Clinical Policy: Imatinib (Gleevec)
Reference Number: ERX.SPA.75
Effective Date: 03.01.14
Last Review Date: 05.18

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

Description
Imatinib mesylate (Gleevec®) is a kinase inhibitor.

FDA Approved Indication(s)
Gleevec is indicated:
- For the treatment of newly diagnosed adult and pediatric patients with Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
- For the treatment of patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
- For the treatment of adult patients with relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL)
- For the treatment of pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
- For the treatment of adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements
- For the treatment of adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown
- For the treatment of adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown
- For the treatment of adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
- For the treatment of patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
- For the treatment of adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST

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.

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

I. Initial Approval Criteria
   A. FDA Labeled Indications (must meet all):
      1. One of the following diagnoses - and mutation if applicable:
         a. CML: Ph/BCR-ABL1-positive;
         b. ALL: Ph/BCR-ABL1-positive;
         c. MDS/MPD: PDGFR-positive;
         d. ASM: D816V c-KIT-negative or c-Kit mutational status unknown;
         e. HES or CEL;
      2. Prescribed by or in consultation with an oncologist or hematologist;
      3. Age ≥ 18 years if diagnosis is MDS/MPD, ASM, DFSP, or GIST;
      4. Dose does not exceed one of the following (a, b, or c):
         a. CML, DFSP, GIST: 800 mg/day;
         b. ALL: 600 mg/day;
c. MDS/MPD, ASM, HES or CEL: 400 mg/day.

**Approval duration: Length of Benefit**

**B. Off-Label Indications** (must meet all):
1. One of the following diagnoses - and mutation if applicable:
   a. Central nervous system metastasis with history of Gleevec treatment for non-small cell lung cancer that is EGFR-positive;
   b. AIDS-related Kaposi sarcoma;
   c. Chordoma (a type of bone cancer);
   d. Melanoma: KIT-positive;
   e. Desmoid tumor (i.e., aggressive fibromatosis);
   f. Pigmented villonodular synovitis/tenosynovial giant cell tumor;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age $\geq$ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 800 mg/day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 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 Gleevec for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed (i, ii, or iii):
      i. CML, DFSP, GIST: 800 mg/day;
      ii. ALL: 600 mg/day;
      iii. MDS/MPD, ASM, HES or CEL: 400 mg/day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: Length of Benefit**

**A. 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**
- ALL: acute lymphoblastic leukemia
- ASM: aggressive systemic mastocytosis
- CEL: chronic eosinophilic leukemia
- CML: chronic myeloid leukemia
Appendix B: Therapeutic Alternatives
Not applicable

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose*</th>
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</thead>
<tbody>
<tr>
<td>CML</td>
<td>Adult: 400-600 mg/day PO for chronic phase 600-800 mg/day PO for accelerated phase or blast crisis (800 mg given as 400 BID) Pediatric: 340 mg/m²/day PO for chronic phase</td>
<td>Adult: 800 mg/day Pediatric: 600 mg/day</td>
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<tr>
<td>ALL</td>
<td>Adult: 600 mg/day PO for relapsed/refractory Ph+ ALL Pediatric: 340 mg/m²/day PO in combination with chemotherapy for newly diagnosed Ph+ ALL</td>
<td>Adult: 600 mg/day Pediatric: 600 mg/day</td>
</tr>
<tr>
<td>MDS/MPD</td>
<td>Adult: 400 mg/day PO</td>
<td>Adult: 400 mg/day</td>
</tr>
<tr>
<td>ASM</td>
<td>Adult: 100-400 mg/day PO</td>
<td>Adult: 400 mg/day</td>
</tr>
<tr>
<td>HES/CEL</td>
<td>Adult: 100-400 mg/day PO</td>
<td>Adult: 400 mg/day</td>
</tr>
<tr>
<td>DESP</td>
<td>Adult: 800 mg/day PO</td>
<td>Adult: 800 mg/day</td>
</tr>
<tr>
<td>GIST</td>
<td>Adult: 400-800 mg/day PO for metastatic or unresectable GIST (800 mg given as 400 BID) 400 mg/day PO or adjuvant GIST</td>
<td>Adult: 800 mg/day; 400 mg/day for adjuvant GIST</td>
</tr>
</tbody>
</table>

*Co-administration with strong CYP3A4 inducers may require an increased dose beyond that listed in the table. Examples of strong CYP3A4 inducers include dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampacin, phenobarbital.

VI. Product Availability
Tablet: 100 mg, 400 mg

VII. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created.</td>
<td>02.14</td>
<td>03.14</td>
</tr>
<tr>
<td>Policy converted to new template.</td>
<td>08.16</td>
<td>09.16</td>
</tr>
<tr>
<td>Added NCCN compendium disease indication and recommendations.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Removed age restrictions, requests for documentation, and safety criteria.</td>
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<tr>
<td>Added max dose criteria for FDA labeled indications without NCCN indication overlap. Changed all durations to 3 months for initial and 6 months for re-auth.</td>
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<tr>
<td>CML- removed monitoring requirements for re-auth.</td>
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</tbody>
</table>
### Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Change Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIST- added option for Kit-positive disease.</td>
<td></td>
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<tr>
<td>HES/CEL- added criteria about FIP1L1-PDGFRα fusion kinase.</td>
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<tr>
<td>Converted to new template.</td>
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<tr>
<td>Age added for MDS/MPD, ASM, HES/CEL, DESP, GIST.</td>
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<tr>
<td>CML NCCN: 1) “myeloid” is inserted to describe blast phase in “As a single agent for accelerated or myeloid blast phase CML”; 2) “In combination with steroids as primary treatment for CML in lymphoid blast phase” is added; 3) continued use of Gleevec in cases of where members are not candidates for other drugs or in cases of poor or partial response is deleted with the assumption that these cases would fall under the continuation criteria; 4) “for relapse” is deleted from “post stem cell transplant therapy” to incorporate history of responsive CML.</td>
<td>07.17</td>
<td>08.17</td>
</tr>
<tr>
<td>ALL NCCN: 1) Gleevec may or may not be used with various regimens as part of induction/consolidation therapy – regimens are therefore deleted; 2) “post stem cell transplant” is added under maintenance therapy.</td>
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<tr>
<td>HES/CEL: “FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) or HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown” is removed as members may or may not have the mutation or the mutation status may be unknown;</td>
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<tr>
<td>GIST NCCN: 1) “resectable disease with risk of significant morbidity” is removed from under primary/preoperative therapy and assumed to fall under unresectable disease; 2) “ongoing treatment for progressive disease” is added.</td>
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<tr>
<td>Maximum dosing added for CML, ALL, DESP, GIST and dose exception due to CYP inducers is added to all indications. Dosing guidance added for off-label use.</td>
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<tr>
<td>All off-label uses are referred to the off-label use policy</td>
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<tr>
<td>Approval periods lengthened from 3/6 to 6/12 months.</td>
<td></td>
<td></td>
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<tr>
<td>References updated.</td>
<td></td>
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</tr>
<tr>
<td>2Q 2018 annual review: NCCN and FDA approved uses summarized for improved clarity; specialist involvement in care added; continuity of care statement added; off-label CNS/NSCLC and Kaposi sarcoma added; approval durations increased to length of benefit; references reviewed and updated.</td>
<td>02.13.18</td>
<td>05.18</td>
</tr>
</tbody>
</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.

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