Clinical Policy: Avapritinib (Ayvakit)
Reference Number: ERX.SPA.372
Effective Date: 03.01.20
Last Review Date: 02.21
Line of Business: Commercial, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Avapritinib (Ayvakit™) is a tyrosine kinase inhibitor.

FDA Approved Indication(s)
Ayvakit is 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Ayvakit is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Gastrointestinal Stromal Tumor (must meet all):
      1. Diagnosis of unresectable or metastatic GIST;
      2. Prescribed by or in consultation with an oncologist;
      3. Age ≥ 18 years;
      4. For Ayvakit request, medical justification supports inability to use avapritinib, if available (e.g., contraindications to excipients);
      5. One of the following (a or b):
         a. Documentation of a PDGFRA exon 18 D842V mutation;
         b. Member meets both of the following (i and ii):
            i. Documentation of a PDGFRA exon 18 mutation other than D842V;
            ii. Failure of imatinib, unless contraindicated or clinically significant adverse effects are experienced;
            *Prior authorization may be required for imatinib
      6. Request meets one of the following (a or b):*
         a. Dose does not exceed 300 mg (1 tablet) per day;
         b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
         *Prescribed regimen must be FDA-approved or recommended by NCCN

   Approval duration:
   Medicaid – 6 months
   Commercial – Length of Benefit

   B. Myeloid/Lymphoid Neoplasm with Eosinophilia and Tyrosine Kinase Fusion Gene (must meet all):
      1. Diagnosis of myeloid/lymphoid neoplasm with eosinophilia (MLNE) and FIP1L1-PDGFRA rearrangement;
      2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For Ayvakit request, medical justification supports inability to use avapritinib, if available (e.g., contraindications to excipients);
5. Member meets both of the following (i and ii):
   a. Documentation of a PDGFRA D842V mutation;
   b. Failure of imatinib*, unless contraindicated or clinically significant adverse effects are experienced;
   *Prior authorization may be required for imatinib
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).*
   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration:
Medicaid – 6 months
Commercial – Length of Benefit

C. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
A. All Indications in Section I (must meet all):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Ayvakit for a covered indication and has received this medication for at least 30 days;
   2. Member is responding positively to therapy;
   3. For Ayvakit request, medical justification supports inability to use avapritinib, if available (e.g., contraindications to excipients);
   4. If request is for a dose increase, request meets one of the following (a or b):*
      a. New dose does not exceed 300 mg (1 tablet) per day;
      b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration:
Medicaid – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GIST: gastrointestinal stromal tumor
MLNE: myeloid/lymphoid neoplasm with eosinophilia
NCCN: National Comprehensive Cancer Network
PDGFR: platelet-derived growth factor receptor
Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>imatinib mesylate (Gleevec®)</td>
<td>GIST 400 mg PO QD up to 400 mg BID [FDA label]</td>
<td>800 mg/day</td>
</tr>
<tr>
<td></td>
<td>MLNE 100-400 mg PO QD [NCCN]</td>
<td></td>
</tr>
</tbody>
</table>

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
None reported

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIST</td>
<td>300 mg PO QD</td>
<td>300 mg/day</td>
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</table>

VI. Product Availability

Tablets: 100 mg, 200 mg, 300 mg

VII. References


Reviews, Revisions, and Approvals

<table>
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<tr>
<th>Policy created</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tr>
<td></td>
<td>01.21.20</td>
<td>02.20</td>
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<tr>
<td>1Q 2021 annual review: oral oncology generic redirection language added; NCCN recommended use for myeloid/lymphoid neoplasm added; references reviewed and updated.</td>
<td>11.05.20</td>
<td>02.21</td>
</tr>
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</table>

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.