Clinical Policy Title:	avapritinib
Policy Number:	RxA.626
Drug(s) Applied:	Ayvakit™
Original Policy Date:	05/21/2020
Last Review Date:	03/09/2021
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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
avapritinib (Ayvakit™)	PDGFRA 18 mutated GIST	300mg 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.	300mg daily

Dosage Forms

- Tablets: 100mg, 200mg and 300mg

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.

I. Initial Approval Criteria

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

1. Diagnosis of unresecttable 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 is 18 years of age or older;

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. 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 is 18 years old or greater;
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 or b):
   a. Dose does not exceed 300 mg orally once daily;
   b. 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

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 Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None

- Boxed Warning(s):
  - None

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

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2. Avapritinib. Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed February 6,2021.
3. AYVAKIT™ (avapritinib) tablets, for oral use prescribing information (per FDA). Cambridge, MA: Blueprint Medicines Corporation;August 2020, Available at: https://ayvakit.com/. Accessed February 6,2021.
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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 February 6,2021.
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7. National Comprehensive Cancer Network Drugs and Biologics Compendium. Accessed with subscription at: http://www.nccn.org. Accessed February 6,2021.
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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	05/21/2020	05/21/2020
Policy was reviewed: 1) Continuation therapy criteria	02/15/2021	03/09/2021

II.A.1. added l”isted in this policy;” 2) Updated Appendix B: added Gleevac as therapeutic alternative and removed previous drugs as those drugs were not present on ESM. 3) References were updated 4) Added initial therapy approval criteria for myeloid/lymphoid neoplasms and updated continued therapy criteria to reflect the same.		