BlueCross BlueShield
Federal Employee Program

AYVAKIT
(avapritinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

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 x 10^9/L.
- 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 x 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 x 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 x 10^9/L, every 4 weeks if values are between 75 and 100 x 10^9/L, and as clinically indicated if values are greater than 100 x 10^9/L (1).

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

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

1. Ayvakit [package insert]. Cambridge, MA; Blueprint Medicines Corporation; November 2024.
2. NCCN Drugs & Biologics Compendium® Avapritinib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 16, 2025.