PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Oral) – Ayvakit Prior Authorization Policy
- Ayvakit® (avapritinib tablets – Blueprint Medicines)

REVIEW DATE: 04/29/2026

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

Ayvakit, a kinase inhibitor, is indicated for the following uses in adults:[1]

- **Gastrointestinal stromal tumor (GIST),** unresectable or metastatic, harboring a platelet-derived growth factor receptor alpha (*PDGFRA*) exon 18 mutation, including *PDGFRA* D842V mutations.
- **Advanced systemic mastocytosis,** including patients with aggressive systemic mastocytosis, systemic mastocytosis with an associated hematological neoplasm, and mast cell leukemia. Limitation of use: Ayvakit is not recommended for the treatment of patients with advanced systemic mastocytosis with platelet counts of < 50 x 10^9/L.
- **Indolent systemic mastocytosis**.
  Limitation of use: Ayvakit is not recommended for the treatment of patients with indolent systemic mastocytosis with platelet counts of < 50 x 10^9/L.

Guidelines

Ayvakit is discussed in the guidelines from National Comprehensive Cancer Network (NCCN):[3]

- **GIST:** NCCN guidelines (version 1.2026 – January 13, 2026) note that Ayvakit is one of the primary treatment options for GIST with *PDGFRA* exon 18 mutation, including *PDGFRA* D842V mutations (category 2A).[2] Imatinib is a category 1 recommended option for primary treatment. The guidelines note that most mutations in the *PDGFRA* gene are associated with a response to imatinib, with the notable exception of *PDGFRA* D842V mutation. Ayvakit (for *PDGFRA* exon 18 mutation that is insensitive to imatinib, including the *D842V* mutation) is recommended for neoadjuvant therapy for resectable GISTs with significant morbidity (category 2A). Ayvakit is listed as an additional option after failure on approved therapies. The approved therapies are imatinib and Ayvakit (for *PDGFRA* mutation) as first-line therapy; sunitinib or Qinlock® (ripretinib tablets) [for patients intolerant to second-line sunitinib]; or dasatinib (for *PDGFRA* exon 18 mutations that are insensitive to imatinib [including the *PDGFRA D842V* mutation]) as second-line therapy; Stivarga® (regorafenib tablets) as third-line therapy; and Qinlock as fourth-line therapy.
- **Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions:** NCCN guidelines (version 1.2026 – October 3, 2025) recommend Ayvakit for the treatment of myeloid/lymphoid neoplasms with eosinophilia and FIP1L1::PDGFRA rearrangement if PDGFRA D842V mutation is found which is resistant to imatinib (category 2A).[4] If this mutation is identified, a clinical trial with Ayvakit is preferred (if available), rather than off-label use.
- **Systemic Mastocytosis:** NCCN guidelines (version 1.2026 – April 9, 2026) recommend single-agent Ayvakit if the patient has platelets ≥ 50 x 10^9/L as "preferred" treatment of aggressive systemic mastocytosis, symptomatic indolent systemic mastocytosis, systemic mastocytosis with an associated neoplasm, and mast cell leukemia with or without an associated hematologic neoplasm (category 2A).[5]

POLICY STATEMENT

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

Ayvakit® (avapritinib tablets - Blueprint Medicines) 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. **Gastrointestinal Stromal Tumor.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND

B) Patient meets ONE of the following (i or ii):
- **i.** The tumor is positive for platelet-derived growth factor receptor alpha (*PDGFRA*) exon 18 mutation; OR
  Note: *PDGFRA* exon 18 mutation includes *PDGFRA* D842V mutations.
- **ii.** Patient has tried ALL of the following (a, b, c, and d):
  - **a)** Imatinib; AND
  - **b)** Sunitinib; AND
  - **c)** Stivarga (regorafenib tablets); AND
  - **d)** Qinlock (ripretinib tablets).

2. **Systemic Mastocytosis.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has a platelet count ≥ 50 x 10^9/L (≥ 50,000/mcL); AND
   C) Patient meets ONE of the following (i or ii):
   - **i.** Patient has indolent systemic mastocytosis; OR
   - **ii.** Patient has ONE of the following subtypes of advanced systemic mastocytosis (a, b, or c):
     - **a)** Aggressive systemic mastocytosis; OR
     - **b)** Systemic mastocytosis with an associated hematological neoplasm; OR
     - **c)** Mast cell leukemia.

Other Uses with Supportive Evidence

3. **Myeloid/Lymphoid Neoplasms.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has eosinophilia; AND
   C) The tumor is positive for platelet-derived growth factor receptor alpha (*PDGFRA*) D842V mutation.

CONDITIONS NOT COVERED

Ayvakit® (avapritinib tablets - Blueprint Medicines) is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Ayvakit® tablets [prescribing information]. Cambridge, MA: Blueprint Medicines Corporation; November 2024.
2. 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 April 22, 2026.
3. The NCCN Drugs & Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 22, 2026. Search term: avapritinib.
4. The NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Clinical Practice Guidelines in Oncology (version 1.2026 – October 3, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 22, 2026.

5. The NCCN Systemic Mastocytosis Clinical Practice Guidelines in Oncology (version 2.2026 – April 9, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 22, 2026.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	05/15/2024
Annual Revision	No criteria changes	05/07/2025
Annual Revision	The name of the policy was changed to as listed. Previously, it was called Oncology – Ayvakit PA. **Gastrointestinal Stromal Tumor:** Sprycel (dasatinib tablets) was removed from the requirement which stated "patient has tried one of sunitinib or Sprycel (dasatinib tablets).	04/29/2026