Submitted by:
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Date of Request: October 20, 2016

Dear NCCN Multiple Myeloma Guidelines Panel:

On behalf of Celgene Corporation, we respectfully request the NCCN Guidelines Panel for Multiple Myeloma review recently *published* data on the use of REVLIMID® (lenalidomide) in combination with daratumumab and dexamethasone for patients with previously treated multiple myeloma.

Specific Changes:
As an update to a previous submission dated June 20, 2016, we respectfully request the addition of daratumumab/lenalidomide/dexamethasone as a preferred regimen in patients with previously treated myeloma with a Category 1 recommendation. In addition, we request an update to the Discussion section (page MS-32) to reflect the latest Phase 3 publication.

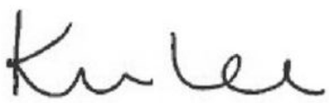
FDA Clearance: REVLIMID is a thalidomide analogue indicated for the treatment of patients with MM in combination with dexamethasone. Please see the enclosed REVLIMID Prescribing information (Celgene Corporation, 2015).

Rationale for Proposed Change:
The following previously submitted data was recently published. An open-label, multicenter, randomized Phase III study (POLLUX) evaluated daratumumab plus lenalidomide and dexamethasone (DRd) vs. lenalidomide and dexamethasone (Rd) in patients with relapsed/refractory multiple myeloma (RRMM) (Dimopoulos et al., 2016).

Treatment of DRd significantly reduced the risk of progression or death by 63% compared with Rd (HR=.37; 95% CI, 0.27-0.52; *P*<.001). With DRd vs. Rd, respectively, median PFS was not estimable vs. 18.4 months and 12-month PFS was 83.2% vs. 60.1%. A treatment benefit of DRd vs. Rd was observed across all sub-groups and was consistent regardless of prior lenalidomide exposure. The 12-month OS was 92.1% with DRd vs. 86.8% with Rd. Median duration of response was not reached with DRd and 17.4 months with Rd. Most common (≥5% in either arm) Grade 3/4 AEs occurring with DRd vs. Rd, respectively, included neutropenia (51.9% vs. 37.0%), febrile neutropenia (5.7% vs. 2.5%), anemia (12.4% vs. 19.6%), thrombocytopenia (12.7% vs. 13.5%), lymphopenia (5.3% vs. 3.6%), infections (28.3% vs. 22.8%), pneumonia (7.8% vs. 8.2%), diarrhea (5.3% vs. 3.2%) and fatigue (6.4% vs. 2.5%). Serious adverse events occurred in 48.8% of DRd and 42.0% of Rd patients, most commonly as pneumonia (8.1% vs. 8.5%, respectively). SPMs occurred in 2.8% of DRd and 3.6% of Rd patients.

A copy of the full publication of this study is enclosed for your review. Your consideration of this submission is greatly appreciated.

Sincerely,



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Executive Director Hematology, US Medical Affairs

CITED REFERENCES:

1. Celgene Corporation. Revlimid (lenalidomide). *Summit, NJ*. 2015; http://www.revlimid.com/.
2. Dimopoulos MA, Oriol A, Nahi H, et al. Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma. . *N Engl J Med* . 2016;375(14):1319-1331. http://www.ncbi.nlm.nih.gov/pubmed/27705267.