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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Antineoplastic Agents	**Original Policy Date:**	February 7, 2020
Subject:	Ayvakit	**Page:**	1 of 4

Last Review Date: March 12, 2021

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 indication: Ayvakit is a kinase inhibitor indicated for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations (1).

Intracranial hemorrhage and various central nervous system (CNS) adverse reactions can occur in patients treated with Ayvakit. Ayvakit should be withheld and then resumed at a reduced dosage upon resolution, or permanently discontinued based on severity (1).

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).

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** in patients that are 18 years of age or older with gastrointestinal stromal tumor (GIST) and if the conditions indicated below are met.

Ayvakit may be considered **investigational** in patients who are less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have 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

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 final 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 final dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Gastrointestinal stromal tumor (GIST)

AND ALL of the following:

a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to monitor for intracranial hemorrhage and CNS adverse reactions
c. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Ayvakit and for 6 weeks after the final dose
d. 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 final 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 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. 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; January 2020.

Policy History

Date	Action
February 2020	Addition to PA
March 2020	Annual review
September 2020	Annual review
March 2021	Annual editorial review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.