Clinical Policy: Imatinib (Gleevec)

Reference Number: CP.PHAR.65
Effective Date: 06.01.11
Last Review Date: 05.20 Revision Log
Line of Business: Commercial, HIM, Medicaid

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
- Patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
- Adult patients with relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL)
- Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
- Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements
- Adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown
- 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
- Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
- Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
- 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 Centene Corporation® 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:
   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;
   c. 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;
   d. 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 the 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM - 6 months
Commercial - Length of Benefit

B. Off-Label Indications (must meet all):

1. One of the following diagnoses:
   a. AIDS-related Kaposi sarcoma;
   b. Chordoma (a bone cancer);
   c. KIT-positive melanoma;
   d. Desmoid tumor (also known as aggressive fibromatosis, a soft tissue sarcoma);
   e. Pigmented villonodular synovitis/tenosynovial giant cell tumor (a soft tissue sarcoma) that is associated with severe morbidity or functional limitations and not amenable to improvement with surgery;
   f. Chronic graft-versus-host disease - as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options;
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*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM - 6 months

Commercial - Length of Benefit

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, 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. Generic version of Gleevec is prescribed, unless medical justification supports inability to use the generic (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 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*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM - 12 months
Commercial - Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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
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

V. 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
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.*

VI. Product Availability
Tablets: 100 mg, 400 mg

VII. 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 11, 2020.

2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 11, 2020.
3. National Comprehensive Cancer Network. Chronic Myeloid Leukemia Version 3.2020. Available at: www.nccn.org. Accessed February 11, 2020.
4. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 1.2020. Available at: www.nccn.org. Accessed February 11, 2020.
5. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 2.2020. Available at: www.nccn.org. Accessed February 11, 2020.
6. National Comprehensive Cancer Network Guidelines. Soft Tissue Sarcoma Version 6.2019. Available at www.nccn.org. Accessed February 11, 2020.
7. National Comprehensive Cancer Network Guidelines. AIDS-Related Kaposi Sarcoma Version 2.2019. Available at www.nccn.org. Accessed February 11, 2020.
8. National Comprehensive Cancer Network Guidelines. Bone Cancer Version 1.2020. Available at www.nccn.org. Accessed February 11, 2020.
9. National Comprehensive Cancer Network Guidelines. Cutaneous Melanoma Version 1.2020. Available at www.nccn.org. Accessed February 11, 2020.
10. National Comprehensive Cancer Network Guidelines. Dermatofibrosarcoma Protuberans Version 1.2020. Available at www.nccn.org. Accessed February 11, 2020.
11. National Comprehensive Cancer Network Guidelines. Myelodysplastic Syndromes Version 1.2020. Available at www.nccn.org. Accessed February 11, 2020.
12. National Comprehensive Cancer Network Guidelines. Systemic Mastocytosis Version 2.2019. Available at www.nccn.org. Accessed February 11, 2020.
13. National Comprehensive Cancer Network Guidelines. Hematopoietic Cell Transplantation Version 1.2020. Available at www.nccn.org. Accessed February 11, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Reworked narrative for CML and ALL per NCCN guidelines. Removed requests for documentation from all algorithms; added age requirements to all algorithms. Figure 1 (CML): added diagnoses questions and questions about age; modified monitoring per NCCN guidelines – see also corresponding narrative and Appendix B. Figure 2 (ALL): changed question about less than or greater than 12 months to initial auth for 3 months and subsequent auths for 6 months – while there is monitoring per NCCN guidelines, Gleevec is always a potential option so specific monitoring questions were not added. Figure 4 (ASM): Added c-Kit mutational status unknown to the first question in the pathway per PI. Restructured safety section into list per the package insert.	05.15	07.15
Policy converted to new template. Added NCCN compendium disease indication and recommendations.	06.16	07.16
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	06.17	07.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
blast phase" is added; 3) continued use of Gleevec in cases where members are not candidates for other drugs or in cases of poor or partial response is deleted in initial criteria and added to continuation criteria; 4) "for relapse" is deleted from "post stem cell transplant therapy." ALL NCCN: 1) Allowed regimens deleted; 2) "post stem cell transplant" is added under maintenance therapy. 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. GIST NCCN: 1) "resectable disease with risk of significant morbidity" is removed from under primary/preoperative therapy; 2) "ongoing treatment for progressive disease" is added. Maximum dose added for CML, ALL and dose exception due to CYP inducers is added to all indications. Reasons to discontinue removed. Approval periods lengthened from 3/6 to 6/12 months.		
2Q 2018 annual review: added Commercial and HIM lines of business; added age; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; added continuity of care statement; off-label CNS/NSCLC, Kaposi sarcoma added; references reviewed and updated.	02.13.18	05.18
2Q 2019 annual review: additional mutations added if chronic meylomonocytic leukemia per NCCN; NSCLC CNS metastasis removed from off-label criteria set; hematologist removed from off-label uses; references reviewed and updated.	02.19.19	05.19
PVNS/TGCT: added requirement that disease is not amenable to improvement with surgery to align with Turalio since both drugs have the same recommendations for use per NCCN.	09.03.19	11.19
2Q 2020 annual review: HIM nonformulary language removed; GVHD NCCN recommended use added; Continued Therapy authorization duration changed to 12 months for consistency with other oral oncology agents; added requirement for use of generic version in section II per Ambetter director's request; references reviewed and updated.	04.28.20	05.20

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. The Health Plan makes no representations and

accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.