UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 1098-13
Program	Prior Authorization/Notification
Medication	Stivarga® (regorafenib)
P&T Approval Date	11/2012, 4/2013, 7/2013, 11/2014, 11/2015, 6/2016, 6/2017, 6/2018, 6/2019, 6/2020, 6/2021, 6/2022, 6/2023, 6/2024
Effective Date	9/1/2024

1. Background:

Stivarga (regorafenib) 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 anti-VEGF 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 (Gleevec) and sunitinib malate (Sutent); hepatocellular carcinoma (HCC) who have been previously treated with Nexavar (sorafenib tosylate).[1]

The National Cancer Comprehensive Network (NCCN) also recommends additional use of Stivarga in colon cancer, rectal cancer, soft tissue sarcoma, hepatocellular carcinoma, biliary tract cancer, bone cancer, gastrointestinal stromal tumor (GIST), and glioblastoma.[2]

Coverage Information:

Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria[a]:

A. <u>Patients less than 19 years of age</u>

1. **Stivarga** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   Authorization will be issued for 12 months.

B. <u>Colorectal Cancer (CRC)</u>

1. **<u>Initial Therapy</u>**

   a. **Stivarga** will be approved based on **<u>all</u>** of the following criteria:

      (1) Diagnosis of advanced or metastatic colorectal cancer

-AND-

(2) History of failure, contraindication, or intolerance to treatment with **all** of the following:

(a) Oxaliplatin-based chemotherapy
(b) Irinotecan-based chemotherapy
(c) Fluoropyrimidine-based chemotherapy
(d) Anti-VEGF therapy -based chemotherapy

-AND-

(3) **One** of the following:

(a) Tumor is *RAS* mutant-type

-OR-

(b) **Both** of the following:

a. Tumor is *RAS* wild-type
b. History of failure, contraindication, or intolerance to anti-EGFR therapy [e.g., Erbitux (cetuximab), Vectibix (panitumumab)]

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Stivarga** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Stivarga therapy

Authorization will be issued for 12 months.

C. Soft Tissue Sarcoma (STS)

1. **Initial Therapy**

a. **Stivarga** will be approved based on **both** of the following criteria:

(1) Diagnosis of soft tissue sarcoma

-AND-

(2) **One** of the following

(a) Extremity/superficial trunk or head/neck that is non-adipocytic with advanced/metastatic disease with disseminated metastases
(b) Retroperitoneal/intra-abdominal that is non-adipocytic with recurrent unresectable or stage IV disease
(c) Advanced/metastatic pleomorphic rhabdomyosarcoma

(d) Angiosarcoma

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Stivarga** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Stivarga therapy

Authorization will be issued for 12 months.

D. Gastrointestinal Stromal Tumor (GIST)

1. **Initial Therapy**

a. **Stivarga** will be approved based on **all** of the following criteria:

(1) Diagnosis of gastrointestinal stromal tumor (GIST)

-AND-

(2) Disease is **one** of the following:

(a) Gross residual (R2 resection)
(b) Unresectable primary
(c) Tumor rupture
(d) Recurrent/metastatic

-AND-

(3) **One** of the following:

(a) SDH-deficient GIST

-OR-

(b) History of failure, contraindication, or intolerance to **both** of the following:

a. Imatinib mesylate (Gleevec)
b. Sutent (sunitinib malate)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Stivarga** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Stivarga therapy

Authorization will be issued for 12 months.

E. Hepatobiliary Cancers

1. **Initial Therapy**

a. **Stivarga** will be approved based on **one** of the following criteria:

(1) **Both** of the following:

(a) Diagnosis of **one** of the following:

a. Gallbladder cancer
b. Extrahepatic cholangiocarcinoma
c. Intrahepatic cholangiocarcinoma

-AND-

(b) Disease is **one** of the following:

a. Unresectable
b. Resected gross residual (R2)
c. Metastatic

-OR-

(2) **Both** of the following:

(a) Diagnosis of hepatocellular carcinoma

-AND-

(b) Used as subsequent-line therapy for disease progression

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Stivarga** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Stivarga therapy

Authorization will be issued for 12 months.

F. Bone Cancer

1. **Initial Therapy**

a. **Stivarga** will be approved based on **all** of the following criteria:

(1) Diagnosis of **one** of the following:

a. Osteosarcoma
b. Dedifferentiated chondrosarcoma
c. High grade undifferentiated pleomorphic sarcoma (UPS)
d. Ewing Sarcoma

-AND-

(2) Disease is **one** of the following:

a. Relapsed/refractory
b. Metastatic

-AND-

(3) Used as second-line therapy

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Stivarga** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Stivarga therapy

Authorization will be issued for 12 months.

G. Glioblastoma

1. **Initial Therapy**

a. **Stivarga** will be approved based on the following criteria:

(1) Diagnosis of recurrent or progressive glioblastoma

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Stivarga** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on Stivarga therapy

Authorization will be issued for 12 months.

H. NCCN Recommended Regimens

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a

Category of Evidence and Consensus of 1, 2A, or 2B

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Stivarga [package insert]. Whippany, NJ: Bayer Healthcare Pharmaceuticals, Inc. December 2020.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at https://www.nccn.org/professionals/drug_compendium/content/. Accessed May 2, 2024.

Program	Prior Authorization/Notification – Stivarga (regorafenib)
Change Control	
9/2014	Administrative change – Tried/Failed exemption for State of New Jersey removed.
11/2014	Annual review. Removed VEGF criteria from colorectal cancer and added disease progression. Added progressive to GIST. Updated background & references.
11/2015	Annual review. Revised CRC and GIST criteria. Increased authorization from 3 months to 12 month. Updated references.
6/2016	Annual review. Revised CRC criteria, removing KRAS/NRAS mutant requirement. Updated references.
6/2017	Annual review. Updated coverage criteria to include hepatocellular cancer to align with updated package insert. Updated background, formatting and references.
6/2018	Annual review. Updated references.
6/2019	Annual review. Updated criteria for colorectal cancer and soft tissue sarcoma based on NCCN guidelines. Updated references.
6/2020	Annual review. Updated criteria for hepatobiliary carcinoma according to NCCN guidelines. Addition of osteosarcoma and glioblastoma according to NCCN. Updated references.
6/2021	Annual review. Updated criteria for soft tissue sarcoma in accordance with NCCN. Updated references.
6/2022	Annual review. Revised criteria to remove indication for solitary fibrous tumor in accordance with NCCN. Updated references.
6/2023	Annual review. Updated background to include SDH-deficient GIST. Updated STS criteria. Updated hepatobiliary cancers criteria. Updated

	glioblastoma criteria. Updated references. Added state mandate footnote.
6/2024	Annual review. Added examples to anti-EGFR therapy. Removed "criteria" from all reauthorization sections. Separated gastrointestinal stromal tumor criteria from soft tissue sarcoma criteria and updated criteria per NCCN guideline. Added disease subtype criteria to hepatobiliary cancer section. Changed osteosarcoma section to bone cancer and added Ewing Sarcoma to criteria per NCCN guideline. Updated background and reference.