

**Clinical Policy: Regorafenib (Stivarga)**

Reference Number: CP.PHAR.107

Effective Date: 12.01.12

Last Review Date: 05.26

Line of Business: Commercial, HIM/ICHRA, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

**Description**

Regorafenib (Stivarga<sup>®</sup>) is a kinase/vascular endothelial growth factor receptor (VEGFR) inhibitor.

**FDA Approved Indication(s)**

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-epidermal growth factor receptor (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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Stivarga is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria****A. Colorectal Cancer (must meet all):**

1. Diagnosis of advanced or metastatic CRC;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;
4. Previously treated with one of the following (a or b):
  - a. For proficient mismatch repair/microsatellite-stable (pMMR/MSS) disease: systemic chemotherapy (*see Appendix B*);
  - b. For deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation disease with ultra-hypermuted phenotype (e.g., tumor mutation burden  $>$  50 mut/Mb): checkpoint inhibitor immunotherapy (*see Appendix B*), unless ineligible;
5. Prescribed as a single agent;
6. For brand Stivarga requests, member must use generic regorafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;

7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 160 mg per day on days 1 to 21 of each 28-day cycle;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM/ICHRA** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**B. Gastrointestinal Stromal Tumor (must meet all):**

1. Diagnosis of GIST;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;
4. Disease is gross residual (R2 resection), unresectable (resectable if succinate dehydrogenase [SDH]-deficient), tumor rupture, recurrent, metastatic, or locally advanced;
5. Prescribed in one of the following ways (a or b):
  - a. As a single agent for one of the following (i or ii):
    - i. Disease previously treated with imatinib (Gleevec<sup>®</sup>)\* and sunitinib (Sutent<sup>®</sup>)\* (Qinlock<sup>®</sup>\* if member is intolerant to sunitinib), unless clinically significant adverse effects are experienced or all are contraindicated;
    - ii. SDH-deficient disease (off-label);
  - b. In combination with everolimus (off-label), and all of the following (i, ii, and iii):
    - i. Disease is gross residual (R2 resection), unresectable, tumor rupture, recurrent/progressive, or metastatic;
    - ii. Disease is imatinib-sensitive, and one of the following (1 or 2):
      - 1) KIT mutant;
      - 2) PDGFRA mutant (except PDGFRA exon 18 mutant GIST that is insensitive to imatinib);
    - iii. Member experienced disease progression on imatinib, sunitinib, Stivarga (as a single agent), and Qinlock\*;

*\*Prior authorization may be required for imatinib, sunitinib, Stivarga, and Qinlock*

6. For brand Stivarga requests, member must use generic regorafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 160 mg per day on days 1 to 21 of each 28-day cycle;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM/ICHRA** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**C. Hepatocellular Carcinoma (must meet all):**

1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;

4. Prescribed as a single agent;
5. Prescribed as a second or subsequent-line therapy (*see Appendix B*);
6. For brand Stivarga requests, member must use generic regorafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 160 mg per day on days 1 to 21 of each 28-day cycle;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM/ICHRA** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**D. Soft Tissue Sarcoma (off-label) (must meet all):**

1. Diagnosis of one of the following soft tissue sarcomas (a, b, c, d, e, or f):
  - a. Non-adipocytic sarcoma as subsequent therapy for advanced, metastatic, recurrent unresectable or recurrent stage IV disease;
  - b. Pleomorphic rhabdomyosarcoma as subsequent therapy for advanced or metastatic disease;
  - c. Angiosarcoma;
  - d. Borderline/malignant phyllodes tumor of the breast as subsequent therapy for unresectable primary, synchronous stage IV, recurrent, or metastatic malignant disease;
  - e. Epithelioid hemangioendothelioma;
  - f. For pediatric members only (age < 18 years): Recurrent or progressive rhabdomyosarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years, unless member has recurrent or progressive rhabdomyosarcoma;
4. Prescribed in one of the following ways (a or b):
  - a. As a single agent;
  - b. For pediatric rhabdomyosarcoma: In combination with vincristine and irinotecan;
5. For brand Stivarga requests, member must use generic regorafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 160 mg per day on days 1 to 21 of each 28-day cycle;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM/ICHRA** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**E. Bone Cancer (off-label) (must meet all):**

1. Diagnosis of one of the following bone cancers (a, b, c, d, or e):
  - a. Osteosarcoma;
  - b. Ewing sarcoma;
  - c. Mesenchymal chondrosarcoma;

- d. Dedifferentiated chondrosarcoma;
- e. High-grade undifferentiated pleomorphic sarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;
4. Request is for second-line therapy for relapsed/refractory, progressive, or metastatic disease (*see Appendix D*);
5. Prescribed as a single agent;
6. For brand Stivarga requests, member must use generic regorafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 160 mg per day on days 1 to 21 of each 28-day cycle;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM/ICHRA** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**F. Uterine Sarcoma (off-label) (must meet all):**

1. Diagnosis of one of the following uterine sarcomas (a, b, c, d, or e):
  - a. Endometrial stromal sarcoma;
  - b. Undifferentiated uterine sarcoma;
  - c. Adenosarcoma;
  - d. PEComa;
  - e. Leiomyosarcoma;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;
4. Disease is advanced, recurrent/metastatic, or inoperable;
5. Prescribed as a single agent;
6. For brand Stivarga requests, member must use generic regorafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 160 mg per day on days 1 to 21 of each 28-day cycle;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM/ICHRA** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**G. Appendiceal Cancer (off-label) (must meet all):**

1. Diagnosis of one of the following appendiceal cancers (a, b, or c):
  - a. Appendiceal adenocarcinoma;
  - b. Undifferentiated carcinoma not otherwise specified;
  - c. Goblet cell adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;

4. Prescribed as a single agent;
5. Member has progressed through all available regimens besides fruquintinib, regorafenib, or trifluridine/tipiracil with or without bevacizumab (*see Appendix B*);
6. Disease is recurrent, progressive, or extraperitoneal;
7. For brand Stivarga requests, member must use generic regorafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Request meets one of the following (a or b):\*
  - a. Dose does not exceed 160 mg per day on days 1 to 21 of each 28-day cycle;
  - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM/ICHRA** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

**H. Other diagnoses/indications** (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Stivarga for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Stivarga requests, member must use generic regorafenib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):\*
  - a. New dose does not exceed 160 mg per day on days 1 to 21 of each 28-day cycle;
  - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*\*Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**

**Medicaid/HIM/ICHRA** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

**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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CRC: colorectal cancer

dMMR/MSI-H: deficient mismatch  
repair/microsatellite instability-high

EGFR: epidermal growth factor receptor

FDA: Food and Drug Administration

GIST: gastrointestinal stromal tumor

HCC: hepatocellular carcinoma

pMMR/MSS: proficient mismatch  
repair/microsatellite-stable

POLE/POLD1: polymerase epsilon/delta

SDH: succinate dehydrogenase

VEGF: vascular endothelial growth factor

VEGFR: vascular endothelial growth factor  
receptor

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| Drug   | Dosing Regimen  | Dose Limit/<br>Maximum Dose |
|--|---|-----------------------------|
| <b>Colorectal Cancer (CRC): Examples of Systemic Chemotherapy and Checkpoint Inhibitors</b>                                |   |                             |
| 5-FU (fluorouracil)†   | Varies upon protocol and patient tolerance  | Varies                      |
| 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  |                             |
| Erbix® (cetuximab)   | Varies upon protocol and patient tolerance  |                             |
| Lonsurf® (trifluridine and tipiracil)  | 35 mg/m <sup>2</sup> /dose PO BID on Days 1 through 5 and Days 8 through 12 of each 28-day cycle  | 70 mg/m <sup>2</sup> /day   |
| Vectibix® (panitumumab)  | Varies upon protocol and patient tolerance  | Varies                      |
| Xeloda® (capecitabine)†  | 1250 mg/m <sup>2</sup> PO BID for 2 weeks followed by a 1-week rest period given as 3-week cycles | 2,500/m <sup>2</sup> /day   |
| Zaltrap® (ziv-aflibercept)   | Varies upon protocol and patient tolerance  | Varies                      |
| 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  |                             |
| Checkpoint inhibitors: Opdivo® (nivolumab) ± Yervoy® (ipilimumab), Keytruda® (pembrolizumab), Jemperli® (dostarlimab-gxly) | Varies  |                             |
| <b>Gastrointestinal Stromal Tumor (GIST)</b>   |   |                             |
| imatinib (Gleevec®)  | 400 mg PO daily up to 400 mg PO BID   | 800 mg/day                  |
| sunitinib (Sutent®)  | 50 mg PO daily for 4 weeks followed by 2 weeks off  | 87.5 mg/day                 |

| Drug  | Dosing Regimen  | Dose Limit/<br>Maximum Dose |
|---|-----------------|-----------------------------|
| Qinlock <sup>®</sup> (ripretinib)   | 150 mg PO daily | 150 mg/day                  |
| <b>Hepatocellular Carcinoma (HCC): Examples of Preferred First-line Systemic Therapy</b>  |                 |                             |
| Nexavar <sup>®</sup> (sorafenib)  | 400 mg PO BID   | 800 mg/day                  |
| Lenvima <sup>®</sup> (lenvatinib)   | 8-12 mg PO QD   | 12 mg/day                   |
| Tecentriq <sup>®</sup> (atezolizumab) + bevacizumab   | Varies          | Varies                      |
| <b>Appendiceal Cancer: Examples of Available Therapies</b>  |                 |                             |
| <u>Initial therapies:</u><br><ul style="list-style-type: none"> <li>• CAPEOX ± bevacizumab</li> <li>• FOLFIRI ± bevacizumab</li> <li>• FOLFIRINOX ± bevacizumab</li> <li>• FOLFOX ± bevacizumab</li> <li>• capecitabine ± bevacizumab</li> <li>• fluorouracil/leucovorin ± bevacizumab</li> </ul>   | Varies          | Varies                      |
| <u>Second-line and subsequent therapies:</u><br><ul style="list-style-type: none"> <li>• (FOLFIRI or irinotecan) ± bevacizumab</li> <li>• FOLFIRINOX ± bevacizumab</li> <li>• (CAPEOX or FOLFOX) ± bevacizumab</li> <li>• IROX ± bevacizumab</li> <li>• Biomarker-directed therapies: encorafenib, cetuximab, panitumumab, adagrasib, sotorasib, pertuzumab, tucatinib, trastuzumab, fam-trastuzumab deruxtecan-nxki, entrectinib, larotrectinib, repotrectinib, selpercatinib</li> </ul> | Varies          | Varies                      |
| <u>For any line of therapy (if dMMR/MSI-H or POLE/POLD1 mutation):</u> cemiplimab-rwlc, dostarlimab-gxly, ipilumab, nivolumab, pembrolizumab, penpulimab-kcqx, retifanlimab-dlwr, tislelizumab-jsgr, toripalimab-tpzi   | Varies          | Varies                      |

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

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

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

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): none reported
- Boxed warning(s): hepatotoxicity

*Appendix D: General Information*

- First-line therapies for osteosarcoma per NCCN:
  - Preferred regimens: cisplatin and doxorubicin, MAP (high-dose methotrexate, cisplatin, and doxorubicin)
  - Other recommended regimen: doxorubicin, cisplatin, ifosfamide, and high-dose methotrexate

**V. Dosage and Administration**

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

**VI. Product Availability**

Tablet: 40 mg

**VII. References**

1. Stivarga Prescribing Information. Whippany, NJ: Bayer HealthCare Pharmaceuticals. Inc.; February 2025. Available at [http://labeling.bayerhealthcare.com/html/products/pi/Stivarga\\_PI.pdf](http://labeling.bayerhealthcare.com/html/products/pi/Stivarga_PI.pdf). Accessed January 28, 2026.
2. Regorafenib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
3. Colon Cancer (Version 5.2026). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
4. Rectal Cancer (Version 4.2025). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
5. Soft Tissue Sarcoma (Version 1.2026). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
6. Hepatocellular Carcinoma (Version 2.2025). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
7. Bone Cancer (Version 2.2026). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
8. Gastrointestinal Stromal Tumors (Version 1.2026). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
9. Uterine Neoplasms (Version 2.2026). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
10. Appendiceal Neoplasms and Cancers (Version 1.2026). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed January 28, 2026.
11. Pediatric Soft Tissue Sarcoma (Version 1.2026). In: National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed March 4, 2026.

| Reviews, Revisions, and Approvals   | Date     | P&T Approval Date |
|---|----------|-------------------|
| 2Q 2022 annual review: modified commercial approval duration from length of benefit to “12 months or duration of request, whichever is less”; WCG.CP.PHAR.107 to be retired and approval durations consolidated to 6 months initial and 12 months continuation of therapy; per NCCN added criteria set for off-label use in glioblastoma; per template added generic oral oncology redirection if available language; clarified dosing in each criteria set to allow 160 mg per day on days 1 to 21 of each 28-day cycle; references reviewed and updated.  | 02.15.22 | 05.22             |
| Template changes applied to other diagnoses/indications.  | 09.30.22 |                   |
| 2Q 2023 annual review: for GIST per prescribing information and NCCN clarified previous treatment requiring imatinib <i>and</i> Sutent, added per NCCN Compendium off label uses in combination with everolimus and SDH mutation positive disease; for soft tissue sarcoma removed solitary fibrous tumor as this off-label use is no longer NCCN Compendium supported, for pleomorphic rhabdomyosarcoma clarified disease is advanced or metastatic, for non-adipocytic sarcoma clarified use is for subsequent therapy for advanced, metastatic, recurrent unresectable or recurrent stage IV disease; references reviewed and updated.   | 01.06.23 | 05.23             |
| 2Q 2024 annual review: for CRC, added that appendiceal carcinoma is a coverable diagnosis and specified the prior therapies required based on disease characteristics (pMMR/MSS, dMMR/MSI-H, POLE/POLD1) per NCCN recommendations; for GIST, added additional disease qualifiers, added that Qinlock should be used if intolerant to Sutent when requested for single agent therapy, and revised from SDH mutation-positive to SDH-deficient per NCCN; for soft tissue sarcoma, added that Stivarga should be used as subsequent therapy for pleomorphic rhabdomyosarcoma per NCCN; for bone cancers, added Ewing sarcoma, mesenchymal chondrosarcoma, dedifferentiated chondrosarcoma, and high-grade undifferentiated pleomorphic sarcoma as coverable cancer types and added an additional disease qualifier of progressive per NCCN; revised glioblastoma to central nervous system cancer and added additional coverable cancers (gliosarcoma, H3-mutated high-grade glioma) and disease qualifier of progressive per NCCN; references reviewed and updated. | 02.01.24 | 05.24             |
| 2Q 2025 annual review: for HCC, removed requirement for Child-Pugh class A disease per NCCN; added off-label criteria set for uterine sarcoma per NCCN; references reviewed and updated.  | 02.05.25 | 05.25             |
| 2Q 2026 annual review: per NCCN, revised the following – for CRC, specified that POLE/POLD1 mutation should have ultra-   | 03.30.26 | 05.26             |

| Reviews, Revisions, and Approvals   | Date | P&T Approval Date |
|---|------|-------------------|
| <p>hypermuted phenotype; for appendiceal carcinoma, moved out of CRC criteria to its own criteria set to reflect additional disease-specific recommendations for use; for GIST, allowed resectable disease if SDH-deficient, and for combination therapy with Stivarga+everolimus, added disease qualifiers, requirement that disease is imatinib-sensitive KIT or PDGFRA mutant, and requirement for prior use of Stivarga as a single agent; for soft tissue sarcoma, added borderline/malignant phyllodes tumor of the breast, epithelioid hemangioendothelioma, and pediatric rhabdomyosarcoma; for uterine sarcoma, corrected “PEGoma” to “PEComa”; removed off-label criteria for central nervous system cancers; for all indications for Medicaid and HIM/ICHRA, extended initial approval duration from 6 to 12 months; references reviewed and updated.</p> <p>Added ICHRA line of business.</p> |      |                   |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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