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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: The submitted use is not approved by the FDA. The supplemental New Drug Application (sNDA) for BOSULIF (bosutinib) for frontline CML use has been accepted for filing and granted Priority Review by FDA. The Prescription Drug User Fee Act (PDUFA) goal date for a decision by the FDA is in December 2017.

Rationale: 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 in a Phase 3 open label, 2-arm, multi-center global trial (BFORE).

The following resources are submitted in support of this requested change:

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*

Cortes BFORE study_JCO_Nov 1 20

BFORE 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. This study enrolled 536 patients with newly diagnosed CP CML. 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 (e13a2 and/or e14a2).

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=0.02). CCyR by 12 months was achieved for 77.2% of patients receiving bosutinib versus 66.4% receiving imatinib (P=0.0075).

Cumulative incidence was favorable with bosutinib (MMR: hazard ratio, 1.34; P=0.0173; CCyR: hazard ratio, 1.38; P=0.001), with earlier response times. Four patients (1.6%) receiving bosutinib and six patients (2.5%) receiving imatinib experienced disease progression to accelerated/blast phase.

The most common Treatment Emergent Adverse Events (TEAEs) of any grade (≥20%) in the bosutinib group were diarrhea (70.1%), nausea (35.1%), thrombocytopenia (35.1%), increased ALT (30.6%), and increased AST (22.8%). Grade 3 or higher TEAEs occurred in 56.3% of patients receiving bosutinib, most commonly (≥10%) ALT increase (19.0%) and thrombocytopenia (13.8%).

We 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

Fiona An, MD
Senior Director, US Medical Affairs
Pfizer Inc.