**09-J1000-84**

**Original Effective Date: 02/15/13**

**Reviewed: 01/14/26**

**Revised: 02/15/26**

# Subject: Bosutinib (Bosulif®) Capsules and Tablets

**THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.**



## DESCRIPTION:

Bosutinib (Bosulif) is a second-generation dual tyrosine kinase inhibitor (TKI) and exerts is therapeutic effects by inhibiting the BCR-ABL kinase that promotes chronic myelogenous leukemia (CML) and Src-family kinases. Bosutinib has demonstrated activity against many of the BCR-ABL kinase domain mutations resistant to imatinib (Gleevec), dasatinib (Sprycel), and nilotinib (Tasigna), except V299L and T315I. Bosutinib was given orphan designation status in 2009 for the treatment of CML and was approved by the US Food and Drug Administration (FDA) in September 2012 for the treatment of adults with chronic phase, accelerated phase, or blast phase Philadelphia (Ph) chromosome-positive CML (CP-CML, AP-CML, and BP-CML, respectively) demonstrating resistance or intolerance to prior therapy. In December 2017, the indication was expanded to include the treatment of adult patients with newly diagnosed, Ph-positive CP-CML. In September 2023, the FDA approved use of bosutinib in certain pediatric populations. The two FDA-approved indications now read as: (1) adult and pediatric patients 1 year of age and older with chronic phase (CP) Ph+ CML, newly-diagnosed or resistant or intolerant to prior therapy, and (2) adult patients with accelerated phase (AP), or blast phase (BP) Ph+ CML with resistance or intolerance to prior therapy. With the approval for pediatric patients, a new capsule formulation in 50 and 100 mg strengths has been released to accommodate lower pediatric dosages. Per the National Comprehensive Cancer Network (NCCN) guidelines, bosutinib has also shown efficacy in the treatment of Ph+ acute lymphoblastic leukemia (ALL) and myeloid/lymphoid neoplasms with eosinophilia and ABL1 rearrangement.

## POSITION STATEMENT:

**Comparative Effectiveness**

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of bosutinib (Bosulif) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

A. **ONE** of the following to support clinical use is met ("1", "2", or "3"):

1. **BOTH** of the following are met regarding FDA labeling or NCCN Compendium ("a" and "b"):

   a. **EITHER** of the following (indication and usage) ["i" or "ii"]:

      i. Member is diagnosed with a condition that is consistent with an indication listed in the bosutinib FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)

      ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation (see Table 2)

   b. **EITHER** of the following (diagnostic testing) ["i" or "ii"]:

      i. The requested indication for bosutinib requires genetic/specific diagnostic testing per FDA labeling* or NCCN Compendium, **AND BOTH** of the following:

         - The genetic/specific diagnostic testing has been completed
         - The results of the testing indicate therapy is appropriate – documentation must be submitted

      ii. The requested indication for bosutinib does **NOT** require specific genetic/diagnostic testing per FDA labeling or NCCN Compendium

      **FDA Companion Diagnostics: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools*

2. Bosutinib is designated as an orphan drug by the FDA for the requested indication **AND** the indication is not included in the FDA labeling or the NCCN compendium as a 1 or 2A recommendation (i.e., "Designated") [orphan drug designations can be found at http://www.accessdata.fda.gov/scripts/opdlisting/oopd/]

3. The indication and usage is supported by the results of **TWO** or more published clinical studies – prescriber must submit full text copies of each article

   **NOTE**:

   - Case reports, posters, and abstracts (including published meeting abstracts) are **NOT** accepted as evidence to support for use.
   - Clinical studies must be supportive of use for a similar patient population (e.g., indication, diagnosis, disease severity, genetic or tumor mutations) and for the intended treatment plan, including any concomitant therapy.

B. For the diagnosis of chronic-phase, Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) **ONLY – ANY** of the following ("1", "2", or "3")**:

1. **BOTH** of the following ("a" and "b"):
    a. Member has a low-risk Sokal, Hasford (EURO), or EUTOS long-term survival (ELTS) score as determined prior to treatment initiation
    b. Member has an FDA-labeled contraindication to, persistent intolerable adverse effects despite appropriate dose modification, or was unable to achieve treatment goals with at least **TWO** of the following products – the member's treatment history, the specific adverse effect(s), and/or contraindication(s) must be provided:
        - A dasatinib product
        - An imatinib product
        - A nilotinib product
2. **BOTH** of the following ("a" and "b"):
    a. Member has an intermediate- or high-risk Sokal, Hasford (EURO), or EUTOS long-term survival (ELTS) score as determined prior to treatment initiation
    b. Member has an FDA-labeled contraindication to, persistent intolerable adverse effects despite appropriate dose modification, or was unable to achieve treatment goals with **BOTH** a dasatinib product **AND** a nilotinib product – the member's treatment history, the specific adverse effect(s), and/or contraindication(s) must be provided
3. Member has an F317V/I/C or T315A mutation (confirmatory laboratory documentation of the mutation must be submitted)

***Step therapy requirement does **NOT** apply if a prior health plan paid for the medication - documentation of a paid claim within the past 90 days must be submitted*

C. The dosage of bosutinib does not exceed the maximum FDA-approved dose and frequency with the following exceptions ("1" or "2"):

1. Dose and frequency for the indication are supported by standard reference compendia (see NCCN Compendium or other compendia in Table 3)
2. Dose and frequency for the indication are supported by the results of **TWO** or more published clinical studies – prescriber must submit full text copies of each article

    **NOTE**: Dose ranging studies, case reports, posters, and abstracts (including published meeting abstracts) are not accepted as evidence to support use

D. For the 100 mg capsule formation **ONLY** – the member is unable to use the tablet formulation due to an inability to swallow a whole tablet (i.e., they need to mix the capsule contents with applesauce or yogurt)

E. The dose will be achieved using the fewest number of capsules or tablets per day [with the exceptions of a 400 mg daily dosage which may be obtained with either four 100 mg tablets or one 400 mg tablet, and a 600 mg daily dosage which may be obtained with six 100 mg tablets]

**Approval duration**: 6 months

Continuation of bosutinib (Bosulif) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

A. Bosutinib has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met **ALL** indication-specific criteria

B. The dosage of bosutinib does not exceed the maximum FDA-approved dose and frequency with the following exceptions:

   i. Dose and frequency for the indication are supported by standard reference compendia (see NCCN Compendium or Table 3)

   ii. Dose and frequency for the indication are supported by the results of **TWO** or more published clinical studies – prescriber must submit full text copies of each article

   **NOTE**: Dose ranging studies, case reports, posters, and abstracts (including published meeting abstracts) are not accepted as evidence to support use

C. For the 100 mg capsule formation **ONLY** – the member is unable to use the tablet formulation due to an inability to swallow a whole tablet (i.e., they need to mix the capsule contents with applesauce or yogurt)

D. The dose of bosutinib will be achieved using the fewest number of capsules or tablets per day [with the exceptions of a 400 mg daily dosage which may be obtained with either four 100 mg tablets or one 400 mg tablet, and a 600 mg daily dosage which may be obtained with six 100 mg tablets]

**Approval duration**: 1 year

## DOSAGE/ADMINISTRATION:

**THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.**

**FDA-approved:** bosutinib is indicated for the treatment of: (1) adult and pediatric patients 1 year of age and older with chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML), newly-diagnosed or resistant or intolerant to prior therapy, and (2) adult patients with accelerated phase (AP), or blast phase (BP) Ph+ CML with resistance or intolerance to prior therapy. The recommended dose and schedule of bosutinib in adult patient is 400 mg orally once daily with food for newly diagnosed CML, and 500 mg orally once daily with food for CML with resistance or intolerance to prior therapy. The recommended dose for pediatric patients with newly-diagnosed CML is 300 mg/$m^2$ orally once daily with food, and, for pediatric patients resistant or intolerant to prior therapy, is 400 mg/$m^2$ orally once daily with food. Continue treatment with bosutinib until disease progression or member intolerance. In clinical studies of adult Ph+ CML patients, dose escalation by increments of 100 mg once daily to a maximum of 600 mg once daily was allowed in patients who did not achieve or maintain a hematologic, cytogenetic, or molecular response and who did not have Grade 3 or higher adverse reactions at the recommended starting dosage. In pediatric patients with BSA <1.1 $m^2$ and an insufficient response after 3 months consider increasing dose by 50 mg increments up to maximum of 100 mg above starting dose. Dose increases for insufficient response in pediatric patients with BSA ≥1.1 $m^2$ can be conducted similarly to adult recommendations in 100 mg increments. The maximum dose in

pediatric and adult patients is 600 mg once daily. Swallow tablets whole. Do not cut, crush, break or chew tablets. Capsules may be swallowed whole. For patients who are unable to swallow a whole capsule(s), each capsule can be opened and the contents mixed with applesauce or yogurt. Mixing the capsule contents with applesauce or yogurt cannot be considered a substitute of a proper meal.

**Dose Modifications (Adults)**

- **Hepatic Impairment:** In adult patients with pre-existing mild, moderate, and severe hepatic impairment, the recommended dose of bosutinib is 200 mg daily.
- **Renal Impairment:** In adult patients with pre-existing moderate renal impairment (CrCl 30 to 50 mL/min), the recommended dose of bosutinib is 300 mg daily for new-diagnosed CML and 400 mg daily for previously-treated CML. In adult patients with pre-existing severe renal impairment (CrCl less than 30 mL/min), the recommended dose of bosutinib is 200 mg daily for new-diagnosed CML and 300 mg daily for previously treated CML.
- **Toxicity:**
    - Elevated liver transaminases: If elevations in liver transaminases greater than 5×institutional upper limit of normal (ULN) occur, withhold bosutinib until recovery to less than or equal to 2.5×ULN and resume at 400 mg once daily thereafter. If recovery takes longer than 4 weeks, discontinue treatment. If transaminase elevations greater than or equal to 3×ULN occur concurrently with bilirubin elevations greater than 2×ULN and alkaline phosphatase less than 2×ULN (Hy's law case definition), discontinue treatment.
    - Diarrhea: For NCI CTCAE Grade 3-4 diarrhea (increase of greater than or equal to 7 stools/day over baseline/pretreatment), withhold bosutinib until recovery to Grade less than or equal to 1. Treatment may be resumed at 400 mg once daily.
    - For other clinically significant, moderate or severe non-hematological toxicity, withhold bosutinib until the toxicity has resolved, then consider resuming at a dose reduced by 100 mg taken once daily. If clinically appropriate, consider re-escalating the dose to the starting dose taken once daily. Doses less than 300 mg/day have been used in patients; however, efficacy has not been established.
    - Neutropenia and thrombocytopenia: ANC less than $1,000\times10^6$/L or platelets less than $50,000\times10^6$/L: Withhold bosutinib until ANC greater than or equal to$1,000\times10^6$/L and platelets greater than or equal to $50,000\times10^6$/L. Resume treatment at the same dose if recovery occurs within 2 weeks. If blood counts remain low for greater than 2 weeks, upon recovery, reduce dose by 100 mg and resume treatment. If cytopenia recurs, reduce dose by an additional 100 mg upon recovery and resume treatment. Doses less than 300 mg/day have been used in patients; however, efficacy has not been established.
- Refer the Bosulif product label for dosage adjustment in pediatric patients.

**Drug Availability:** bosutinib is supplied as 100 mg, 400 mg, and 500 mg tablets, and as 50 mg and 100 mg capsules.

## PRECAUTIONS:

**CONTRAINDICATIONS**

- Hypersensitivity to bosutinib.

**WARNINGS**

- **Concomitant Use with CYP3A Inhibitors and Inducers:** Avoid the concomitant use of bosutinib with strong or moderate CYP3A inhibitors **OR** strong CYP3A inducers
    - Strong CYP3A inhibitors - ritonavir, indinavir, nelfinavir, saquinavir, ketoconazole, boceprevir, telaprevir, itraconazole, voriconazole, posaconazole, clarithromycin, telithromycin, nefazodone and conivaptan
    - Moderate CYP3A inhibitors - fluconazole, darunavir, erythromycin, diltiazem, atazanavir, aprepitant, amprenavir, fosamprevir, crizotinib, imatinib, verapamil, grapefruit products and ciprofloxacin
    - Strong CYP3A inducers - rifampin, phenytoin, carbamazepine, St. John's Wort, rifabutin and phenobarbital
- **Gastrointestinal Toxicity:** Diarrhea, nausea, vomiting, and abdominal pain occur with bosutinib treatment. Monitor and manage members using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold dose, dose reduce or discontinue bosutinib as necessary.
- **Myelosuppression:** Thrombocytopenia, anemia and neutropenia occur with bosutinib treatment. Members with CML who are receiving bosutinib should have a complete blood count performed weekly for the first month and then monthly thereafter, or as clinically indicated. To manage myelosuppression, withhold, dose reduce, or discontinue bosutinib as necessary.
- **Hepatic Toxicity:** Bosutinib may cause elevations in serum transaminases (alanine aminotransferase [ALT], aspartate aminotransferase [AST]). Perform at least monthly hepatic enzyme tests for the first three months of treatment with bosutinib and as clinically indicated thereafter. In members with transaminase elevations, monitor liver enzymes more frequently. Withhold, dose reduce, or discontinue bosutinib as necessary.
- **Cardiovascular Toxicity**: Bosutinib can cause cardiovascular toxicity including cardiac failure, left ventricular dysfunction, and cardiac ischemic events. Cardiac failure events occurred more frequently in previously treated patients than in patients with newly diagnosed CML and were more frequent in patients with advanced age or risk factors, including previous medical history of cardiac failure. Cardiac ischemic events occurred in both previously treated patients and in patients with newly diagnosed CML and were more common in patients with coronary artery disease risk factors, including history of diabetes, body mass index greater than 30, hypertension, and vascular disorders. Monitor patients for signs and symptoms consistent with cardiac failure and cardiac ischemia and treat as clinically indicated. Interrupt, dose reduce, or discontinue bosutinib as necessary.
- **Renal Toxicity**: An on-treatment decline in estimated glomerular filtration rate (eGFR) has occurred in patients treated with bosutinib. Monitor patients for renal function at baseline and during therapy.
- **Fluid Retention:** Fluid retention occurs with bosutinib and may manifest as pericardial effusion, pleural effusion, pulmonary edema, and/or peripheral edema. Monitor and manage members using standards of care. Interrupt, dose reduce or discontinue bosutinib as necessary.
- **Embryofetal toxicity:** Based on findings from animal studies and its mechanism of action, bosutinib can cause fetal harm when administered to a pregnant woman. Advise females of reproductive

potential to use effective contraception during treatment and for at least 2 weeks after the last dose.

## BILLING/CODING INFORMATION:

The following codes may be used to describe:

### HCPCS Coding

| | |
|---|---|
| J8999 | Prescription drug, oral, chemotherapeutic, nos |

### ICD-10 Diagnosis Codes That Support Medical Necessity

| | |
|---|---|
| C83.50 – C83.59 | Lymphoblastic (diffuse) lymphoma |
| 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 |
| C94.80 – C94.82 | Other specified leukemias |
| C95.10 – C95.12 | Chronic leukemia of unspecified cell type |
| C96.Z | Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue |
| C96.9 | Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified |

## REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

**Medicare Advantage:** No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

**Medicare Part D:** Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

## DEFINITIONS:

**Accelerated Phase CML:** is a phase of chronic myelogenous leukemia in which the disease is progressing.

**Acute lymphoblastic leukemia:** an aggressive (fast-growing) type of leukemia (blood cancer) in which too many immature white blood cells are found in the blood and bone marrow. Also called acute lymphocytic leukemia and ALL.

**Blast Phase CML:** is the final phase in the evolution of CML, and behaves like an acute leukemia, with rapid progression and short survival.

**Chronic Phase CML:** approximately 85% of members with CML are in the chronic phase at the time of diagnosis. During this phase, members are usually asymptomatic or have only mild symptoms of fatigue, left side pain, joint and/or hip pain, or abdominal fullness.

**Chronic Myelogenous Leukemia (CML):** also known as chronic granulocytic leukemia (CGL), is a cancer of the white blood cells. It is a form of leukemia characterized by the increased and unregulated growth of predominantly myeloid cells in the bone marrow and the accumulation of these cells in the blood.

**Cytogenetic:** is a branch of genetics that is concerned with the study of the structure and function of the cell, especially the chromosomes. It includes routine analysis of G-banded chromosomes, other cytogenetic banding techniques, as well as molecular cytogenetics such as fluorescent in situ hybridization (FISH) and comparative genomic hybridization (CGH).

**Induction Chemotherapy:** the use of drug therapy as the initial treatment for patients presenting with advanced cancer that cannot be treated by other means.

**Philadelphia chromosome or Philadelphia translocation:** is a specific chromosomal abnormality that is associated with chronic myelogenous leukemia (CML).

## RELATED GUIDELINES:

**Allogeneic Bone Marrow and Stem Cell Transplantation, 02-38240-01**
**Nilotinib Capsules (Nilceya and Tasigna) and Tablets (Danziten), 09-J1000-48**
**Oral Oncology Medications, 09-J3000-65**

## OTHER:

### Table 1: CML Risk Scores

| Score | Calculation | Risk Definition by Calculation |
|---|---|---|
| Sokal score | Exp 0.0116 x (age - 43.4) + (spleen size - 7.51) + 0.188 x [(platelet count/700)$^2$ - 0.562] + 0.0887 x (blast cells - 2.10) | • Low: <0.8<br>• Intermediate: 0.8 to 1.2<br>• High: >1.2 |
| Hasford (EURO) score | [0.666 when age ≥50 + (0.042 x spleen size) + 1.0956 when platelet count ≥1,500 x $10^3$/L + (0.0584 x blast | • Low: ≤780<br>• Intermediate: >780 to 1,480 |

| | | |
|---|---|---|
| | cells) + 0.2039 when basophils ≥3% + (0.0413 x eosinophils)] x 1,000 | • High: >1,480 |
| EUTOS long-term survival (ELTS) score | 0.0025 x (age/10)$^3$ + 0.0615 x spleen size + 0.1052 x blasts cells + 0.4104 x (platelet count/1,000)$^{-0.5}$ | • Low: ≤1.5680<br>• Intermediate: >1.5680 to ≤2.2185<br>• High: >2.2185 |

Age is in years. Spleen is in centimeters below the costal margin (maximum distance). Blast cells, eosinophils, and basophils are in percent of peripheral blood differential. All factors must be collected prior to any treatment.

Online calculator for Sokal and Hasford (EURO) scores can be found at:
https://www.leukemia-net.org/content/leukemias/cml/euro__and_sokal_score/index_eng.html

Online calculator for the ELTS score can be found at:
https://www.leukemia-net.org/content/leukemias/cml/elts_score/index_eng.html

## Table 2

| **NCCN Categories of Evidence Consensus** | |
|---|---|
| Category 1 | Based upon high-level evidence; there is uniform NCCN consensus that the intervention is appropriate |
| Category 2A | Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate |
| Category 2B | Based upon lower-level evidence, there NCCN consensus that the intervention is appropriate |
| Category 3 | Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate |

## Table 3

| **Other Compendia** | |
|---|---|
| **Compendium** | **Covered Uses** |
| AHFS-DI | Narrative text is supportive |
| Clinical Pharmacology | Narrative text is supportive |
| Lexicomp | Evidence rating A, B or G |
| Thomson Micromedex DrugDex | Meets requirements for **BOTH** of the following:<br>• Strength of recommendation: Class I (Recommended) or IIa (Recommended, In Most Cases)<br>• Efficacy: Class I (Effective) or IIa (Evidence Favors Efficacy) |
| | |
| AHFS-DI - American Hospital Formulary Service Drug Information | |

## Table 4

| **Lexicomp Recommendation Ratings** |
|---|

| | |
|---|---|
| **A** | Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form (e.g., results of the introduction of penicillin treatment) to support the off-label use. Further research is unlikely to change confidence in the estimate of benefit. |
| **B** | Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate. |
| **C** | Evidence from observational studies (e.g., retrospective case series/reports providing significant impact on patient care), unsystematic clinical experience, or from potentially flawed randomized, controlled trials (e.g., when limited options exist for condition). Any estimate of effect is uncertain. |
| **G** | Use has been substantiated by inclusion in at least one evidence-based or consensus-based clinical practice guideline. |

## Table 5

| **Thomson Micromedex DrugDex Recommendation Ratings: Strength of Recommendation** | | |
|---|---|---|
| **Class I** | Recommended | The given test or treatment has been proven to be useful, and should be performed or administered |
| **Class IIa** | Recommended, in most cases | The given test or treatment is generally considered to be useful and is indicated in most cases. |
| **Class IIb** | Recommended in some cases | The given test or treatment may be useful, and is indicated in some, but not most, cases |
| **Class III** | Not recommended | The given test or treatment is not useful and should be avoided |
| **Class Indeterminate** | Evidence Inconclusive | |

## Table 6

| **Thomson Micromedex DrugDex Recommendation Ratings: Efficacy** | | |
|---|---|---|
| **Class I** | Effective | Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is effective |
| **Class IIa** | Evidence favors efficacy | Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion favors efficacy. |
| **Class IIb** | Evidence is inconclusive | Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion argues against efficacy. |

| | | |
|---|---|---|
| **Class III** | Ineffective | Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is ineffective |

## REFERENCES:


1. Bosulif (bosutinib) [package insert]. Pfizer, Inc. New York (NY): December 2024.
2. Brümmendorf TH, Cortes JE, de Souza CA, et al. Bosutinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukaemia: results from the 24-month follow-up of the BELA trial. Br J Haematol. 2015 Jan;168(1):69-81. doi: 10.1111/bjh.13108. Epub 2014 Sep 8.
3. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2026. Available at: https://www.clinicalkey.com/pharmacology/. Accessed 01/02/26.
4. Cortes JE, Kantarjian HM, Brümmendorf TH, et al. Safety and efficacy of bosutinib (SKI-606) in chronic phase Philadelphia chromosome-positive chronic myeloid leukemia patients with resistance or intolerance to imatinib. Blood. 2011 Oct 27;118(17):4567-76.
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6. Khoury HJ, Cortes JE, Kantarjian HM, et al. Bosutinib is active in chronic phase chronic myeloid leukemia after imatinib and dasatinib and/or nilotinib therapy failure. Blood. 2012 Apr 12;119(15):3403-12.
7. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 01/02/26.
8. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 01/02/26.


## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/14/26.

## GUIDELINE UPDATE INFORMATION:

| | |
|---|---|
| 02/15/13 | New Medical Coverage Guideline. |
| 03/15/14 | Review and revision to guideline; consisting of reformatting position statement, updating dosage/administration, references, program exceptions, and related guidelines. |
| 03/15/15 | Review and revision to guideline; consisting of revising position statement, and updating the description, dosage/administration, and references. |
| 11/01/15 | Revision: ICD-9 Codes deleted. |
| 03/15/16 | Review and revision to guideline consisting of description, position statement, definitions, and references. |
| 03/15/17 | Review and revision to guideline consisting of removal of the age requirement and acute lymphoblastic leukemia (ALL) indication in the position statement, and updates to description section, dosage/administration section, precautions section, billing/coding section, definitions, and references. |

| | |
|---|---|
| 02/15/18 | Review and revision to guideline consisting of updates to description, dosage/administration, position statement, billing/coding, other, and references sections. |
| 02/15/19 | Review and revision to guideline consisting of updates to description, position statement, definitions, and references sections. |
| 02/15/20 | Review and revision to guideline consisting of updates to the description, warnings/precautions, billing/coding, and references. |
| 02/15/21 | Review and revision to guideline consisting of updates to the description, position statement, precautions, other section, related guidelines, and references. |
| 02/15/22 | Review and revision to guideline consisting of updates to the description, precautions, and references. |
| 02/15/23 | Review and revision to guideline consisting of updates to the related guidelines and references. |
| 02/15/24 | Review and revision to guideline consisting of updates to the description, position statement, dosage/administration, and references. Bosutinib is now FDA approved in certain pediatric populations, and 50 and 100 mg capsules are now available. |
| 03/15/24 | Revision to guideline consisting of updates to the position statement related to the maximum number of capsules or tablets permitted per day, and a new requirement that the 100 mg capsule may only be used for members unable to swallow a whole tablet. |
| 02/15/25 | Review and revision to guideline consisting of updates to the references. |
| 02/15/26 | Review and revision to guideline consisting of updates to the position statement, related guidelines, and references. For newly treated, chronic-phase CML, the step requirement was expanded to two products (vs. one). |