Clinical Policy: Imatinib (Gleevec)

Reference Number: PA.CP.PHAR.65
Effective Date: 06/11
Last Review Date: 04/19 Revision Log

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
It is the policy of health plans affiliated with Pennsylvania Health and Wellness® that imatinib (Gleevec) is **medically necessary** when one of the following criteria is met:

I. Initial Approval Criteria

A. FDA Labeled Indications (must meet all):

1. One of the following diagnoses::
   a. Ph+ (BCR-ABL1-positive) CML or Ph+ (BCR-ABL-positive) ALL;
   b. MDS/MPD and member meets one of the following (i or ii):
      i. Disease is positive for a PDGFR mutation;
      ii. If the member has a diagnosis of chronic myelomonocytic leukemia (an MDS/MPD subtype), disease is positive for either a 5q31-33 or a PDGFR

mutation;
b. ASM and member meets one of the following (i or ii):
i. Disease is negative for the D816V c-KIT mutation;
ii. c-Kit mutational status is unknown;
b. HES/CEL, DESP, or GIST (a soft tissue sarcoma);
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. Request meets one of the following (a or b):
a. Dose does not exceed any of the following (i, ii, or iii):
i. 800 mg per day: CML, DFSP, GIST;
ii. 600 mg per day: ALL;
iii. 400 mg per day: MDS/MPD, ASM, HES/CEL;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

B. Off-Label Indications (must meet all):
1. One of the following diagnoses:
a. Central nervous system metastasis with history of Gleevec treatment for EGFR-positive non-small cell lung cancer;
b. AIDS-related Kaposi sarcoma;
c. Chordoma (a bone cancer);
d. KIT-positive melanoma;
e. Desmoid tumor (also known as aggressive fibromatosis, a soft tissue sarcoma);
f. Pigmented villonodular synovitis/tenosynovial giant cell tumor (a soft tissue sarcoma);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. 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).

Approval duration: 6 months

C. Other diagnoses/indications:
1. Refer to PA.CP.PMN.53

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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 any of the following (i, ii or iii):
i. 800 mg per day: CML, DFSP, GIST;

ii. 600 mg per day: ALL;
iii. 400 mg per day: MDS/MPD, ASM, HES/CEL;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications (1 or 2):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
ASM: aggressive systemic mastocytosis
CEL: chronic eosinophilic leukemia
CML: chronic myeloid leukemia
DFSP: dermatofibrosarcoma protuberans
FDA: Food and Drug Administration
GIST: gastrointestinal stromal tumor
HES: hypereosinophilic syndrome
MDS: myelodysplastic syndromes
MPD: myeloproliferative diseases
PDGFR: platelet-derived growth factor receptor
Ph+: Philadelphia chromosome positive
PVNS/TGCT: pigmented villonodular synovitis/tenosynovial giant cell tumor

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CML	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	Adult: 800 mg/day Pediatric: 600 mg/day
ALL	Adult: 600 mg/day PO for relapsed / refractory Ph+ ALL Pediatric: 340 mg/m^2/day PO in combination with chemotherapy for newly diagnosed Ph+ ALL	Adult: 600 mg/day Pediatric: 600 mg/day
MDS/MPD	Adult: 400 mg/day PO	Adult: 400 mg/day
ASM	Adult: 100-400 mg/day PO	Adult: 400 mg/day

Indication	Dosing Regimen	Maximum Dose
HES/CEL	Adult: 100-400 mg/day PO	Adult: 400 mg/day
DESP	Adult: 800 mg/day PO	Adult: 800 mg/day
GIST	Adult: 400-800 mg/day PO for metastatic or unresectable GIST (800 mg given as 400 BID) and 400 mg/day PO or adjuvant GIST	Adult: 800 mg/day; 400 mg/day for adjuvant GIST

**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.*

V. Product Availability

Tablets: 100 mg, 400 mg

VI. References

1. Gleevec Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2018. Available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gleevec_tabs.pdf. Accessed February 5, 2019.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 5, 2019.
3. National Comprehensive Cancer Network. Chronic Myeloid Leukemia Version 1.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed February 4, 2019.
4. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 1.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed February 4, 2019.
5. National Comprehensive Cancer Network Guidelines. Soft Tissue Sarcoma Version 2.2019. Available at www.nccn.org. Accessed February 5, 2019.
6. National Comprehensive Cancer Network Guidelines. AIDS-Related Kaposi Sarcoma Version 2.2019. Available at www.nccn.org. Accessed February 5, 2019.
7. National Comprehensive Cancer Network Guidelines. Bone Cancer Version 1.2019. Available at www.nccn.org. Accessed February 5, 2019.
8. National Comprehensive Cancer Network Guidelines. Cutaneous Melanoma Version 1.2019. Available at www.nccn.org. Accessed February 5, 2019.
9. National Comprehensive Cancer Network Guidelines. Dermatofibrosarcoma Protuberans Version 1.2019. Available at www.nccn.org. Accessed February 5, 2019.
10. National Comprehensive Cancer Network Guidelines. Myelodysplastic Syndromes Version 1.2019. Available at www.nccn.org. Accessed February 5, 2019.
11. National Comprehensive Cancer Network Guidelines. Systemic Mastocytosis Version 2.2019. Available at www.nccn.org. Accessed February 5, 2019.

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: added age; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; off-label CNS/NSCLC, Kaposi sarcoma added; references reviewed and updated.	02.13.18	
2Q 2019 annual review: additional mutations added if chronic myelomonocytic leukemia per NCCN; hematologist removed from off-label uses; references reviewed and updated.	04/19	