Clinical Policy: Bosutinib (Bosulif)

Reference Number: CP.PHAR.105
Effective Date: 10.01.12
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Bosutinib (Bosulif®) is a kinase inhibitor.

FDA Approved Indication(s)

Bosulif is indicated for the treatment of patients with:

- Adult and pediatric patients one year of age or older with chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML), newly diagnosed or resistant or intolerant to prior therapy.
- Adult patients with accelerated phase (AP), or blast phase (BP) Ph+ CML with resistance or intolerance to prior therapy.

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 Bosulif is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Myelogenous Leukemia (must meet all)**:**

1. Diagnosis of Ph+ (BCR-ABL1-positive) CML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. One of the following (a or b);
   a. Age ≥ 1 years with chronic phase (CP) CML;
   b. Age ≥ 18 years with accelerated phase (AP), or blast phase (BP) CML;
4. Member does not have the following mutations: T315I, V299L, G250E, or F317L;
5. One of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395.*
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
6. For brand Bosulif requests, member must use generic bosutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a, b, or c):*≠
   a. For an adult member, dose does not exceed 600 mg per day;
   b. For a pediatric member, dose not exceed the body surface area (BSA)-based dosing listed in section V;

c. 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 - 6 months
Commercial - 12 months or duration of request, whichever is less

B. Acute Lymphoblastic Leukemia (off-label) (must meet all)**:**
1. Diagnosis of Ph+ (BCR-ABL1-positive) acute lymphoblastic leukemia (ALL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member does not have the following mutations: T315I, V299L, G250E, or F317L;
4. One of the following (a or b):*
   **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395.*
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
5. For brand Bosulif requests, member must use generic bosutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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 - 6 months
Commercial - 12 months or duration of request, whichever is less

C. Myeloid/Lymphoid Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of myeloid/lymphoid neoplasm with eosinophilia and tyrosine kinase fusion genes (i.e., ABL1 rearrangement);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Disease is BCR-ABL1-positive;
4. One of the following (a or b):
   **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395.*
   a. Member has contraindication, intolerance, or disease progression on imatinib;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;
5. For brand Bosulif requests, member must use generic bosutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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 - 6 months
Commercial - 12 months or duration of request, whichever is less

D. 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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 Bosulif for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Bosulif requests, member must use generic bosutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed the following (a or b):*≠
   a. Dose does not exceed 600 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 - 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) 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, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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
AP: accelerated phase
BP: blast phase
CML: chronic myelogenous leukemia
CP: chronic phase
FDA: Food and Drug Administration
MLNE: Myeloid/lymphoid neoplasms with eosinophilia
Ph+: Philadelphia chromosome-positive

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
imatinib (Gleevec)	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 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)	800 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• Pediatric: 340 mg/m^2/day PO for chronic phase MLNE: 100-400 mg PO QD [NCCN]	

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

- Contraindication(s): hypersensitivity to Bosulif
- Boxed warning(s): 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.

Appendix E: States with Regulations against Redirections in Certain Oncology Settings

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
MS	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to Commercial and HIM requests only** For stage 4 metastatic cancer and associated conditions
OK	Yes	**Applies to HIM requests only** For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication:	Dosing Regimen	Maximum Dose
	Adult: 400 mg/day PO	Adults:600 mg/day

Indication:	Dosing Regimen	Maximum Dose
Newly diagnosed Ph+ CP CML		
	Pediatrics: body surface area (BSA) dosing • < 0.55 m^2 = 150 mg/day PO • 0.55 to <0.75 m^2 = 200 mg/day PO • 0.75 to 0.9 m^2 = 250 mg/day PO • 0.9 to <1.1 m^2 = 300 mg/day PO • ≥1.1 m^2 = 400 mg/day PO	Pediatrics: BSA dosing • < 0.55 m^2 = 250 mg/day • 0.55 to <0.75 m^2 = 200 mg/day • 0.75 to 0.9 m^2 = 350 mg/day • 0.9 to <1.1 m^2 = 400 mg/day • ≥1.1 m^2 = 600 mg/day
Ph+ CP CML With resistance or intolerance to previous therapy	Adults: 500 mg PO QD	Adults: 600 mg/day
	Pediatrics: BSA dosing • <0.55 m^2 = 200 mg/day PO • 0.55 to <0.63 m^2 = 250 mg/day PO • 0.63 to < 0.75 m^2 =300 mg/day PO • 0.75 to <0.9 m^2 = 350 mg/day PO • 0.9 to <1.1 m^2 = 400 mg/day PO • ≥1.1 m^2 = 500 mg/day PO	Pediatrics: BSA dosing • <0.55 m^2 = 300 mg/day • 0.55 to <0.63 m^2 = 350 mg/day • 0.63 to < 0.75 m^2 =400 mg/day • 0.75 to <0.9 m^2 = 450 mg/day • 0.9 to <1.1 m^2 = 500 mg/day • ≥1.1 m^2 = 600 mg/day
AP, or BP Ph+ CML with resistance or intolerance to prior therapy	Adults: 500mg/day PO	Adults: 600mg/day

VI. Product Availability

- Tablets: 100 mg, 400 mg, 500 mg
- Capsules: 50 mg, 100 mg

VII. References

1. Bosulif Prescribing Information. New York, NJ: Pfizer Inc.; December 2024. Available at https://www.bosulif.com. Accessed January 16, 2025.
2. Bosutinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 10, 2025.
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia. Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed February 10, 2025.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia. Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed February 10, 2025.

5. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes. Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed February 10, 2025.

Reviews, Revision, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: added that member does not have any of the following mutations: T315I, V299L, G250E, or F317L per NCCN; added generic redirection language to "must use" since oral oncology product; added approval criteria for myeloid/lymphoid neoplasm with eosinophilia and tyrosine kinase fusion genes; added that member has contraindication, intolerance, or disease progression on imatinib; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.20.21	05.21
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.105 to be retired and approval durations consolidated to 6 months initial and 12 months for continuation of therapy; for imatinib redirection added by-passing of redirection if state regulations do not allow step therapy in Stage IV or metastatic cancer settings; references reviewed and updated.	01.25.22	05.22
Template changes applied to other diagnoses/indications.	09.30.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.06.23	05.23
RT4: added new FDA approved pediatric age extension to 1 year old for CML; added new oral capsule formulation.	10.10.23	
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; for myeloid/lymphoid neoplasm tyrosine kinase fusion genes requirement added reference to ABL1 rearrangement per NCCN Compendium; for Appendix E, added state OK and updated state OH notes to include Commercial line of business; references reviewed and updated.	01.08.24	05.24
Updated Appendix E to include Mississippi.	06.05.24	
2Q 2025 annual review: no significant changes; references reviewed and updated. Added step therapy bypass for IL HIM per IL HB 5395.	01.16.25	05.25

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.