Submitted by:
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Dear NCCN Multiple Myeloma Guidelines Panel:

On behalf of Bristol Myers Squibb, we respectfully request the NCCN Multiple Myeloma Guidelines Panel review the enclosed data regarding the use of Empliciti®(elotuzumab) in patients with relapsed and refractory multiple myeloma (RRMM).

Specific Changes:

We respectfully request the panel's consideration of the enclosed data to update the recommendation of elotuzumab in combination with pomalidomide and dexamethasone (EPd) from Other Recommended Regimens for Early Relapses (1-3 prior therapies), Category 2A to Preferred Regimens for Early Relapses (1-3 prior Therapies), Category 1 for previously treated multiple myeloma [MYEL-G 3 of 4] as well as the respective Discussion section (Page MS-34).

FDA Clearance:

EMPLICITI®(elotuzumab) is a SLAMF7-directed immunostimulatory antibody indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor (PI).[1]

Rationale:

Despite treatment advances for RRMM, new therapies that improve overall survival (OS) are still needed, especially in those patients' that have received and are refractory to lenalidomide (LEN) and a PI.[2] Elotuzumab is a humanized IgG1 monoclonal antibody that specifically targets the SLAMF7 (Signaling Lymphocytic Activation Molecule Family member 7) protein; and when combined with pomalidomide offers a treatment option for these LEN-exposed patients.[1,3] The summary below demonstrates both significant improvement in progression-free survival (PFS) and OS data with EPd in patients who received ≥ 2 lines of therapy including LEN and PI.

This data is being submitted in response to a standing request from NCCN for new data.

On behalf of Bristol Myers Squibb, we request the NCCN Panel to review data recently presented at the 18th International Myeloma Workshop (IMW) 2021 Meeting regarding the use of EMPLICITI® in RRMM.

Dimopoulos et al. reported the final analysis of OS results from the ELOQUENT-3 Study (NCT 02654132), an open-label, international, multicenter, randomized phase II study investigating the use of EPd [n=60] vs Pd [n=57] in patients with RRMM and ≥ 2 prior therapies including LEN and a PI.[4]

Baseline characteristics were similar across treatment groups with patients receiving a median of 3 (2-8) prior lines of therapy. Majority of patients received LEN as previous therapy (98% EPd vs 100% Pd) while 100% received a PI across both treatment groups with 68% EPd vs 72% Pd patients, refractory to both. The primary endpoint, previously reported, was significantly improved PFS (10.3 months EPd vs 4.7 months Pd, *P* = 0.008).[3]

At final analysis (data cutoff January 11, 2021, minimum follow up 45 months) there were 61.7% and 74.5% deaths reported across the EPd and Pd groups, respectively with disease progression being the most common cause (41.7% EPd and 49.1% Pd).

- Median OS was significantly improved:
  - EPd, 29.8 mo, [95% CI, 22.9-45.7] vs Pd, 17.4 mo [95% CI, 13.8–27.7]), hazard ratio (HR) of 0.59 (95% CI, 0.37–0.93; 2-sided stratified log-rank *P* = 0.0217),
  - 41% reduction in the risk of death with EPd
  - 1-year increase in median OS
- OS rates were higher with EPd than Pd at 1, 2 and 3 years (79% vs 68%), (63% vs 44%) and (39% vs 29%), respectively.

No new safety signals were detected, and the safety profile was consistent with previous reports. Adverse events (AEs) leading to discontinuation occurred in 18.3% and 23.6% of EPd vs Pd groups, respectively. Secondary primary malignancies (SPMs) occurred in 4 patients in the EPd group and 2 in the Pd group.

	EPd (%)	Pd (%)
Any AEs Any Grade	96.7	96.4
Most frequent treatment-related AEs		
Neutropenia	20.0	21.8
Hyperglycemia	20.0	12.7
Any AEs Grade 3/4	60.0	61.8
Grade 3/4 infections	25.5	21.8
Grade 5 AEs	13.3	20.0

Your consideration of this submission is greatly appreciated.

Sincerely,

Kaleen Barbary, PharmD
Director| Worldwide Scientific Content & US Market Capabilities- Hematology/Cell Therapy

Fiona An, MD
Executive Director | US Medical Hematology

References:

1. EMPLICITI [package insert]. Princeton, NJ: Bristol-Myers Squibb Company. October 2019.
2. Moreau P, Zamagni E, Mateos MV, et al. Treatment of patients with multiple myeloma progressing on frontline-therapy with lenalidomide. Blood Cancer Journal (2019) 9:38.

3. Dimopoulos MA, Dytfeld D, Grosicki S et al. Elotuzumab plus pomalidomide and dexamethasone for multiple myeloma. N Engl J Med 2018;379:1811-1822.
4. Dimopoulos MA, Dytfeld D, Grosicki S, et al. Elotuzumab plus pomalidomide and dexamethasone for relapsed/refractory multiple myeloma: final overall survival from the phase 2, randomized ELOQUENT-3 study. Poster presented at: the 18th International Myeloma Workshop (IMW); September 8-11, 2019; Vienna, Austria. P-193.