

## **Clinical Policy: Imatinib (Gleevec)**

Reference Number: CP.PHAR.65

Effective Date: 06.01.11

Last Review Date: 05.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Imatinib mesylate (Gleevec<sup>®</sup>) 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-PDGFR $\alpha$  fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFR $\alpha$  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<sup>®</sup> that Gleevec is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. FDA Labeled Indications (must meet all):**

1. Diagnosis of one of the following:
  - 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, DFSP, or GIST (a soft tissue sarcoma);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. For brand Gleevec, member must use generic imatinib, unless contraindicated or clinically significant adverse effects are experienced;
4. Age  $\geq$  18 years if the diagnosis is MDS/MPD, ASM, DFSP, or GIST;
5. 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. Diagnosis of one of the following:
  - a. AIDS-related Kaposi sarcoma (KS), and both of the following (i and ii):
    - i. Imatinib is prescribed in combination with antiretroviral therapy;
    - ii. Failure of liposomal doxorubicin and paclitaxel, unless clinically significant adverse effects are experienced or both are contraindicated;
  - b. Recurrent conventional or chondroid chordoma (a bone cancer);
  - c. KIT-positive melanoma as second-line or subsequent therapy;
  - d. Desmoid tumor (also known as aggressive fibromatosis, a soft tissue sarcoma);
  - e. Myeloid/lymphoid neoplasm with eosinophilia and tyrosine kinase fusion genes;
  - f. 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;
  - g. 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 one of the following specialists (a or b):

- a. AIDS-related KS: an oncologist or immunologist;
- b. All other diagnoses: an oncologist;
3. Age  $\geq$  18 years;
4. For brand Gleevec requests, member must use generic imatinib, unless contraindicated or clinically significant adverse effects are experienced;
5. 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.PA.154 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. For brand Gleevec requests, member must use generic imatinib, unless contraindicated or clinically significant adverse effects are experienced;
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.PA.154 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.PA.154 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

KS: Kaposi sarcoma  
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*

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
liposomal doxorubicin (Doxil <sup>®</sup> , Lipodox <sup>®</sup> 50)	<b>AIDS-related KS</b> 20 mg/m <sup>2</sup> IV every 2-3 weeks with a cumulative lifetime dose of 400-450 mg/m <sup>2</sup> due to cardiotoxicity	See regimen
paclitaxel	<b>AIDS-related KS</b> 135 mg/m <sup>2</sup> IV every 3 weeks <b>or</b> 100 mg/m <sup>2</sup> every 2 weeks	See regimen

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*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/m <sup>2</sup> /day PO for chronic phase	Adult: 800 mg/day Pediatric: 600 mg/day
ALL	Adult:	Adult: 600 mg/day

Indication	Dosing Regimen	Maximum Dose
	600 mg/day PO for relapsed / refractory Ph+ ALL Pediatric: 340 mg/m <sup>2</sup> /day PO in combination with chemotherapy for newly diagnosed Ph+ ALL	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; August 2020. Available at [https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gleevec\\_tabs.pdf](https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/gleevec_tabs.pdf). Accessed February 21, 2021.
2. Imatinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed February 21, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 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-PDGFR $\alpha$ fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) or HES and/or CEL who are FIP1L1-PDGFR $\alpha$ fusion kinase negative or unknown” is removed.	06.17	07.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 myelomonocytic 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
AIDS-related KS: updated criteria to require concurrent use with antiretroviral therapy and failure of first line agents per NCCN guidelines; added immunologist as a prescriber option per specialist feedback.	06.29.20	11.20
2Q 2021 annual review: added off-label indication for myeloid/lymphoid neoplasm with eosinophilia and tyrosine kinase fusion genes; added generic redirection language to “must use” since oral oncology product; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.20.21	05.21

**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

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**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.

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