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| **Clinical Policy Title:** | avapritinib |
| **Policy Number:** | RxA.626 |
| **Drug(s) Applied:** | Ayvakit™ |
| **Original Policy Date:** | 05/21/2020 |
| **Last Review Date:** | 01/17/2022 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

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.
An FDA-approved test to detect exon 18 mutations is not currently available.

Avapritinib is also indicated for the treatment of adult patients with AdvSM (Advanced Systemic Mastocytosis). 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.

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| avapritinib (Ayvakit™) | PDGFRA 18 mutated GIST | 300 mg orally once daily, (1 hour before or 2 hours after meals). Continue treatment until disease progression or unacceptable toxicity. Do not make up missed doses within 8 hours of the next scheduled dose. | 300 mg orally once daily |
| | AdvSM | 200 mg orally once daily, (1 hour before or 2 hours after meals). Continue treatment until disease progression or unacceptable toxicity. | 200 mg orally once daily |

## Dosage Forms

- Tablets: 25 mg, 50 mg, 100 mg, 200 mg and 300 mg

## Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

**I. Initial Approval Criteria**

**A. Gastrointestinal stromal tumor (GIST)** (must meet all):

1. Diagnosis of unresectable or metastatic GIST;
2. Member has one of the following (a or b):
   a. PDGFR exon 18 mutations indicating the PDGGFRA D842V mutation;
   b. PDGFR exon 18 mutation other than D842V and were insensitive to imatinib unless contraindicated or clinically significant adverse effects are experienced;
3. Member ≥ 18 years;
4. Prescribed by or in consultation with an oncologist;
5. Prescribed as monotherapy;
6. Dose does not exceed 300 mg orally once daily;

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**B. Advanced Systemic Mastocytosis (AdvSM)** (must meet all):

1. Individual has one of the following subtypes of advanced systemic mastocytosis (a, b or c):
   a. Aggressive systemic mastocytosis (ASM);
   b. Systemic mastocytosis with an associated hematological neoplasm (SM-AHN);
   c. Mast cell leukemia (MCL);
2. Member ≥ 18 years;
3. Individual has a platelet count ≥ 50 x $10^9$/L ( ≥ 50,000/mcL);
4. Prescribed by or in consultation with an oncologist;
5. Dose does not exceed 200 mg orally once daily;

**Approval Duration**
**Commercial**: 6 months
**Medicaid**: 6 months

**C. Myeloid/Lymphoid neoplasms with eosinophilia and tyrosine kinase fusion genes** (Off-label) (must meet all):

1. Diagnosis of FIP1L1-PDGFRA -positive myeloid/lymphoid neoplasms with eosinophilia;
2. Member has PDGFRA D842V mutation and had a failure of imatinib therapy, unless contraindicated or clinically significant adverse effects are experienced;
3. Member ≥ 18 years;
4. Prescribed by or in consultation with an oncologist;
5. Dose is FDA-approved or supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence);

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months

**II. Continued Therapy Approval**

**A. All indications listed in Section I** (must meet all):

1. Member is currently receiving avapritinib that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (i.e. absence of disease progression);
3. Meets one of the following (a, b or c):
   a. GIST: Dose does not exceed 300 mg orally once daily;
   b. AdvSM: Dose does not exceed 200 mg orally once daily;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence);

**Approval Duration**
**Commercial:** 12 months
**Medicaid:** 12 months

## III. Appendices

**APPENDIX A: Abbreviation/Acronym Key**
FDA: Food and Drug Administration
GIST: Gastrointestinal Stromal Tumor
NCCN: National Comprehensive Cancer Network
PDGFRA: Platelet-Derived Growth Factor Receptor Alpha
MCL: Mast cell leukemia
ASM: Aggressive systemic mastocytosis

**APPENDIX B: Therapeutic Alternatives**
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| imatinib mesylate (Gleevec®) | 400 mg orally once daily up to 400 mg twice a day | 800 mg/day |

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

**APPENDIX C: Contraindications/Boxed Warnings**
- Contraindication(s):
  - None Reported.

- Boxed Warning(s):
  - None Reported.

**APPENDIX D: General Information**
The NCCN soft tissue sarcoma guidelines have been updated to add avapritinib as a treatment option:
- As a treatment option for unresectable/metastatic GIST with PDGFRA exon 18 mutation, including PDGFRA D842V mutations (NCCN category 2A recommendation);
- As a treatment option following persistent gross residual disease (R2 resection) in patients with PDGFRA D842V mutation (NCCN category 2A recommendation);
- As a continued treatment option for limited progression for unresectable/metastatic GIST with PDGFRA exon 18 mutation, including PDGFRA D842V mutations (NCCN category 2A recommendation; and

- As a treatment option for metastatic/unresectable GIST with disease progression after therapy with imatinib, sunitinib and regorafenib (NCCN category 2A recommendation)

**References**


1. Ayvakit™ (avapritinib) tablets, for oral use prescribing information (per FDA). Cambridge, MA: Blueprint Medicines Corporation; June 2021, Available at: https://ayvakit.com/. Accessed December 8, 2021.
2. Avapritinib. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, March 17. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed December 8, 2021.
3. Avapritinib. Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed December 8, 2021.
4. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed December 8, 2021.
5. Morgan, J. Tyrosine kinase inhibitor therapy for advanced gastrointestinal stromal tumors. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, Ma, 2020. Accessed with subscription at: http://uptodate.com. Accessed December 8, 2021.
6. Morgan, J; Chandrajit, P; Duensing, A; Keedy, VL. Epidemiology, classification, clinical presentation, prognostic features and diagnostic work-up of gastrointestinal tumors (GIST). In: UpToDate, Post, TW (Ed), UpToDate, Waltham, Ma, 2020. Accessed with subscription at: http://uptodate.com. Accessed December 8, 2021.
7. National Comprehensive Cancer Network Drugs and Biologics Compendium. Accessed with subscription at: http://www.nccn.org. Accessed December 8 ,2021.
8. National Comprehensive Cancer Network Guidelines. Soft Tissue Sarcoma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed December 8, 2021.
9. National Comprehensive Cancer Network Guidelines. Gastrointestinal tumors (GIST). Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed December 8, 2021.
10. National Comprehensive Cancer Network Guidelines. Systemic Mastocytosis Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed December 8, 2021.


| Review/Revision History | Review/Revised Date | P&T Approval Date |
|---|---|---|
| Policy established. | 05/21/2020 | 05/21/2020 |
| Policy was reviewed:<br>1) Continuation therapy criteria II.A.1. added l"isted in this policy;"<br>2) Updated Appendix B: added Gleevac as therapeutic alternative and removed previous drugs as those drugs were not present on ESM.<br>3) References were updated<br>4) Added initial therapy approval criteria for myeloid/lymphoid neoplasms and updated continued therapy criteria to reflect the same. | 02/15/2021 | 03/09/2021 |

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| Policy was reviewed:<br>1) Background: Updated to include:<br>a. New indication: Advanced Systemic Mastocytosis (AdvSM).<br>b. 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.<br>2) Dosing Information, Indication: Updated to include new indication AdvSM.<br>3) Dosage Forms: Updated dosage form from Tablets: 100 mg, 200 mg and 300 mg to Tablets: 25 mg, 50 mg, 100 mg, 200 mg and 300 mg.<br>4) Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy.<br>5) Initial Approval Criteria, 1.B: Updated to include approval criteria for indication AdvSM.<br>6) Continued Therapy Approval, II.A.3.b: Updated to include new dosing criteria AdvSM: Dose does not exceed 200 mg orally once daily.<br>7) Appendix A: Updated to include abbreviations MCL & ASM.<br>8) Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only"<br>9) References were reviewed and updated. | 12/08/2021 | 01/17/2021 |