Submitted by:
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Dear NCCN Multiple Myeloma Guidelines Panel Members:

On behalf of Bristol-Myers Squibb Company, we respectfully request the NCCN Guidelines Panel for Multiple Myeloma review data recently published in the Journal of Clinical Oncology, from the Phase III ECOG-E3A06 study (NCT01169337) on the use of lenalidomide (REVLIMID®) versus observation in patients with smoldering multiple myeloma (SMM).

Specific Changes:

We request an update within the guidelines to reflect the results from the Phase III study of lenalidomide versus observation in patients with asymptomatic intermediate or high-risk SMM, described below (Lonial et al., 2019).

FDA Clearance:

REVLIMID® is a thalidomide analogue indicated for the treatment of adult patients with multiple myeloma in combination with dexamethasone and as maintenance therapy in patients with multiple myeloma following autologous hematopoietic stem cell transplantation. Please see the enclosed full Prescribing Information for approved indications (Celgene Corporation).

Lenalidomide is not approved by the FDA for the treatment of patients with SMM.

Rationale for Proposed Change:

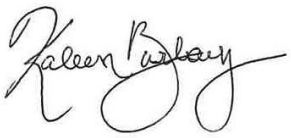
This open-label, randomized, multicenter, Phase III study evaluated lenalidomide 25 mg on days 1 to 21 of a 28-day cycle (n=90) vs. observation (n=92) in patients with asymptomatic intermediate or high-risk SMM (median age 64 years), until disease progression or toxicity or withdrawal for other reasons (Lonial et al., 2019). The primary endpoint was progression-free survival (PFS) defined as the time from randomization to development of symptomatic multiple myeloma as per the American Society of Hematology/US Food and Drug Administration panel consensus. Other assessments included response, toxicity, secondary primary cancers (SPC), and health related quality of life.

Median follow up was 35 months. One-, 2- and 3-year PFS was 98%, 93%, and 91% for lenalidomide arm, and 89%, 76%, and 66% for the observation arm; (HR 0.28 [95% CI 0.12 – 0.62]; *P*=0.002). Patient response rates among lenalidomide treated patients (n=88) included ≥VGPR 4.5% (95% CI 1.2% – 11.2%) and ≥PR 50.0% (95% CI 39.1% – 60.8%). Median time to response was 5 (range, 1-23) months. There were no responses in the observation arm.

Among lenalidomide treated patients, grade 3 or 4 non-hematologic adverse events were reported in 25 patients (28.4%); grade 3 or 4 hematologic and non-hematologic adverse events were reported in 36 patients (40.9%). The 3-year cumulative incidence of total SPC was 11.0% for lenalidomide and 4.8% for observation. Six deaths occurred, 2 in lenalidomide arm and 4 in the observation arm, (HR 0.46 [95% CI, 0.08 to 2.53]).

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

Sincerely,



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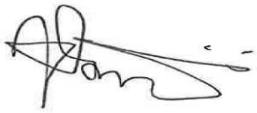

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REFERENCES

1. Celgene Corporation. Revlimid (lenalidomide) [Package Insert]. Summit, NJ: Celgene Corporation. http://www.revlimid.com/.
2. Lonial S, Jacobus S, Fonseca R, et al. Randomized Trial of Lenalidomide Versus Observation in Smoldering Multiple Myeloma. *J Clin Oncol*. 2019. http://www.ncbi.nlm.nih.gov/pubmed/31652094.

Revlimid ® is a registered trademark of Celgene Corp