

Submitted by:  
Awny Farajallah, MD, FACP  
Vice President, Head US Medical Oncology  
Bristol-Myers Squibb Company  
777 Scudders Mill Road  
Plainsboro, NJ 08536  
609-897-3945; awny.farajallah@bms.com  
April 21, 2016

**NCCN Guidelines® Panel: Multiple Myeloma**

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed, recently published data on the use of elotuzumab in combination with bortezomib and dexamethasone as a treatment option for previously treated multiple myeloma for the Panel's consideration.<sup>1</sup>

These data are being submitted in response to a standing request from NCCN for new clinical data.

**FDA Clearance:**

On November 30, 2015, the FDA approved EMPLICITI™ (elotuzumab) in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.<sup>2</sup> An initial analysis of data from a non-registrational study on the use of elotuzumab in combination with bortezomib and dexamethasone was also submitted to the FDA for consideration as part of the initial FDA filing of elotuzumab in combination with lenalidomide and dexamethasone and was not included in the final approval.

**Rationale:** Survival data, including an extended 2-year follow-up, on the use of elotuzumab plus bortezomib and dexamethasone (EBd) versus bortezomib and dexamethasone (Bd) in patients with previously treated multiple myeloma have been published in Blood.<sup>1</sup> In this open-label, phase 2 study, patients were randomized 1:1 to receive either EBd or Bd, until disease progression or unacceptable toxicity.

**Efficacy findings, highlights**

- Results of the interim analysis, demonstrated a 28% reduction in risk of disease progression or death for patients in the EBd arm compared to patients in the Bd arm (HR, 0.72; 70% CI, 0.59-0.88), which is statistically significant. Median PFS was 9.7 months vs. 6.9 months in the EBd and Bd treatment arms, respectively.
- PFS rates at 1-year for EBd vs Bd, respectively, were 39% (95% CI, 28% to 50%) versus 33% (95% CI, 22% to 44%)
- At the 2 year follow-up, EBd continued to show an efficacy benefit compared to Bd alone with a 24% relative risk reduction in PFS (HR, 0.76; 70% CI, 0.63-0.91). These results were statistically significant.
- 2-year PFS rates were 18% (95% CI, 10% to 28%) for EBd versus 11% (95% CI, 5% to 20%) for Bd

**Safety findings, highlights**

- Adverse events (AEs) were comparable across treatment arms and were reported in 75 (100%) patients and 72 (96%) patients in the EBd and Bd treatment arms, respectively
- Grade 3 to 4 AEs were reported in 53 (71%) patients with EBd versus 45 (60%) with Bd. The most common grade 3 or higher AEs were infections [EBd, n=16 (21%); Bd, n=10 (13%)] and thrombocytopenia [EBd, n=7 (9%); Bd, n=13 (17%)]
- Serious AEs were reported in 51% of patients treated with EBd and 41% of patients treated with Bd.
- Grade 1-2 infusion reactions occurred in 4 patients in the EBd arm. There were no discontinuations due to infusion reactions.

The following resources are submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications/presentations.

1. Jakubowiak A, Offidani M, Pegourie B, et al. Randomized phase 2 study of elotuzumab plus bortezomib/dexamethasone (Bd) versus Bd for relapsed/refractory multiple myeloma. *Blood*. 2016. DOI 10.1182/blood-2016-01-694604
2. EMPLICITI™ Prescribing Information. Bristol-Myers Squibb Company, Princeton, NJ; 2015.

Thank you for your consideration of this request.

Sincerely,

A handwritten signature in black ink, appearing to read "Awny Farajallah". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Awny Farajallah, MD, FACP  
Vice President, Head US Medical Oncology  
Bristol-Myers Squibb Company