI, and previous imatinib (defined as disease progression or intolerance) and previous sunitinib (defined as progression only) therapy were randomized to receive either regorafenib 160 mg once daily (n=133) or placebo (n=66) for the first 3 weeks of each 4-week cycle until disease progression or occurrence of toxic effects. All patients also received best supportive care. Patients in the placebo group could cross over to receive open-label regorafenib in the event of tumor progression. Analysis was performed by central radiology reviewers using RECIST criteria uniquely modified for this study to apply to GIST (no lymph nodes or bone lesions chosen as target lesions, and positron emission tomography scans could not be used). After 144 PFS events, the difference in median PFS (primary endpoint) was 3.9 months (4.8 months [interquartile range [IQR], 1.4 to 9.2 months] in the regorafenib group vs.0.9 months [IQR, 0.9 to 1.8 months] in the placebo group; hazard ratio, 0.27; 95% CI, 0.19 to 0.39; p < 0.0001). The final analysis of overall survival (OS) will occur following 136 events;

however, in a *preliminary assessment OS was not significantly different between the regorafenib and placebo groups* (HR, 0.77; 95% CI, 0.42 to 1.41; p=0.199).
- Grade 3 or greater adverse events in the regorafenib group included hypertension (23%), hand-foot skin reactions (20%), and diarrhea (5%); two grade 5 events (cardiac arrest and hepatic failure) were determined to be drug-related.

FORMULARY COVERAGE

Prior authorization: Required
Good Health Formulary: Tier 3
Commercial Formulary: Tier 3
Medicare Part D coverage: Tier 5

COVERAGE CRITERIA

Stivarga® (regorafenib) meets the definition of **medical necessity** for the following:
- Treatment of patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and if KRAS wild type, an anti-EGFR therapy. Documentation required includes:
  - Supporting documentation of diagnosis
  - Documentation of prior therapies for the treatment of CRC
  - Documentation of KRAS mutation status if no prior anti-EGFR therapy
- Treatment of patients with locally advanced, unresectable, or metastatic gastrointestinal stromal tumor (GIST) after treatment with imatinib and sunitinib. Documentation of prior treatment with Gleevec (imatinib) with either intolerance or disease progression AND documentation of disease progression on Sutent (sunitinib) is required.

Stivarga® (regorafenib) is considered **experimental** for the following:
- Any condition or diagnosis not FDA approved or Compendia supported.

Required Provider Specialty:
- Approval is limited to Oncologists

DOSAGE/ADMINISTRATION

Adult Dosing (safety and efficacy has not been determined for pediatric patients less than 18 years):
- mCRC: Dose 160 mg orally once daily with a low-fat breakfast that contains less than 30% fat on days 1 through 21 of every 28-day cycle. Regorafenib treatment may continue until disease progression or unacceptable toxicity occurs.
- GIST that is locally advanced, unresectable, or metastatic, after treatment with imatinib and sunitinib: recommended adult dose of regorafenib is 160 mg orally once daily with a low-fat breakfast (< 30% fat) on days 1 through 21 of every 28-day cycle. Regorafenib treatment may continue until disease progression or unacceptable toxicity occurs.
- Refer to Stivarga's prescribing information for dose modifications in the event of hepatotoxicity, any adverse reaction that is grade 3 or 4, Hand-Foot Skin Reaction, and Hypertension

PRECAUTIONS

Black Box Warning:
- Severe and sometimes fatal hepatotoxicity has been observed in clinical trials. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue regorafenib for hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis, depending upon severity and persistence.

Precautions:

- Cardiac ischemia and infarction have been reported (1.2% for regorafenib-treated patients vs. 0.4% of placebo-treated patients); discontinue for new or acute onset ischemia or infarction and resume after resolution of ischemic events if benefits outweigh the risks of further cardiac ischemia.
- Avoid concomitant use with strong CYP3A4 inducers (e.g., rifampin, phenytoin, carbamazepine, phenobarbital, St. John's Wort).
- Avoid concomitant use with strong CYP3A4 inhibitors (e.g., clarithromycin, grapefruit juice, itraconazole, ketoconazole, posaconazole, telithromycin, voriconazole).
- Dermatologic reactions including hand-foot skin reaction and rash have been reported; interrupt and reduce dose or discontinue depending on severity and/or persistence.
- Hemorrhage, including fatal hemorrhages of the respiratory, gastrointestinal, or genitourinary tracts, has been reported; permanently discontinue for severe or life-threatening hemorrhage.
- Gastrointestinal perforation or fistulae have been reported; permanently discontinue regorafenib if this occurs.
- Severe hepatic impairment (Child-Pugh Class C); use not recommended.
- Hypertension, including hypertensive crisis, has been reported (30% of regorafenib-treated vs. 8% of placebo-treated). Monitoring is recommended. Interrupt or discontinue treatment for severe or uncontrolled hypertension.
- May cause fetal harm.
- Reversible Posterior Leukoencephalopathy Syndrome (RPLS) occurred in 1 of 1100 regorafenib-treated patients; discontinue if confirmed RPLS develops.
- Discontinue regorafenib if wound dehiscence occurs.
- Discontinue regorafenib before surgery and reconsider resuming if wound healing adequate.

Billing/Coding information

HCPCS Coding:

C9399	Unclassified drugs or biologicals (This code should only be used for drugs and biologicals that are approved by the FDA on or after January 1, 2004) (Hospital Outpatient Use ONLY)
J8999	Prescription drug, oral, chemotherapeutic, Not Otherwise Specified

COST

- AWP (November 2012): Stivarga 40mg oral tablets (84): $11,219.88
- AWP (May 2013): Stivarga 40mg oral tablets (84): $11,219.88
- AWP (January 2014): Stivarga 40mg oral tablets (84): $12,369.84

COMMITTEE APPROVAL

- November 2012

GUIDELINE UPDATE INFORMATION

November 2012	Prior Authorization and Coverage Policy created
May 2013	Prior Authorization and Coverage Policy updated
May 2014	Coverage policy updated

REFERENCES

- DRUGDEX®, accessed 11/02/12, 5/31/2013, 5/11/2014
- Product Information: Stivarga® (regorafenib) tablet, oral. Bayer HealthCare, Wayne, NJ, 2012, 2013.