BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

AYVAKIT™ (avapritinib) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for AYVAKIT (avapritinib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an oncologist

Indication
- Treatment of unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring platelet derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutation

ORIGINAL EFFECTIVE DATE: 02/18/2021 | ARCHIVE DATE: | LAST REVIEW DATE: 05/21/2026 | LAST CRITERIA REVISION DATE: 05/16/2024

- Advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM AHN), and mast cell leukemia (MCL), with platelet count greater than 50 × 10^9/L
- Indolent systemic mastocytosis (ISM) with platelet count greater than 50 × 10^9/L
- Other oncologic direct treatment uses listed in National Comprehensive Cancer Network (NCCN) Guidelines with Category 1 or 2A evidence and consensus

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- GIST or ISM indication: Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2
- ADvSM indication: Eastern Cooperative Oncology Group (ECOG) performance status 0 to 3

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No severe renal impairment (creatinine clearance less than or equal to 29 mL/min)
- No concomitant use with strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, etc.)

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (including platelet count and creatinine clearance)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualification
- Continues to be seen by a physician specializing in or in consultation with an oncologist

Clinical Response
- No evidence of disease progression or unacceptable toxicity

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Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No significant adverse drug effects such as:
  - Intracranial hemorrhage (e.g., subdural hematoma, cerebral hemorrhage)
  - Severe cognitive impairment, dizziness, sleep disorders, mood disorders, speech disorders, hallucinations
- No severe renal impairment (creatinine clearance less than or equal to 29 mL/min)
- No concomitant use with strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, etc.)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications
2. Off-Label Use of Cancer Medications

Description:

Ayvakit (avapritinib) 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; for the treatment of patients with Advanced Systemic Mastocytosis (AdvSM) including patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL) whose platelet counts are greater than 50 ×

10^9/L; and for the treatment of Indolent Systemic Mastocytosis (ISM) whose platelet counts are greater than 50 × 10^9/L

Ayvakit (avapritinib) is a potent tyrosine kinase inhibitor that blocks PDGFRA; it targets PDGFRA and PDGFR D842 mutants, as well as KIT exon 11, 11/17, and 17 mutants. Certain PDGFRA and KIT mutations may result in autophosphorylation and constitutive activation of these receptors, which may contribute to tumor cell proliferation. Ayvakit (avapritinib) inhibits autophosphorylation of KIT D816V and PDGFRA D842V, which are mutants associated with resistance to approved kinase inhibitors.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

NCCN recommendation definitions:
Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status (also known as Zubrod Score)	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Symptomatic, fully ambulatory, restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Symptomatic, ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Symptomatic, capable of only limited self-care, confined to bed or chair more than 50% of waking hours but not bedridden
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*

Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

Activities of daily living (ADL):

Instrumental ADL:

Prepare meals, shop for groceries or clothes, use the telephone, manage money, etc.

Self-care ADL:

Bathe, dress and undress, feed self, use the toilet, take medications, not bedridden

Resources:

Ayvakit (avapritinib) product information, revised by Blueprint Medicines Corporation. 11-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed January 29, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Gastrointestinal Stromal Tumors (GISTs) Version 1.2026 – Updated January 13, 2026. Available at https://www.nccn.org. Accessed March 10, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Systemic Mastocytosis Version 1.2026 – Updated January 22, 2026. Available at https://www.nccn.org. Accessed March 10, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Version 1.2026 – Updated October 03, 2025. Available at https://www.nccn.org. Accessed March 10, 2026.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions