Clinical Policy: Imatinib (Gleevec)

Reference Number: ERX.SPMN.116
Effective Date: 03/14
Last Review Date: 09/16 Revision Log

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that imatinib (Gleevec®) is **medically necessary** when one of the following criteria is met:

I. Initial Approval Criteria

A. Chronic Myeloid Leukemia (must meet all):

1. Diagnosis of chronic myeloid leukemia (CML);
2. CML is Philadelphia chromosome positive (Ph+) or BCR-ABL1 positive;
3. Member meets a or b:
   a. FDA approved use (i or ii):
      i. Newly diagnosed CML in chronic phase;
      ii. Blast, accelerated or chronic phase CML after failure of interferon-alpha therapy;
   b. Off-label NCCN recommended use (any of the following):
      i. Gleevec will be used at high dose following poor response to standard-dose Gleevec, in members who are not candidates for alternate-generation tyrosine kinase inhibitors (nilotinin, dasatinib, etc.);
      ii. Gleevec will be used at high dose following partial cytogenetic response, (BCR-ABL1 transcript levels ≤10% but >1%) or in cytogenetic relapse at 12 months and beyond, after standard-dose Gleevec in members who are not candidate for alternate-generation tyrosine kinase inhibitors (nilotinin, dasatinib, etc.) or omacetaxine;
      iii. As a single agent for accelerated or blast phase CML;
      iv. In combination with induction chemotherapy followed by hematopoietic stem cell transplant for blast phase CML;
      v. Post-transplant treatment in the presence of relapse.

Approval duration: 3 months

B. Acute Lymphoblastic Leukemia (must meet all):

1. Diagnosis of Ph+ acute lymphoblastic leukemia (ALL);
2. Member meets a or b:
   a. FDA approved use (i or ii):
      i. Relapsed or refractory Ph+ ALL;
      ii. Newly diagnosed Ph+ ALL in combination with chemotherapy;
   b. Off-label NCCN recommended use (i or ii):
      i. Induction/consolidation therapy in combination with (a or b):
         a) Vincristine containing regimen and other therapies;

b) Corticosteroids for members aged ≥ 65 years or with substantial comorbidities;

ii. Maintenance therapy in combination with vincristine and prednisone with or without methotrexate and mercaptopurine.

Approval duration: 3 months

C. Gastrointestinal Stromal Tumors (must meet all):

1. Diagnosis gastrointestinal stromal tumors (GIST);
2. Member meets a or b:
   a. FDA approved use (i or ii):
      i. Disease is Kit (CD117) positive, unresectable and/or metastatic;
      ii. Adjuvant treatment following resection in Kit (CD117) positive GIST;
   b. Off-label NCCN recommended use (any of the following):
      i. Primary or preoperative treatment for unresectable, recurrent, metastatic or resectable disease with risk of significant morbidity;
      ii. Postoperative treatment following complete resection or persistent residual disease.

Approval duration: 3 months

D. Myelodysplastic/Myeloproliferative Diseases (must meet all):

1. Diagnosis of myelodysplastic/myeloproliferative diseases (MDS/MPD);
2. Disease is associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements;
3. Prescribed dose of Gleevec does not exceed 400 mg/day.

Approval duration: 3 months

E. Dermatofibrosarcoma Protuberans (must meet all):

1. Diagnosis of dermatofibrosarcoma protuberans (DFSP);
2. Member meets (a or b):
   a. FDA approved use:
      i. Disease is unresectable, recurrent and/or metastatic;
   b. Off-label NCCN recommended use:
      i. As adjuvant therapy for positive surgical margins following excision.

Approval duration: 3 months

F. Aggressive Systemic Mastocytosis (ASM) (must meet all):

1. Diagnosis of aggressive systemic mastocytosis;
2. Disease is without the D816V c-Kit mutation or with c-Kit mutational status unknown;
3. Prescribed dose of Gleevec does not exceed 400 mg/day.

Approval duration: 3 months

G. **Hypereosinophilic Syndrome and/or Chronic Eosinophilic Leukemia** (must meet all):
   1. Diagnosis of hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL);
   2. FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) positive, negative, or unknown;
   3. Prescribed dose of Gleevec does not exceed 400 mg/day.

Approval duration: 3 months

H. **Other diagnoses/indications:** Refer to ERX.SPMN.16 - Global Biopharm Policy.
   1. Additional Gleevec uses outlined in the NCCN compendium and which meet NCCN category 1, 2a, or 2b, are covered for the following indications per the USS.SPMN.16 Global Biopharm Policy:
      a. Bone cancer – chordoma;
      b. Melanoma;
      c. NHL – lymphoblastic lymphoma;
      d. Soft tissue sarcoma:
         i. Desmoid tumors (aggressive fibromatosis);
         ii. Pigmented villonodular synovitis/tenosynovial giant cell tumor (PVNS/TGCT).

II. Continued Approval

A. **All Indications** (must meet all)**:**
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Responding positively to therapy.

Approval duration: 6 months

B. **Other diagnoses/indications** (must meet 1 or 2):
   1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
   2. Refer to ERX.SPMN.16 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Imatinib mesylate is a small molecule protein-kinase inhibitor that inhibits the BCR-ABL tyrosine kinase, the constitutive abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in CML. Imatinib inhibits proliferation and induces apoptosis in BCR-ABL positive cell lines as well as fresh leukemic cells from Philadelphia chromosome positive chronic myeloid leukemia. Imatinib inhibits colony formation in assays using ex vivo peripheral blood and bone marrow samples from CML patients. Imatinib is also an inhibitor of the receptor tyrosine kinases for platelet-derived growth factor (PDGF) and stem cell factor (SCF), c-kit, and inhibits PDGF- and SCF-mediated cellular events.

Formulations:
Gleevec is available in 100 mg and 400 mg tablets for oral administration.

FDA Approved Indication(s):
Gleevec (imatinib) is a kinase inhibitor/oral tablet indicated for the treatment of:

- Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia in chronic phase.
- Patients with Philadelphia chromosome positive chronic myeloid leukemia in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.
- Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia.
- Pediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) in combination with chemotherapy.
- Adult patients with myelodysplastic/myeloproliferative diseases associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements.
- Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation or with c-Kit mutational status unknown.
- Adult patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia 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.
- Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans.
- Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors.
- Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST.

Appendices
Appendix A: Abbreviation Key
ALL: acute lymphoblastic leukemia
ASM: aggressive systemic mastocytosis
CEL: chronic eosinophilic leukemia
CML: chronic myelogenous leukemia
DFSP: dermatofibrosarcoma protuberans
FISH: fluorescent in situ hybridization
GIST: gastrointestinal stromal tumor
HES: hypereosinophilic syndrome
MDS: myelodysplastic syndromes
MPD: myeloproliferative diseases
PDGFR: platelet-derived growth factor receptor
Ph+: Philadelphia chromosome positive
PVNS: pigmented villonodular synovitis
TGCT: tenosynovial giant cell tumor
TKI: tyrosine kinase inhibitor

Reviews, Revisions, and Approvals	Date	Approval Date
Policy created.	02/14	03/14

Reviews, Revisions, and Approvals	Date	Approval Date
Policy converted to new template. Added NCCN compendium disease indication and recommendations. Removed age restrictions, requests for documentation, and safety criteria. 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. CML- removed monitoring requirements for re-auth. GIST- added option for Kit-positive disease. HES/CEL- added criteria about FIP1L1-PDGFRα fusion kinase.	08/16	09/16

References

1. Gleevec Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2015. Available at http://www.pharma.us.novartis.com/. Accessed June 6, 2016.
2. Imatinib mesylate. In: National Comprehensive Cancer network Drug and Biologics Compendium. Available at www. NCCN.org. Accessed June 6, 2016.

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.