Clinical Policy: Imatinib (Gleevec, Imkeldi)

Reference Number: CP.PHAR.65
Effective Date: 06.01.11
Last Review Date: 05.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

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

Description

Imatinib mesylate (Gleevec®, Imkeldi™) is a kinase inhibitor.

FDA Approved Indication(s)

Gleevec and Imkeldi are 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 (BC), accelerated phase (AP), or in chronic phase (CP) 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 re-arrangements
- 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 fluorescence in situ hybridization [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 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 imatinib, Gleevec, and Imkeldi are **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 t(5;12) translocation associated with the ETV6-PDGFRβ fusion gene or PDGFRβ gene rearrangements at 5q32 (off-label);
   c. ASM and member meets one of the following (i-iv):
      i. Disease is negative for the D816V c-KIT mutation;
      ii. c-Kit mutational status is unknown;
      iii. Well-differentiated systemic mastocytosis (off-label);
      iv. Eosinophilia is present with FIP1L1-PDGFRA fusion gene (off-label);
   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 and Imkeldi*, member must use generic imatinib, unless contraindicated, clinically significant adverse effects are experienced, or for Imkeldi requests member is unable to swallow tablets;
   **For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395 for Imkeldi requests*
4. Age ≥ 18 years if the diagnosis is MDS/MPD, ASM, HES/CEL, 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. CML, DFSP, GIST: 800 mg per day;
      ii. ALL: 600 mg per day;
      iii. MDS/MPD, ASM, HES/CEL: 400 mg per day;
   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*
   ≠ Dose optimization is required; refer to Appendix D

Approval duration:
Medicaid/HIM/ICHRA - 12 months
Commercial - 12 months or duration of request, whichever is less

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

1. Diagnosis of one of the following (a-g):
   a. Kaposi sarcoma (KS), and both of the following (i and ii):
      i. If request is for AIDS-related KS, 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 metastatic or unresectable melanoma as second-line or subsequent therapy (i.e., following BRAF-targeted 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) as single-agent therapy;
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 ≥ 18 years;
4. For brand Gleevec and Imkeldi* requests, member must use generic imatinib, unless contraindicated, clinically significant adverse effects are experienced, or for Imkeldi requests member is unable to swallow tablets;
   **For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395 for Imkeldi requests*
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*
   ≠ Dose optimization is required; refer to Appendix D

Approval duration:
Medicaid/HIM/ICHRA - 12 months
Commercial - 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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 imatinib, Gleevec, or Imkeldi 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 and Imkeldi* requests, member must use generic imatinib, unless contraindicated, clinically significant adverse effects are experienced, or for Imkeldi requests member is unable to swallow tablets;
   **For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395 for Imkeldi requests*
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. CML, DFSP, GIST: 800 mg per day;
      ii. ALL: 600 mg per day;
      iii. MDS/MPD, ASM, HES/CEL: 400 mg per day;
   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*
   ≠ Dose optimization is required; refer to Appendix D

Approval duration:
Medicaid/HIM/ICHRA - 12 months
Commercial - 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
AP: accerlated phase
ASM: aggressive systemic mastocytosis
BC: blast crisis

CEL: chronic eosinophilic leukemia
CML: chronic myeloid leukemia
CP: chronic phase
DFSP: dermatofibrosarcoma protuberans
FDA: Food and Drug Administration
FISH: fluorescence in situ hypridization
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®, Lipodox® 50)	**AIDS-related KS** 20 mg/m^2 IV every 2-3 weeks with a cumulative lifetime dose of 400-450 mg/m^2 due to cardiotoxicity	See regimen
paclitaxel	**AIDS-related KS** 135 mg/m^2 IV every 3 weeks **or** 100 mg/m^2 every 2 weeks	See regimen

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

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- Dose optimization is the consolidation of multiple units of lower strength to the fewest units required to achieve the desired daily dose/regimen based on commercially available dosage strengths. Requests for multiple units of a lower strength will be denied when the plan-approved QL for such medication is exceeded and higher strength units are commercially available to achieve the desired daily dose/regimen.

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^2/day PO for chronic phase	Adult: 800 mg/day Pediatric: 600 mg/day
ALL	Adult: • 600 mg/day PO for relapsed / refractory Ph+ ALL	Adult: 600 mg/day Pediatric: 600 mg/day

Indication	Dosing Regimen	Maximum Dose
	Pediatric: • 340 mg/m^2/day PO in combination with chemotherapy for newly diagnosed Ph+ ALL	
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, rifampicin, phenobarbital.*

VI. Product Availability

Drug Name	Availability
Imatinib (Gleevec)	Tablets: 100 mg, 400 mg
Imatinib (Imkeldi)	Oral solution: 80 mg/mL (140 mL bottle)

VII. References

1. Gleevec Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2026. Available at: https://www.novartis.com/us-en/sites/novartis_us/files/gleevec_tabs.pdf . Accessed January 27, 2026.
2. Imkeldi Prescribing Information. Cambridge, MA: Shorla Oncology Inc.; November 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/219097s000lbl.pdf. Accessed January 13, 2026.
3. Imatinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 27, 2026.
4. National Comprehensive Cancer Network Guidelines. Chronic Myeloid Leukemia Version 1.2026. Available at https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed January 27, 2026.
5. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia Version 2.2025. Available at https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed January 27, 2026.
6. National Comprehensive Cancer Network Guidelines. Gastrointestinal Stromal Tumors (GISTs) Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed January 27, 2026.
7. National Comprehensive Cancer Network Guidelines. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed January 27, 2026.
8. National Comprehensive Cancer Network Guidelines. Dermatofibrosarcoma Protuberans Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/dfsp.pdf. Accessed January 27, 2026.

9. National Comprehensive Cancer Network Guidelines. Hematopoietic Cell Transplantation Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed January 27, 2026.
10. National Comprehensive Cancer Network Guidelines. Kaposi Sarcoma Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kaposi.pdf. Accessed January 27, 2026.
11. National Comprehensive Cancer Network Guidelines. Melanoma: Cutaneous Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed January 27, 2026.
12. National Comprehensive Cancer Network Guidelines. Soft Tissue Sarcoma Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed January 27, 2026.
13. National Comprehensive Cancer Network Guidelines. Systemic Mastocytosis Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf. Accessed January 27, 2026.
14. National Comprehensive Cancer Network Guidelines. Bone Cancer Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed January 27, 2026.
15. National Comprehensive Cancer Network Guidelines. Pediatric Acute Lymphoblastic Leukemia Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed January 27, 2026.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2022 annual review: modified commercial approval duration from length of benefit to "12 months or duration of request, whichever is less"; WCG.CP.PHAR.65 to be retired and approval durations consolidated to 6 months initial and 12 months for continuation of therapy; per NCCN clarified off label use in chronic myelomonocytic leukemia is positive for either a t(5;12) translocation associated with the ETV6-PDGFRβ fusion gene or PDGFRβ gene rearrangements at 5q32, for ASM added additional indications for well-differentiated systemic mastocytosis and when eosinophilia is present with FIP1L1-PDGFRA fusion gene, for KS added allowance for non-AIDS-related KS, for melanoma added requirement that disease is metastatic or unresectable, for pigmented villonodular synovitis/tenosynovial giant cell tumor revised to only require use as single-agent therapy and removing previous requirements for morbidity and functional limitations; for HES/CEL applied 18 years or older age requirement per prescribing information; references reviewed and updated.	01.31.22	05.22
Template changes applied to other diagnoses/indications.	10.12.22	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2023 annual review: no significant changes; clarified for melanoma imatinib should be used following BRAF-targeted therapy; references reviewed and updated.	01.06.23	05.23
2Q 2024 annual review: no significant changes; for dosing limits added clarification that dose optimization is required in each criteria set; added Appendix D to define dose optimization; references reviewed and updated.	01.10.24	05.24
RT4: added new oral solution formulation Imkeldi to criteria requiring redirection to generic imatinib with an additional bypass if member is unable to swallow tablets; revised policy/criteria section to also include generic imatinib.	12.02.24	
2Q 2025 annual review: no significant changes; references reviewed and updated.	01.17.25	05.25
2Q 2026 annual review: no significant changes; for Imkeldi, added step therapy bypass for IL HIM per IL HB 5395; revised initial approval durations for HIM/Medicaid from 6 months to 12 months; references reviewed and updated. Added ICHRA line of business.	03.26.26	05.26

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.