Clinical Policy: Avapritinib (Ayvakit)

Reference Number: CP.PHAR.454
Effective Date: 03.01.20
Last Review Date: 02.26
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Avapritinib (Ayvakit®) is a tyrosine kinase inhibitor.

FDA Approved Indication(s)

Ayvakit is indicated for the treatment of adults with:

- Unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations
- Advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL)
- Indolent Systemic Mastocytosis (ISM)

Limitation(s) of use: Ayvakit is not recommended for the treatment of patients with platelet counts of less than 50 X 10^9/L with AdvSM or ISM.

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® that Ayvakit is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of unresectable, recurrent, progressive, or metastatic GIST;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For brand Ayvakit requests, member must use generic avapritinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. One of the following (a or b):
   a. Documentation of a PDGFRA exon 18 D842V mutation;
   b. Member meets both of the following (i and ii):
      i. Documentation of a PDGFRA exon 18 mutation other than D842V;
      ii. Member meets one of the following (1 or 2);
      ** For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*

1) Failure of imatinib, Qinlock™, Sutent®, or Stivarga*, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization may be required for imatinib, Qinlock, Sutent, or Stivarga*
2) Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix D);*

6. Prescribed as single-agent therapy;
7. Request does not exceed health plan-approved quantity limit, if applicable;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 300 mg per day;
      ii. 1 tablet per day;
   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 – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Advanced Systemic Mastocytosis (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. ASM;
   b. SM-AHN;
   c. MCL;
2. Prescribed by or in consultation with an oncologist, allergist, or immunologist;
3. Age ≥ 18 years;
4. Prescribed as single-agent therapy;
5. For brand Ayvakit requests, member must use generic avapritinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Documentation of platelet count ≥ 50 x 10^9/L (≥ 50,000/mcL);
7. Request does not exceed health plan-approved quantity limit, if applicable;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 200 mg per day;
      ii. 1 tablet per day;
   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 – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Indolent Systemic Mastocytosis (must meet all):
1. Diagnosis of ISM;
2. Prescribed by or in consultation with an oncologist, allergist, or immunologist;
3. Age ≥ 18 years;
4. Prescribed as single-agent therapy;

5. For brand Ayvakit requests, member must use generic avapritinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Documentation of platelet count ≥ 50 x 10^9/L (≥ 50,000/mcL);
7. Request does not exceed health plan-approved quantity limit, if applicable;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 25 mg per day;
      ii. 1 tablet per day;
   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 – 12 months
Commercial – 12 months or duration of request, whichever is less

D. Myeloid/Lymphoid Neoplasm with Eosinophilia and Tyrosine Kinase Fusion Gene (off-label) (must meet all)**:**

1. Diagnosis of myeloid/lymphoid neoplasm with eosinophilia (MLNE) and FIP1L1-PDGFRA rearrangement;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. For brand Ayvakit requests, member must use generic avapritinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Documentation of a PDGFRA D842V mutation that is resistant to imatinib;
6. Request does not exceed health plan-approved quantity limit, if applicable;
7. Dose is within FDA maximum limit for any FDA-approved indication or 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 – 12 months
Commercial – 12 months or duration of request, whichever is less

E. 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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 Ayvakit for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Ayvakit requests, member must use generic avapritinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. Request does not exceed health plan-approved quantity limit, if applicable;
5. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed any of the following (i, ii, or iii):
      i. GIST: 300 mg (1 tablet) per day;
      ii. AdvSM: 200 mg (1 tablet) per day;
      iii. ISM: 25 mg (1 tablet) per day;
   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 – 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AdvSM: advanced systemic mastocytosis
ASM: aggressive systemic mastocytosis
FDA: Food and Drug Administration
GIST: gastrointestinal stromal tumor
ISM: indolent systemic mastocytosis
MCL: mast cell leukemia
MLNE: myeloid/lymphoid neoplasm with eosinophilia
NCCN: National Comprehensive Cancer Network
PDGFR: platelet-derived growth factor receptor
SM-AHN: systemic mastocytosis with an associated hematological neoplasm

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 Name	Dosing Regimen	Dose Limit/ Maximum Dose
imatinib mesylate (Gleevec®)	**GIST** 400 mg PO QD up to 400 mg BID [FDA label]	800 mg/day
Qinlock™ (ripretinib)	**GIST:** 150 mg PO QD	150 mg/day
Sutent® (sunitinib)	**GIST:** 50 mg PO QD	150 mg/day
Stivarga® (regorafenib)	**GIST:** 160 mg PO QD for the first 21 days of each 28-day cycle	160 mg/day

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

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: States with Regulations against Redirections in Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA
IN	Yes	For advanced, metastatic cancer and associated conditions
LA	Yes[≠]	For stage 4 advanced, metastatic cancer or associated conditions. [≠]Exception if clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy

State	Step Therapy Prohibited?	Notes
MS	Yes	For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	For stage 4 metastatic cancer and associated conditions
OK	Yes	For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes^	For advanced metastatic cancer, metastatic blood cancer, and associated conditions ^Exception if step therapy is for AB-rated generic equivalent, interchangeable biological product, or biosimilar product to the equivalent brand drug
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
GIST	300 mg PO QD	300 mg/day
AdvSM, including ASM, MCL, SM-AHN	200 mg PO QD	200 mg/day
ISM	25 mg PO QD	25 mg/day

VI. Product Availability

Tablets: 25 mg, 50 mg, 100 mg, 200 mg, 300 mg

VII. References

1. Ayvakit Prescribing Information. Cambridge, MA: Blueprint Medicines Corporation; November 2024. Available at: www.ayvakit.com. Accessed December 2, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 19, 2025.
3. National Comprehensive Cancer Network. Gastrointestinal Stromal Tumors (GISTs) Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed November 19, 2025.
4. National Comprehensive Cancer Network. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed November 19, 2025.
5. National Comprehensive Cancer Network. Systemic Mastocytosis Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed November 19, 2025.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: oral oncology generic redirection language added; NCCN recommended use for myeloid/lymphoid neoplasm	11.05.20	02.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
added; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.		
RT4: added criteria for newly approved indication of advanced systemic mastocytosis; added separate approval duration for legacy WCG Medicaid (WCG.CP.PHAR.454 to be retired).	07.01.21	08.21
1Q 2022 annual review: added documentation of platelet count ≥ 50 x 10^9/L (≥ 50,000/mcL) based on NCCN Compendia and prescribing information for systemic mastocystosis; references reviewed and updated.	09.13.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
Template changes applied to other diagnoses/indications.	09.28.22	
1Q 2023 annual review: Per NCCN Compendium, added "recurrent, progressive" GIST diagnosis option and requirement for single-agent therapy; added hematology specialist option to MLNE indication to align with other Centene policies with MLNE coverage criteria; removed legacy WellCare approval durations as these should align with Medicaid; references reviewed and updated.	10.25.22	02.23
RT4: added crtieria for newly approved indication of indolent systemic mastocytosis.	07.30.23	
1Q 2024 annual review: no significant changes; references reviewed and updated.	10.13.23	02.24
1Q 2025 annual review: added oncology bypass language to existing redirections; references reviewed and updated.	10.21.24	02.25
1Q 2026 annual review: for GIST, added Qinlock, Sutent, and Stivarga as examples of prior lines of therapy; for MLNE and FIP1L1-PDGFRA, revised criteria from "failure of imatinib" to "documentation of PDGFRA D842 mutation that is resistant to imatinib"; added step therapy bypass for IL HIM per IL HB 5395; Medicaid/HIM line of business, extended initial approval duration from 6 to 12 months for this maintenance medication for a chronic condition; added request does not exceed health plan-approved quantity limit, if applicable; references reviewed and updated.	11.21.24	02.26
For Appendix E, added state IN and revised language and exception for Tennessee.	04.09.26	

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.