



PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Stivarga Prior Authorization Policy

- Stivarga® (regorafenib tablets – Bayer)

REVIEW DATE: 03/25/2026

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Stivarga, a kinase inhibitor, is indicated for the following uses:¹

- **Colorectal cancer**, metastatic, in patients 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-epidermal growth factor receptor (EGFR) therapy.
- **Gastrointestinal stromal tumor (GIST)**, locally advanced, unresectable, or metastatic in patients who have been previously treated with imatinib and sunitinib.
- **Hepatocellular carcinoma**, in patients who have been previously treated with sorafenib.

Guidelines

Stivarga is discussed in National Comprehensive Cancer Network (NCCN) guidelines:²⁻¹⁰

- **Appendiceal Neoplasms and Cancers:** NCCN guidelines (version 1.2026 – October 30, 2025) recommend Stivarga for second-line and subsequent therapy for disease that has progressed through all available regimens except Stivarga,

Fruzaqla® (fruquintinib capsules), or Lonsurf® (trifluridine and tipiracil tablets) with or without bevacizumab (category 2A).¹⁰

- **Biliary Tract Cancers:** NCCN guidelines (version 1.2026 – March 10, 2026) recommend Stivarga under “Other Recommended” regimen as a subsequent therapy for biliary tract cancers upon disease progression (category 2B).
- **Bone Cancer:** NCCN guidelines (version 2.2026 – December 19, 2025) recommend Stivarga as a single agent “Preferred Regimen” for second-line therapy for relapsed/refractory or metastatic disease for patients with osteosarcoma (category 1).³ Stivarga is also recommended under “Other Recommended Regimens” for second-line treatment (relapsed/refractory or metastatic disease) of Ewing sarcoma (category 2A) or mesenchymal chondrosarcoma (category 2B).
- **Colon Cancer and Rectal Cancer:** NCCN guidelines (colon cancer [version 1.2026 – March 5, 2026] and rectal cancer [version 1.2026 – March 5, 2026]) recommend Stivarga as subsequent therapy as a single agent for advanced or metastatic disease not previously treated with Stivarga in patients who have progressed through all available regimens except Stivarga, Fruzaqla® (fruquintinib capsules), or Lonsurf® (trifluridine and tipiracil tablets) with or without bevacizumab.^{5,6}
- **Gastrointestinal Stromal Tumors (GIST):** NCCN guidelines (version 1.2026 – January 13, 2026) recommend Stivarga as a “Preferred Regimen” in the third-line setting (category 1) for treatment of unresectable, progressive, or metastatic disease after single-agent therapy with imatinib or sunitinib [both category 1].⁷ If patient is intolerant to sunitinib, they can use Qinlock® (ripretinib tablets) instead as second-line therapy. Stivarga in combination with everolimus tablets is recommended as “Useful in Certain Circumstances” for unresectable, recurrent, or metastatic disease after failure on approved therapies. Stivarga is also recommended as “Useful in Certain Circumstances” for neoadjuvant therapy in succinate dehydrogenase (SDH)-deficient GIST that are resectable with significant morbidity. It is also recommended for unresectable, succinate dehydrogenase (SDH)-deficient disease (category 2A) in the first-line setting.
- **Hepatocellular Carcinoma:** NCCN guidelines (version 1.2026 – March 10, 2026) recommend Stivarga for subsequent treatment for patients with hepatocellular carcinoma (category 1).⁸
- **Soft Tissue Sarcoma:** NCCN guidelines (version 3.2026 – March 12, 2026) recommend Stivarga as a single-agent subsequent therapy for patients with non-adipocytic sarcoma with advanced/metastatic disease (retroperitoneal/intra-abdominal, extremity/body wall of head/neck), advanced/metastatic pleomorphic rhabdomyosarcoma, borderline/malignant phyllodes tumor of the breast, epithelioid hemangioendothelioma, or angiosarcoma (all category 2A).⁹
- **Uterine Neoplasms:** NCCN guidelines (version 2.2026 – November 14, 2025) recommend Stivarga as a second-line or subsequent therapy option for uterine sarcoma as one of the “Other Recommended Regimens” for patients with recurrent/metastatic, advanced or inoperable disease (category 2A).¹⁰

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Stivarga. All approvals are provided for the duration noted below.

- **Stivarga® (regorafenib tablets (Bayer)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

- 1. Colon, Rectal, or Appendiceal Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
 - A)** Patient is \geq 18 years of age; AND
 - B)** Patient has advanced or metastatic disease; AND
 - C)** Patient has been previously treated with a fluoropyrimidine; AND
Note: Examples include capecitabine and 5-fluorouracil [5-FU].
 - D)** Patient has been previously treated with oxaliplatin; AND
 - E)** Patient has been previously treated with irinotecan; AND

- 2. Gastrointestinal Stromal Tumor.** Approve for 1 year if the patient meets BOTH of the following (A and B):
 - A)** Patient is \geq 18 years of age; AND
 - B)** Patient meets ONE of the following (i or ii):
 - i.** Patient has tried BOTH of the following (a and b):
 - a)** Imatinib; AND
 - b)** Patient meets ONE of the following (1 or 2):
 - 1.** Patient has tried sunitinib; OR
 - 2.** Patient is intolerant to sunitinib and has tried Qinlock (ripretinib tablets);
OR
 - ii.** The medication is used for succinate dehydrogenase (SDH)-deficient disease.

- 3. Hepatocellular Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
 - A)** Patient is \geq 18 years of age; AND
 - B)** Patient has been previously treated with one systemic regimen.
Note: Examples of a systemic regimen include Tecentriq (atezolizumab intravenous infusion), bevacizumab, sorafenib, Lenvima (lenvatinib capsules), Opdivo (nivolumab intravenous infusion), Imjudo (tremelimumab-actl intravenous infusion), and Imfinzi (durvalumab intravenous infusion).

Other Uses with Supportive Evidence

- 4. Biliary Tract Cancers.** Approve for 1 year if the patient meets BOTH of the following (A and B):
 - A)** Patient is \geq 18 years of age; AND
 - B)** Patient has tried at least one systemic therapy.
Note: Examples of systemic therapy are cisplatin/gemcitabine, FOLFOX, capecitabine, and oxaliplatin.

- 5. Bone Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
 - A)** Patient is \geq 18 years of age; AND
 - B)** Patient has relapsed/refractory or metastatic disease; AND
 - C)** Patient has tried one systemic chemotherapy regimen; ANDS
Note: Examples of a systemic chemotherapy regimen contain one of more of the following: cisplatin, doxorubicin, methotrexate, ifosfamide, cyclophosphamide, etoposide, topotecan, irinotecan, vincristine, and temozolomide.
 - D)** Patient has ONE of the following (i, ii, or iii):
 - i.** Ewing sarcoma; OR
 - ii.** Mesenchymal chondrosarcoma; OR
 - iii.** Osteosarcoma.

6. Soft Tissue Sarcoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is \geq 18 years of age; AND

B) Patient has advanced or metastatic disease; AND

C) Patient has ONE of the following (i, ii, iii, iv, or v):

i. Borderline/malignant phyllodes tumor of the breast; OR

ii. Epithelioid hemangioendothelioma; OR

iii. Non-adipocytic sarcoma; OR

iv. Pleomorphic rhabdomyosarcoma; OR

v. Angiosarcoma.

7. Uterine Sarcoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

Note: Examples of uterine sarcoma include endometrial stromal sarcoma, undifferentiated uterine sarcoma, or uterine leiomyosarcomas.

A) Patient is \geq 18 years of age; AND

B) Patient has recurrent, advanced, inoperable, or metastatic disease; AND

C) Patient has tried at least one systemic regimen.

Note: Examples of systemic regimen include one or more of the following: doxorubicin, docetaxel, gemcitabine, ifosfamide, dacarbazine, epirubicin, or vinorelbine.

CONDITIONS NOT COVERED

- **Stivarga® (regorafenib tablets (Bayer)**

is(are) considered not medically necessary for ANY other use(s).

REFERENCES

1. Stivarga® tablets [prescribing information]. Whippany, NJ: Bayer; February 2026.
2. The NCCN Drugs and Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2026. Search term: regorafenib.
3. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2026 – December 19, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2026.
4. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 1.2026 – March 5, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2026.
5. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 1.2026 – March 5, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2026.
6. The NCCN Gastrointestinal Stromal Tumors Clinical Practice Guidelines in Oncology (version 1.2026 – January 13, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 22, 2026.
7. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 1.2026 – March 10, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 22, 2026.
8. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 3.2026 – March 12, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2026.
9. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 2.2026 – November 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed March 20, 2026.
10. The NCCN Appendiceal Neoplasms and Cancers Clinical Practice Guidelines in Oncology (version 1.2026 – October 30, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 20, 2026.
11. The NCCN Biliary Tract Cancers Clinical Practice Guidelines in Oncology (version 1.2026 – March 10, 2026). © 2026 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 22, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	Bone Cancer: Changed indication name from "Osteosarcoma" to "Bone Cancer". Added new criteria to approve for use in Ewing sarcoma or osteosarcoma. Added more examples of drugs, such as cyclophosphamide, etoposide, irinotecan, topotecan, vincristine, temozolomide, to the Note. Glioblastoma: While referring to disease description, added "or progressive" disease, in addition to recurrent disease.	03/06/2024

Annual Revision	<p>Gastrointestinal Stromal Tumor: Added criteria for Stivarga use as first-line therapy for succinate dehydrogenase (SDH)-deficient disease.</p> <p>Central Nervous System Tumors: Changed indication name from Glioblastoma. Added new criterion to approve for Glioblastoma or <i>H3</i>-mutated high-grade glioma.</p> <p>Uterine Sarcoma: This condition and criteria for approval were added to the policy.</p>	03/19/2025
Annual Revision	<p>Biliary Tract Cancers: Added new approval condition and criteria.</p> <p>Bone Cancer: Added mesenchymal chondrosarcoma as one of the options for approval.</p> <p>Central Nervous System Tumors: Removed condition of approval.</p> <p>Colon, Rectal, or Appendiceal Cancer: Approval indication was named as noted. Previously it was, "Colon, Rectal and Appendiceal Cancer". Moved examples of fluoropyrimidine to a Note. Removed option for approval for tumor that is wild-type <i>RAS</i> (<i>KRAS</i> wild-type and <i>NRAS</i> wild-type) along with options of trial of Erbitux or Vectibix or the tumor did not originate on the left side of colon. Also removed option for approval for tumor with <i>RAS</i> mutation (<i>KRAS</i> or <i>NRAS</i> mutation).</p> <p>Gastrointestinal Stromal Tumors: Removed option of trial for Ayvakit or Sprycel. Added option of trying Qinlock in patients intolerant to sunitinib. For succinate dehydrogenase-deficient disease removed requirement of first-line therapy.</p> <p>Soft Tissue Sarcoma: Added borderline/malignant phyllodes tumor of the breast and epithelioid hemangioendothelioma as options for approval.</p>	03/25/2026

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