Bosulif® (bosutinib)
(Oral)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Bosulif 100 mg tablets: 6 tablets per day
- Bosulif 400 mg tablets: 1 tablet per day
- Bosulif 500 mg tablets: 1 tablet per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 600 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age unless otherwise specified; **AND**

Universal Criteria [1]

- Patient will avoid concomitant therapy with all of the following:
  - Coadministration with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
  - Coadministration with moderate or strong CYP3A inhibitors (e.g., itraconazole, fluconazole, clarithromycin, etc.); **AND**
  - Coadministration with proton pump inhibitors (e.g., lansoprazole, esomeprazole, omeprazole), or if acid-reduction therapy is required, use of short-acting antacids or H2 blockers may be used at staggered administration times; **AND**

Chronic Myelogenous Leukemia (CML) † Φ [1-3,6-8]

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- Patient has Philadelphia chromosome-positive (Ph+) or *BCR-ABL1* positive disease; **AND**
- Patient does not have any of the following *BCR-ABL1* mutations: T315I, V299L, G250E, or F317L (****NOTE:** This does not apply to newly diagnosed chronic phase disease or continued therapy); **AND**
  - Patient is resistant, or intolerant, or had an inadequate response to prior therapy consisting of a 3 month trial or longer with a tyrosine kinase inhibitor (e.g., imatinib, dasatinib, ponatinib, nilotinib, etc.) †; **AND**
    - Patient has chronic, accelerated, or blast phase disease; **OR**
  - Used post-allogeneic hematopoietic stem cell transplant (HCT) ‡; **AND**
    - Used as follow-up therapy in patients with molecular relapse (BCR-ABL1 transcript positive) following complete cytogenetic response (CCyR); **OR**
    - Used for at least one year in patients with prior CCyR for accelerated or blast phase disease; **OR**
    - Used as follow-up therapy in patients with relapse or less than CCyR; **OR**
  - Used as primary treatment † ‡; **AND**
    - Used as a single agent for newly diagnosed chronic; **OR**
    - Used as a single agent for accelerated or myeloid blast phase disease; **OR**
    - Used in combination with corticosteroids for lymphoid blast phase disease; **OR**
    - Used in combination with induction chemotherapy for disease in lymphoid blast phase or myeloid blast phase; **OR**
  - Used as switch therapy ‡; **AND**
    - Patient received primary treatment with one of the following: imatinib, dasatinib, or nilotinib; **AND**
    - Patient has *BCR-ABL1* transcript levels:
      - >0.1% to 1% at 12 months (if treatment goal is treatment-free remission); **OR**
      - >1% to 10% at 12 months; **OR**
      - >10% at any response milestone; **OR**
  - Used as continued therapy ‡; **AND**
    - Patient has *BCR-ABL1* transcript levels:
      - ≤10% at any response milestone; **OR**
      - >10% at 3 months

Acute Lymphoblastic Leukemia (ALL) ‡ [2,4,5,10]

- Patient has Philadelphia chromosome-positive (Ph+) B-ALL; **AND**
- Patient does not have any of the following *BCR-ABL1* mutations: T315I, V299L, G250E, or F317L; **AND**
  - Used for relapsed or refractory disease; **AND**
    - Used as a single agent; **OR**

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        - Used in combination with an induction therapy not previously used; **OR**
        - Used in combination inotuzumab ozogamicin; **OR**
        - Used in combination with blinatumomab; **OR**
    - Used as maintenance therapy; **AND**
        - Used in combination with vincristine and prednisone with or without methotrexate and mercaptopurine for patients with negative minimal residual disease after complete response to induction therapy; **OR**
        - Used as a single agent; **AND**
            - Used post-hematopoietic stem cell transplant; **OR**
            - Used in patients unfit for additional therapies; **OR**
    - Used as consolidation therapy; **AND**
        - Used for negative minimal residual disease after complete response to induction therapy; **AND**
            - Used as a single agent therapy in patients unfit for additional therapies; **OR**
            - Used combination with combination with blinatumomab for patients who are not candidates for multi-agent chemotherapy; **OR**
        - Used for persistent/rising minimal residual disease following a complete response to induction therapy; **AND**
            - Used in combination with blinatumomab; **OR**
            - Used as a single agent for patients who are unfit for additional therapies; **OR**
    - Patient is at least 15 years of age OR < 65 years of age without substantial comorbidities; **AND**
        - Used in a multiagent chemotherapy regimen for induction or consolidation therapy; **OR**
        - Used in combination with a corticosteroid for induction therapy; **OR**
        - Used in combination with vincristine and dexamethasone for induction therapy; **OR**
    - Patient is ≥65 years of age OR with substantial comorbidities; **AND**
        - Used as induction therapy as part of one of the following regimens:
            - As a single agent or in combination with a corticosteroid; **OR**
            - In combination with vincristine and dexamethasone; **OR**
            - In combination with a multiagent chemotherapy regimen

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes ‡ [2,9]

- Patient has eosinophilia and ABL1 rearrangement; **AND**
    - Patient has chronic or blast phase myeloid or lymphoid neoplasms; **AND**
        - Used as a single agent; **OR**
    - Patient has blast phase lymphoid, myeloid, or mixed lineage neoplasms; **AND**

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- Used in combination with ALL- or AML-type induction chemotherapy followed by allogeneic HCT (if eligible)

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-4,9]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in Section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: hepatic toxicity, renal toxicity, fluid retention, myelosuppression, gastrointestinal toxicity, cardiovascular toxicity (cardiac failure, left ventricular dysfunction, cardiac ischemic events), etc.; **AND**

Chronic Myelogenous Leukemia (CML)

- Treatment response as indicated by one of the following *BCR-ABL1* (IS) transcript levels:
  - > 0.1% to 10% at 3 months or 6 months; **OR**
  - > 0.1% to 1% at 12 months and beyond (if treatment goal is long-term survival); **OR**
  - ≤ 0.1% at 12 months and beyond (if treatment goal is treatment-free remission)

  NOTE: cytogenetic assessment of response may be used if quantitative RT-PCR (QPCR) using International Scale (IS) for *BCR-ABL1* is not available

Acute Lymphoblastic Leukemia (ALL)

- Treatment response or stabilization of disease as indicated by CBC, bone marrow cytogenic analysis, QPCR, or FISH

Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes

- Disease response as evidenced by at least one of the following:
  - Decrease in spleen size or improvements in other myelofibrosis symptoms (such as fatigue, bone pain, frequent infections, fever, night sweats, easy bruising/bleeding, etc.)
  - Stabilization or improvement as evidenced by a complete response [CR] (i.e. morphologic, cytogenetic or molecular complete response CR), complete hematologic response, or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

V. Dosage/Administration [1,3,5,9,10]

Indication	Dose
CML	Newly diagnosed chronic phase Ph+ CML:

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	400 mg orally once daily with food until disease progression or intolerance to therapy. All other treatment settings: 500 mg orally once daily with food until disease progression or intolerance to therapy.
ALL	500 mg orally once daily with food until disease progression or intolerance to therapy.
Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes	400 mg OR 500 mg orally once daily with food until disease progression or intolerance to therapy.
***NOTE:** Consider dose escalation to 600 mg orally once daily in patients who do not reach complete hematologic response by week 8 or complete cytogenetic response by week 12 and do not have Grade 3 or greater adverse reactions.	

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug, oral, chemotherapeutic, NOS

NDC:

- Bosulif 100 mg tablet: 00069-0135-xx
- Bosulif 400 mg tablet: 00069-0193-xx
- Bosulif 500 mg tablet: 00069-0136-xx

VII. References

1. Bosulif [package insert]. New York, NY; Pfizer, Inc; October 2021. Accessed June 2022.
2. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium®) for bosutinib. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2022.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Chronic Myelogenous Leukemia 3.2022. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2022.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Acute Lymphoblastic Leukemia 1.2022. National Comprehensive

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9. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes. Version 1.2022. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed June 2022.
10. Kantarjian HM, Cortes JE, Kim DW, et al. Bosutinib safety and management of toxicity in leukemia patients with resistance or intolerance to imatinib and other tyrosine kinase inhibitors. Blood. 2014 Feb 27;123(9):1309-18. doi: 10.1182/blood-2013-07-513937. Epub 2013 Dec 17. Erratum in: Blood. 2014 Aug 7;124(6):981.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.50	Lymphoblastic (diffuse) lymphoma, unspecified site
C83.51	Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb

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C83.56	Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma, spleen
C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse
C92.10	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
C92.11	Chronic myeloid leukemia, BCR/ABL-positive, in remission
C92.12	Chronic myeloid leukemia, BCR/ABL-positive, in relapse
C94.8	Other specified leukemias
C94.80	Other specified leukemias not having achieved remission
C94.81	Other specified leukemias, in remission
C94.82	Other specified leukemias, in relapse
C95.1	Chronic leukemia of unspecified cell type
C95.10	Chronic leukemia of unspecified cell type not having achieved remission
C95.11	Chronic leukemia of unspecified cell type, in remission
C95.12	Chronic leukemia of unspecified cell type, in relapse
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.

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Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

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