UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

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| Program Number | 2024 P 1308-6 |
| Program | Prior Authorization/Notification |
| Medication | Ayvakit® (avapritinib) |
| P&T Approval Date | 2/2020, 2/2021, 9/2021, 9/2022, 7/2023, 7/2024 |
| Effective Date | 10/1/2024 |

**1. Background:**

Ayvakit (avapritinib) 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. Ayvakit is indicated for the treatment of adult patients with advanced systemic mastocytosis (AdvSM), including patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), and mast cell leukemia (MCL). Ayvakit is not recommended for the treatment of patients with AdvSM with platelet counts of less than 50 x $10^9$/L. Ayvakit is also indicated for the treatment of indolent systemic mastocytosis (ISM). Ayvakit is not recommended for the treatment of patients with ISM with platelet counts of less than 50 X $10^9$/L.

The National Comprehensive Cancer Network (NCCN) also recommends use as single agent therapy as continued treatment for limited progression of GIST, for unresectable, recurrent, or metastatic disease after failure on approved therapies. Additionally, NCCN recommends use for treatment of GIST with PDGFRA exon 18 mutations, including the PDGFRA D842V mutation, for disease that is unresectable, recurrent, metastatic, gross residual disease (R2 resection), or as treatment for resectable disease with significant morbidity that is insensitive to imatinib.

The NCCN also recommends use of Ayvakit for treatment for myeloid/lymphoid neoplasms with eosinophilia and FIP1L1-PDGFRA rearrangement if PDGFRA D842V mutation is found which is resistant to imatinib.

**Coverage Information:**

Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

**2. Coverage Criteria[a]:**

**A. <u>Patients less than 19 years of age</u>**

1. **Ayvakit** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   **Authorization will be issued for 12 months.**

**B. Gastrointestinal Stromal Tumor (GIST)**

1. **Initial Authorization**

a. **Ayvakit** will be approved based on **all** of the following criteria:

(1) Diagnosis of gastrointestinal stromal tumor (GIST)

**-AND-**

(2) **One** of the following:

(a) Patient has unresectable, recurrent, or metastatic disease after failure on approved therapies (e.g., imatinib, sunitinib, dasatinib, regorafenib, ripretinib)

**-OR-**

(b) **Both** of the following:

i. Disease is **one** of the following:
- Unresectable
- Resectable with significant morbidity
- Metastatic
- Recurrent
- Limited progression
- Gross residual disease (R2 resection)
- Residual disease with significant morbidity

**-AND-**

ii. Presence of a platelet-derived growth factor receptor alpha (PDGFRA) exon mutation, including 18 D842V mutation

**Authorization will be issued for 12 months.**

2. **Reauthorization**

a. **Ayvakit** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on **Ayvakit** therapy

**Authorization will be issued for 12 months.**

**C. Myeloid/Lymphoid Neoplasms**

1. **Initial Authorization**

a. **Ayvakit** will be approved based on **all** of the following criteria:

(1) Diagnosis of myeloid/lymphoid neoplasms with eosinophilia

**-AND-**

(2) Presence of a FIP1L1-PDGFRA rearrangement

**-AND-**

(3) Presence of a PDGFRA D842V mutation

**Authorization will be issued for 12 months.**

2. **Reauthorization**

a. **Ayvakit** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on **Ayvakit** therapy

**Authorization will be issued for 12 months.**

**D. Systemic Mastocytosis**

1. **Initial Authorization**

a. **Ayvakit** will be approved based on **both** of the following criteria:

(1) Diagnosis of one of the following:

(a) Advanced systemic mastocytosis
(b) Aggressive systemic mastocytosis
(c) Systemic mastocytosis with an associated hematologic neoplasm
(d) Mast cell leukemia
(e) Indolent systemic mastocytosis

**-AND-**

(2) Platelet count is greater than or equal to $50 \times 10^9/L$

**Authorization will be issued for 12 months.**

2. **Reauthorization**

a. **Ayvakit** will be approved based on the following criterion:

(1) Patient does not show evidence of progressive disease while on **Ayvakit** therapy

**Authorization will be issued for 12 months.**

**E. NCCN Recommended Regimens**

The drug has been recognized for treatment of the cancer indication by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B

**Authorization will be issued for 12 months.**

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

**3. Additional Clinical Rules:**

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

**4. References:**


1. Ayvakit [package insert]. Cambridge, MA: Blueprint Medicines Corporation, May 2023.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at https://www.nccn.org/compendia-templates/compendia/nccn-compendia . Accessed on May 29, 2024.


| Program | Prior Authorization/Notification – Ayvakit (avapritinib) |
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| **Change Control** | |
| 2/2020 | New program. |
| 2/2021 | Annual review. Updated criteria for GIST according to NCCN recommendations. Added criteria for Myeloid/Lymphoid neoplasms according to NCCN recommendations. |
| 9/2021 | Added criteria for systemic mastocytosis according to label and NCCN recommendations. |
| 9/2022 | Annual review. Updated GIST criteria per label and NCCN recommendations. Added state mandate footnote. Updated reference. |
| 7/2023 | Annual review. Added criteria for indolent systemic mastocytosis according to label. Updated GIST criteria following resection per NCCN recommendations. |
| 7/2024 | Annual review. Updated wording of systemic mastocytosis criteria per NCCN without change to clinical intent. Updated references. |