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NCCN Guidelines Panel: Chronic Myeloid Leukemia

Dear NCCN CML Panel Members:

On behalf of Pfizer Oncology, I respectfully request the NCCN Guideline Panel for Chronic Myeloid Leukemia (CML) to review the enclosed information for inclusion of BOSULIF (bosutinib) as a treatment option for patients with newly diagnosed Chronic Phase (CP) Ph+ CML.

**Specific Changes Requested:** Recommend the addition of BOSULIF (bosutinib) as a treatment option for newly diagnosed CP Ph+ CML patients.

**FDA Clearance:** On December 19<sup>th</sup> 2017, FDA approved BOSULIF (bosutinib) for Newly-diagnosed chronic phase Ph+ CML. This indication is approved under accelerated approval based on molecular and cytogenetic response rates. Continued approval for this indication may be contingent upon verification and confirmation of clinical benefit in an ongoing long-term follow up trial.

**Rationale:** The efficacy of BOSULIF in patients with newly-diagnosed chronic phase Ph+ CML was evaluated in the **B**osutinib trial in **F**irst-line chr**O**nic myelogenous leukemia **tRE**atment (BFORE) Trial [NCT02130557]: "A Multicenter Phase 3, Open-Label Study of Bosutinib Versus Imatinib in Adult Patients With Newly Diagnosed Chronic Phase Chronic Myelogenous Leukemia". BOSULIF (bosutinib) 400mg once daily demonstrated higher rate of MMR at 12 months (Primary Endpoint) and CCyR by 12 months (Key Secondary Endpoint) over imatinib 400mg once daily.

**The following resources are submitted along with this letter in support of this requested change:**

1. BOSULIF (bosutinib) prescribing information. Pfizer Inc.
2. Cortes J et al. Bosutinib Versus Imatinib for Newly Diagnosed Chronic Myeloid Leukemia: Results From the Randomized BFORE Trial. *J Clin Oncol.* 2017 Nov 1. DOI: 10.1200/JCO.2017.74.7162



The basis of the approval was based on the 12 months analysis data for BFORE trial. The trial was conducted to evaluate the efficacy and safety of bosutinib 400 mg once daily alone compared with imatinib 400 mg once daily alone in adult patients with newly diagnosed Ph+ CP CML. The trial randomized 536 patients (268 in each arm) with Ph+ or Ph- newly-diagnosed CP CML (Intent-to-treat population). The primary endpoint analysis was based on modified intent-to-treat (mITT) population consisting of 487 patients with Ph+ CML with typical BCR-ABL1 transcript types (e2a2 and/or e3a2) at baseline and baseline BCR-ABL copies >0.

The primary efficacy endpoint for the study was rate of MMR at 12 months. In the mITT population of those receiving bosutinib (n=246), 47.2% achieved MMR at 12 months compared to 36.9% in patients receiving imatinib (n=241) (P=0.0200). CCyR by 12 months was achieved for 77.2% of patients receiving bosutinib versus 66.4% receiving imatinib (P=0.0075). After a minimum of 12 months of follow-up, 5 bosutinib patients and 7 imatinib patients transformed to AP CML or BP CML while on treatment.

Adverse reactions reported for greater than or equal to 20% of bosutinib patients with newly-diagnosed CML (N=268) were diarrhea (70%), nausea (35%), thrombocytopenia (35%), rash (34%), increased ALT (31%), abdominal pain (25%), and increased AST (23%). Grade 3 or higher TEAEs occurred in 56.3% of patients receiving bosutinib, most commonly ( $\geq 10\%$ ) ALT increase (19.0%) and thrombocytopenia (13.8%).

We greatly appreciate the Panel's thorough consideration of the data for BOSULIF (bosutinib) for the treatment of patients with newly diagnosed Chronic Phase Ph+ CML.

Sincerely,  
Fiona

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