**PRODUCT DESCRIPTION**

BOSULIF® (bosutinib) is an oral, once-daily, tyrosine kinase inhibitor (TKI) which inhibits the Bcr-Abl kinase that promotes chronic myelogenous leukemia (CML); it is also an inhibitor of Src-family kinases.¹

BOSULIF is approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with chronic phase, accelerated phase or blast phase Philadelphia chromosome positive (Ph+) CML with resistance, or intolerance to prior therapy.¹

**RATIONALE**

Chronic myelogenous leukemia is one of four types of leukemia, with almost 6,000 new cases diagnosed per year in the U.S.⁵ Approximately 34,000 people are living with CML in the U.S.³,⁴ Treatment is usually chronic but not curative. Multiple alternative treatment options are needed as approximately one in three patients may not respond, may develop drug-resistant disease or may not be able to tolerate their therapy during the course of treatment.⁵,⁶

**MECHANISM OF ACTION**

The Philadelphia Chromosome, a hallmark abnormal chromosome of CML, initiates a series of events leading to the development of Bcr-Abl, a tyrosine kinase that causes CML cells to reproduce rapidly.² BOSULIF, an inhibitor of both Abl and Src kinases, disrupts signaling in CML cells that allows the cells to grow, survive and reproduce.¹,⁷

**STUDY 200**

The U.S. approval of BOSULIF was based on data from Study 200, a global, single arm, open-label, multi-cohort, Phase 1/2 study, which investigated the use of BOSULIF in 546 patients with Ph+ CML. The study had separate cohorts for patients in the chronic phase previously treated with imatinib; the chronic phase previously treated with imatinib followed by nilotinib and/or dasatinib; and the accelerated and blast phases previously treated with at least imatinib.¹

Results of the study demonstrated:¹

- The major cytogenetic response (MCyR) at 24 weeks for patients with chronic phase CML who had been previously treated with imatinib only (n=266) was 33.8 percent (95% CI: 28.2, 39.9). With a minimum follow-up of 23 months, 53.4 percent of patients achieved a MCyR. At the time of this analysis, the median duration of MCyR was not reached. Of patients who achieved MCyR, 52.8 percent had a MCyR lasting at least 18 months.
- The MCyR by 24 weeks for patients with chronic phase CML who had been treated with imatinib and at least one other TKI (n=108) was 26.9 percent (95% CI: 18.8, 36.2). With a minimum follow-up of 13 months, 32.4 percent of patients achieved a MCyR. At the time of this analysis, the median duration of MCyR was not reached. Of patients who achieved MCyR, 51.4 percent had a MCyR lasting at least nine months.
- A low rate of transformation (4 percent, n=16) from the chronic phase to the accelerated or blast phase was also observed in patients treated with BOSULIF.
- In Study 200, the most common all grade adverse reactions (ARs) observed in patients in the chronic phase included diarrhea (84 percent), nausea (46 percent), abdominal pain (40 percent), thrombocytopenia (40 percent) and vomiting (37 percent). Grade 3/4 ARs included thrombocytopenia (26 percent), neutropenia (11 percent), diarrhea (9 percent), anemia (9 percent) and rash (8 percent).

**PATIENT ACCESS TO BOSULIF IN THE U.S.**

Pfizer believes eligible patients should have access to a range of support services, including insurance counseling, co-pay assistance, and access to medicines for free or at a savings.

In the U.S., Pfizer offers BOSULIF STEPS, a support program created specifically for patients who are prescribed BOSULIF. The goal of BOSULIF STEPS is to provide patients with important information they can use throughout each step of their treatment.

Patients can visit [www.BOSULIF.com](http://www.BOSULIF.com) or call Pfizer RxPathways at 1-866-706-2400 to learn more.
**Contraindication:** Hypersensitivity to BOSULIF. Anaphylactic shock occurred in less than 0.2% of treated patients.

**Gastrointestinal Toxicity:** Diarrhea, nausea, vomiting, and abdominal pain can occur. In the clinical trial, median time to onset for diarrhea was 2 days, median duration was 1 day, and median number of episodes per patient was 3 (range 1-221). Monitor and manage patients using standards of care, including antidiarrheals, antiemetics, and/or fluid replacement. Withhold, dose reduce, or discontinue BOSULIF as necessary.

**Myelosuppression:** Thrombocytopenia, anemia, and neutropenia can occur. Perform complete blood counts weekly for the first month and then monthly or as clinically indicated. Withhold, dose reduce, or discontinue BOSULIF as necessary.

**Hepatic Toxicity:** Twenty percent of patients experienced an increase in either ALT or AST. Liver enzyme elevation usually occurs early in treatment. Perform hepatic enzyme tests monthly for the first 3 months and as clinically indicated. In patients with transaminase elevations, monitor liver enzymes more frequently. Drug-induced liver injury has occurred. Withhold, dose reduce, or discontinue BOSULIF as necessary. In patients with mild, moderate, and severe hepatic impairment, the recommended starting dose is 200 mg daily.

**Renal Toxicity:** An on-treatment decline in estimated glomerular filtration rate has occurred in patients treated with BOSULIF. Monitor renal function at baseline and during therapy, with particular attention to patients with preexisting renal impairment or risk factors. Consider dose adjustment in patients with baseline and treatment emergent renal impairment. The recommended starting doses for patients with severe renal impairment (CrCL<30 mL/min) or moderate renal impairment (CrCL 30-50 mL/min) are 300 mg and 400 mg daily, respectively.

**Fluid Retention:** Fluid retention can occur and may cause pericardial effusion, pleural effusion, pulmonary edema, and/or peripheral edema. Monitor and manage patients using standards of care. Interrupt, dose reduce, or discontinue BOSULIF as necessary.

**Embryofetal Toxicity:** BOSULIF may cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be advised of potential hazard to the fetus and to avoid becoming pregnant while receiving BOSULIF.

**Adverse Reactions:** The most common adverse reactions observed in greater than 20% of patients in the Phase 1/2 safety population (N=546) were diarrhea, nausea, thrombocytopenia, vomiting, abdominal pain, rash, anemia, pyrexia, and fatigue. The most common Grade 3/4 adverse reactions and laboratory abnormalities observed in greater than 10% of patients were thrombocytopenia, anemia, and neutropenia.

**CYP3A Inhibitors and Inducers:** Avoid concurrent use with strong or moderate CYP3A inhibitors or inducers.

**Proton Pump Inhibitors:** Consider using short-acting antacids or H2 blockers instead of PPIs. Separate antacid or H2 blocker dosing and BOSULIF dosing by more than 2 hours.

**Substrates of P-glycoprotein:** BOSULIF may increase the plasma concentrations of drugs that are P-gp substrates, such as digoxin.

**Nursing Mothers:** Given the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or BOSULIF.

For more information, please see the BOSULIF Patient Information and full Prescribing Information.