PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 05/31/2023

INSTRUCTIONS FOR USE

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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. Patients should be selected for treatment with Ayvakit based on the presence of a *PDGFRA* exon 18 mutation; an FDA-approved test for the detection of this mutation is not currently available.
- **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 less than 50 x 10^9/L.
- **Indolent systemic mastocytosis**.

Guidelines

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

- **GIST:** NCCN guidelines (version 1.2023 – March 13, 2023) 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 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® (ripretinib tablets) as fourth-line therapy.

- **Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions:** NCCN guidelines (version 1.2023 – May 19, 2023) note that since Ayvakit targets *PDGFRA* exon 18 mutation, it may have a role for use in patients with *FIP1L1-PDGFRA* positive myeloid/lymphoid neoplasms with eosinophilia harboring *PDGFRA* D842V mutation, 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 1.2023 – May 24, 2023) recommend single-agent Ayvakit if the patient has platelets ≥ 50 x 10^9/L as preferred treatment of aggressive 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 the following criteria (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following criteria (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 each 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 the following criteria (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 criteria (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 the following criteria (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 experimental, investigational, or unproven for ANY other use(s).

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 1.2023 – March 13, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2023.
3. The NCCN Drugs & Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2023. Search term: avapritinib.
4. The NCCN Myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase fusion genes Clinical Practice Guidelines in Oncology (version 1.2023 – May 19, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2023.
5. The NCCN Systemic Mastocytosis Clinical Practice Guidelines in Oncology (version 1.2023 – May 24, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Gastrointestinal Stromal Tumor:** An option of trial of Sprycel (dasatinib tablets) was added to trial of Sutent (sunitinib capsules).	07/13/2022

	Myeloid/Lymphoid Neoplasms: The wording "with eosinophilia" was removed from the condition of approval and added as a criteria requirement.	
Early Annual Revision	**Systemic mastocytosis:** Criterion was added a patient who has indolent systemic mastocytosis based on new FDA approval.	05/31/2023