Ayvakit® (avapritinib)
(Oral)

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I. Length of Authorization

Coverage is provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Ayvakit 25 mg tablet: 1 tablet per day
- Ayvakit 50 mg tablet: 1 tablet per day
- Ayvakit 100 mg tablet: 1 tablet per day
- Ayvakit 200 mg tablet: 1 tablet per day
- Ayvakit 300 mg tablet: 1 tablet per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- Gastrointestinal Stromal Tumors (GIST) and Myeloid/Lymphoid Neoplasms with Eosinophilia: 300 mg per day
- Advanced Systemic Mastocytosis (AdvSM): 200 mg per day
- Indolent Systemic Mastocytosis (ISM): 25 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1,2]

- Used as a single agent; **AND**
- Patient will avoid concomitant therapy with all of the following:
  - Coadministration with moderate or strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, bosentan, efavirenz, etc.); **AND**
  - Coadministration with strong CYP3A inhibitors (e.g., itraconazole, ketoconazole, clarithromycin, etc.); **AND**

- Coadministration with moderate CYP3A inhibitors (e.g., aprepitant, fluconazole, ciprofloxacin, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

Gastrointestinal Stromal Tumors (GIST) † ‡ Φ [1-5]

- Patient has the presence of platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutations (including the PDGFRA D842V mutation); **AND**
  - Patient's PDGFRA exon 18 mutations are insensitive to imatinib; **AND**
    - Used as first-line therapy for gross residual (R2 resection), unresectable primary, recurrent, or metastatic disease OR tumor rupture; **OR**
    - Used as first-line therapy as continued treatment for limited progression; **OR**
    - Used as neoadjuvant therapy for resectable disease with significant morbidity; **OR**
  - Patient has gross residual (R2 resection), unresectable primary, recurrent, or metastatic disease OR tumor rupture; **AND**
    - Disease has progressed on prior treatment with at least ONE of the following: imatinib, sunitinib, regorafenib, or ripretinib

Advanced Systemic Mastocytosis (AdvSM) † ‡ Φ [1]

- Patient has a confirmed diagnosis of one of the following: aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL); **AND**
- Patient has a platelet count ≥ 50 X 10^9/L obtained within the last 4 weeks and is not receiving platelet transfusions

Indolent Systemic Mastocytosis (ISM) † Φ [1]

- Patient has a platelet count ≥ 50 X 10^9/L obtained within the last 4 weeks

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes ‡ [2,6]

- Patient has eosinophilia and FIP1L1-PDGFRA gene rearrangement; **AND**
- Patient has the presence of a D842V mutation in the PDGFRA gene that is resistant to imatinib

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious intracranial hemorrhages, cognitive effects, photosensitivity reactions, etc.; **AND**

Advanced Systemic Mastocytosis (AdvSM) [10]

- Disease stabilization or improvement as evidenced by a complete remission, partial remission, or clinical improvement by bone marrow biopsy or extracutaneous organ biopsy, serum tryptase level, CBC, or resolution of organ damage

Indolent Systemic Mastocytosis (ISM) † Φ [1]

- Disease response as evidenced by stabilization or improvement in signs and symptoms such as abdominal pain, nausea, diarrhea, spots, itching, flushing, bone pain, fatigue, dizziness, headache, brain fog, etc.

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes [6]

- Disease response as evidenced by at least one of the following:
  - Decrease in spleen size or improvements in other myelofibrosis symptoms (such as weakness, fatigue, cough, dyspnea, myalgias, angioedema, rash, fever, rhinitis, etc.)
  - Stabilization or improvement as evidenced by a complete response [CR] (i.e. morphologic, cytogenetic or molecular complete response CR), complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

Gastrointestinal Stromal Tumors (GIST)

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration [1,6,11,12,14]

Indication	Dose
Gastrointestinal Stromal Tumors (GIST) and Myeloid/Lymphoid Neoplasms with Eosinophilia	Administer 300 mg orally once daily on an empty stomach, at least 1 hour before or 2 hours after a meal, until disease progression or unacceptable toxicity.
Advanced Systemic Mastocytosis (AdvSM)	Administer 200 mg orally once daily on an empty stomach, at least 1 hour before or 2 hours after a meal, until disease progression or unacceptable toxicity.
Indolent Systemic Mastocytosis (ISM)	Administer 25 mg orally once daily on an empty stomach, at least 1 hour before or 2 hours after a meal.

VI. Billing Code/Availability Information

HCPCS Code:

- J8999: Prescription drug, oral, chemotherapeutic, not otherwise specified
- C9399: Unclassified drugs or biologicals

NDC:

- Ayvakit 25 mg tablet: 72064-0125-xx
- Ayvakit 50 mg tablet: 72064-0150-xx
- Ayvakit 100 mg tablet: 72064-0110-xx
- Ayvakit 200 mg tablet: 72064-0120-xx
- Ayvakit 300 mg tablet: 72064-0130-xx

VII. References

1. Ayvakit [package insert]. Cambridge, MA; Blueprint Medicines Corporation.; May 2023. Accessed June 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) avapritinib. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2023.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastrointestinal Stromal Tumors (GISTs) Version 1.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed June 2023.
4. Gebreyohannes YK, Wozniak A, Zhai ME, et al. Robust Activity of Avapritinib, Potent and Highly Selective Inhibitor of Mutated KIT, in Patient-derived Xenograft Models of Gastrointestinal Stromal Tumors. Clin Cancer Res. 2019 Jan 15;25(2):609-618. doi: 10.1158/1078-0432.CCR-18-1858. Epub 2018 Oct 1.
5. Heinrich MC, Jones RL, von Mehren M, et al. Clinical activity of avapritinib in ≥ fourth-line (4L+) and PDGFRA Exon 18 gastrointestinal stromal tumors (GIST). Journal of Clinical Oncology 2019 37:15_suppl, 11022-11022.
6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 1.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed June 2023.
7. Heinrich MC, Jones RL, von Mehren M, et al. Clinical Response to avapritinib by RECIST and Choi Criteria in ≥4th Line and PDGFRA exon 18 gastrointestinal stromal tumors (GIST) [abstract]. Connective Tissue Oncology Society Annual Meeting, Tokyo, Japan. 2019:Abstract 3027631.
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10. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Systemic Mastocytosis Version 1.2023. National Comprehensive Cancer Network, 2023. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed June 2023.
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12. Gotlib J, Reiter A, Radia DH, et al. Efficacy and safety of avapritinib in advanced systemic mastocytosis: interim analysis of the phase 2 PATHFINDER trial. Nat Med. 2021 Dec;27(12):2192-2199. doi: 10.1038/s41591-021-01539-8.
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14. Heinrich MC, Jones RL, von Mehren M, et al. Avapritinib in advanced PDGFRA D842V-mutant gastrointestinal stromal tumour (NAVIGATOR): a multicentre, open-label, phase 1 trial. Lancet Oncol. 2020 Jul;21(7):935-946. doi: 10.1016/S1470-2045(20)30269-2.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C49.A0	Gastrointestinal stromal tumor unspecified site
C49.A1	Gastrointestinal stromal tumor of esophagus
C49.A2	Gastrointestinal stromal tumor of stomach
C49.A3	Gastrointestinal stromal tumor of small intestine
C49.A4	Gastrointestinal stromal tumor of large intestine
C49.A5	Gastrointestinal stromal tumor of rectum
C49.A9	Gastrointestinal stromal tumor of other sites
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C94.30	Mast cell leukemia not having achieved remission
C94.31	Mast cell leukemia, in remission
C94.32	Mast cell leukemia, in relapse
C94.8	Other specified leukemias
C94.80	Other specified leukemias not having achieved remission
C94.81	Other specified leukemias, in remission
C94.82	Other specified leukemias, in relapse
C95.1	Chronic leukemia of unspecified cell type

C95.10	Chronic leukemia of unspecified cell type not having achieved remission
C95.11	Chronic leukemia of unspecified cell type, in remission
C95.12	Chronic leukemia of unspecified cell type, in relapse
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
C96.20	Malignant mast cell neoplasm, unspecified
C96.21	Aggressive systemic mastocytosis
C96.22	Mast cell sarcoma
C96.29	Other malignant mast cell neoplasm
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
D47.02	Systemic mastocytosis
Z85.831	Personal history of malignant neoplasm of soft tissue

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC