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# 5.21.139

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2026
<b>Subsection:</b>	Antineoplastic Agents	<b>Original Policy Date:</b>	February 7, 2020
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**Last Review Date:** March 6, 2026

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## Ayvakit

### Description

#### Ayvakit (avapritinib)

#### Background

Ayvakit (avapritinib) is a tyrosine kinase inhibitor that targets platelet-derived growth factor receptor alpha (PDGFRA) and PDGFRA D842 mutants as well as multiple KIT exon 11, 11/17 and 17 mutants. Certain mutations in PDGFRA and KIT can result in the autophosphorylation and constitutive activation of these receptors which can contribute to tumor cell proliferation. Other potential targets for Ayvakit include wild type KIT, PDGFRB, and CSFR1. Ayvakit inhibits the autophosphorylation of KIT D816V and PDGFRA D842V, mutants associated with resistance to approved kinase inhibitors. This could contribute to its inhibition of tumor cell proliferation (1).

#### Regulatory Status

FDA-approved indications: Ayvakit is a kinase inhibitor indicated for: (1)

- **Gastrointestinal Stromal Tumor (GIST)**
  - the treatment of adults with unresectable or metastatic GIST harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.
- **Advanced Systemic Mastocytosis (AdvSM)**
  - the treatment of adult patients with AdvSM. AdvSM includes patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL).
  - Limitations of Use: Ayvakit is not recommended for the treatment of patients with AdvSM with platelet counts of less than  $50 \times 10^9/L$ .

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- Indolent Systemic Mastocytosis (ISM)
  - the treatment of adult patients with ISM.
  - Limitations of Use: Ayvakit is not recommended for the treatment of patients with ISM with platelet counts of less than  $50 \times 10^9/L$ .

Ayvakit has warnings regarding intracranial hemorrhage, cognitive effects, and embryo-fetal toxicity. Serious intracranial hemorrhage may occur in patients treated with Ayvakit. Ayvakit should be discontinued if intracranial hemorrhage of any grade occurs. A broad spectrum of cognitive adverse reactions can occur in patients receiving Ayvakit. Ayvakit can cause fetal harm when administered to pregnant women. Females and males of reproductive potential should be advised to use effective contraception during treatment with Ayvakit and for 6 weeks after the final dose (1).

In patients with AdvSM, a platelet count must be performed prior to initiating therapy; Ayvakit is not recommended in patients with AdvSM with platelet counts less than  $50 \times 10^9/L$ . Following treatment initiation, platelet counts must be performed every 2 weeks for the first 8 weeks regardless of baseline platelet count. After 8 weeks of treatment, monitor platelet counts every 2 weeks (or more frequently as clinically indicated) if values are less than  $75 \times 10^9/L$ , every 4 weeks if values are between 75 and  $100 \times 10^9/L$ , and as clinically indicated if values are greater than  $100 \times 10^9/L$  (1).

The safety and effectiveness of Ayvakit in pediatric patients have not been established (1).

## Related policies

Nexavar, Qinlock, Sprycel, Stivarga, Sutent, Votrient

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Ayvakit may be considered **medically necessary** if the conditions indicated below are met.

Ayvakit may be considered **investigational** for all other indications.

## Prior-Approval Requirements

**Age** 18 years of age or older

## Diagnoses

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Patient must have **ONE** of the following:

1. Unresectable or metastatic gastrointestinal stromal tumor (GIST)
  - a. Platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations
2. Advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL)
  - a. Platelet count  $\geq 50 \times 10^9/L$
3. Indolent Systemic Mastocytosis (ISM)
  - a. Platelet count  $\geq 50 \times 10^9/L$

**AND ALL** of the following:

- a. Prescriber agrees to monitor for intracranial hemorrhage and CNS adverse reactions
- b. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Ayvakit and for 6 weeks after the last dose
- c. Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Ayvakit and for 6 weeks after the last dose

## Prior – Approval *Renewal* Requirements

**Age** 18 years of age or older

### Diagnoses

Patient must have **ONE** of the following:

1. Gastrointestinal stromal tumor (GIST)
  - a. **NO** disease progression or unacceptable toxicity
2. Advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL)
  - a. Platelet count  $\geq 50 \times 10^9/L$
  - b. **NO** disease progression or unacceptable toxicity
3. Indolent Systemic Mastocytosis (ISM)
  - a. Platelet count  $\geq 50 \times 10^9/L$

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**AND ALL** of the following:

- Prescriber agrees to monitor for intracranial hemorrhage and CNS adverse reactions
- Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Ayvakit and for 6 weeks after the last dose
- Males with female partners of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Ayvakit and for 6 weeks after the last dose

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Quantity** 90 tablets per 90 days

**Duration** 12 months

### Prior – Approval *Renewal* Limits

Same as above

## Rationale

### Summary

Ayvakit (avapritinib) is a tyrosine kinase inhibitor indicated for the treatment of gastrointestinal stromal tumor (GIST), advanced systemic mastocytosis (AdvSM), and indolent systemic mastocytosis (ISM). Ayvakit has warnings regarding intracranial hemorrhage, cognitive effects, and embryo-fetal toxicity. Females and males of reproductive potential should be advised to use effective contraception during treatment with Ayvakit and for 6 weeks after the final dose. The safety and effectiveness of Ayvakit in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Ayvakit while maintaining optimal therapeutic outcomes.

### References

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1. Ayvakit [package insert]. Cambridge, MA; Blueprint Medicines Corporation; November 2024.
2. NCCN Drugs & Biologics Compendium<sup>®</sup> Avapritinib 2026. National Comprehensive Cancer Network, Inc. Accessed on January 21, 2026.

### Policy History

Date	Action
February 2020	Addition to PA
March 2020	Annual review
September 2020	Annual review
March 2021	Annual editorial review
July 2021	Addition of indication: advanced systemic mastocytosis (AdvSM)
September 2021	Annual review and reference update
March 2022	Annual review and reference update
March 2023	Annual review and reference update
June 2023	Per PI update, added indication of indolent systemic mastocytosis (ISM)
September 2023	Annual review and reference update
March 2024	Annual review and reference update
September 2024	Annual review and reference update
December 2024	Annual review and reference update
March 2025	Annual review and reference update
June 2025	Annual review and reference update
March 2026	Annual review and reference update

### Keywords

**This policy was approved by the FEP<sup>®</sup> Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.**