# PRIOR AUTHORIZATION POLICY

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

**REVIEW DATE:** 05/15/2024

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## 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. Ayvakit is not recommended for the treatment of patients with advanced systemic mastocytosis with platelet counts of $< 50 \times 10^9$/L.
- **Indolent systemic mastocytosis**.
  Ayvakit is not recommended for the treatment of patients with indolent systemic mastocytosis with platelet counts of $< 50 \times 10^9$/L.

## Guidelines

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

- **GIST:** NCCN guidelines (version 1.2024 – March 8, 2024) 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 listed as a preferred regimen 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 Sprycel® (dasatinib tablets; 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 1.2024 – December 21, 2023) 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 3.2024 – April 24, 2024) recommend single-agent Ayvakit if the patient has platelets $\geq 50 \times 10^9$/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.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ayvakit is recommended in those who meet one of the following criteria:

### 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)** One of sunitinib or Sprycel (dasatinib tablets); 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 RECOMMENDED FOR APPROVAL

Coverage of Ayvakit is not recommended in the following situations:

**1.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## REFERENCES

1. Ayvakit® tablets [prescribing information]. Cambridge, MA: Blueprint Medicines Corporation; May 2023.
2. The NCCN Gastrointestinal Stromal Tumors Clinical Practice Guidelines in Oncology (version 1.2024 – March 8, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 13, 2024
3. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 13, 2024. Search term: avapritinib.
4. The NCCN Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions Clinical Practice Guidelines in Oncology (version 1.2024 – December 21, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 13, 2024.
5. The NCCN Systemic Mastocytosis Clinical Practice Guidelines in Oncology (version 3.2024 – April 24, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 13, 2024.