BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**2/18/2021**
LAST REVIEW DATE:	**5/19/2022**
LAST CRITERIA REVISION DATE:	**5/19/2022**
ARCHIVE DATE:	

AYVAKIT™ (avapritinib) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Ayvakit (avapritinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Treatment for unresectable or metastatic Gastrointestinal Stromal Tumor (GIST) harboring platelet-derived growth factor receptor alpha (PDGFRA) exon 18-mutation, including PDGFRA D842V mutations

     b. 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

     c. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  4. Individual has an Eastern Co-operative Oncology Group (ECOG) performance status (PS) of ONE of the following:
     a. For GIST: ECOG PS 0-2
     b. For AdvSM: ECOG PS 0-3

  5. Individual does not have severe renal impairment (CrCl $\leq$ 29 mL/min)

  6. Individual does not have severe hepatic impairment (total bilirubin > 3x ULN and any AST)

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Ayvakit (avapritinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

  2. Individual's condition responded while on therapy
     a. Response is defined as **ONE** of the following:
        i. No evidence of disease progression
        ii. Documented evidence of efficacy, disease stability and/or improvement

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3. Individual has been adherent with the medication

4. Individual has not developed any significant adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Intracranial hemorrhage including subdural hematoma and cerebral hemorrhage
        ii. Severe cognitive impairment, dizziness, sleep disorders, mood disorders, speech disorders, and hallucinations

5. Individual does not have severe renal impairment (CrCl ≤ 29 mL/min)

6. Individual does not have severe hepatic impairment (total bilirubin > 3x ULN and any AST)

7. There are no significant interacting drugs

Renewal duration: 12 months

- 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. It is also indicated 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.

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:

NCCN recommendation definitions:
Category 1:

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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	

Resources:

Ayvakit (avapritinib) product information, revised by Blueprint Medicines Corporation. 06-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 10, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Gastrointestinal Stromal Tumors (GISTs) Version 1.2022 – Updated January 21, 2022. Available at https://www.nccn.org. Accessed May 10, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Systemic Mastocytosis Version 1.2022 – Updated April 14, 2022. Available at https://www.nccn.org. Accessed May 10, 2022.

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