Submitted by:
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Dear NCCN B-Cell Lymphoma Guidelines Panel:

On behalf of Celgene Corporation, we respectfully request that the NCCN Guidelines Panel for B-Cell Lymphoma review the enclosed, recently presented data regarding the use of REVLIMID® (lenalidomide) in combination with rituximab in patients with relapsed/refractory follicular or marginal zone lymphoma.

Specific Changes:
We respectfully request updating the recommendation for the lenalidomide + rituximab combination to a Category 1, preferred regimen for second-line and subsequent therapy in follicular lymphoma.

FDA Status:
REVLIMID is not approved for the treatment of follicular or marginal zone lymphoma. Please see the enclosed full Prescribing Information.

Rationale:
In support of the proposed change, results from the phase III clinical study (AUGMENT) evaluating the efficacy and safety of lenalidomide plus rituximab (R^2) compared to rituximab-placebo (control) in patients with relapsed/refractory follicular or marginal zone lymphoma (n=358) are enclosed for your review. In the R^2 arm, patients received oral REVLIMID 20 mg daily on Days 1-21 every 28 days for 12 cycles and intravenous rituximab 375 mg/m^2 weekly in Cycle 1 and Day 1 of Cycles 2-5. Patients in the control arm received rituximab and placebo on the same schedule.

The study met its primary endpoint of progression-free survival (PFS) at median follow-up of 28.3 months (HR [95% CI]: 0.46 [0.34-0.62]; P<0.0001). Median PFS was 39.4 months and 14.1 months for R^2 and control arms, respectively. Overall response rate was observed in 78% and 53% of patients (P<0.0001) for R^2 and control, respectively.

Complete response was observed in 34% of patients treated with R^2 vs 18% of patients in the control arm (*P*=0.001). Grade 3/4 treatment-emergent adverse events (TEAEs) were reported in 69% and 32% of patients in the R^2 and control arms, respectively. More frequent Grade 3/4 TEAEs in the R^2 vs control arms were attributable to increased neutropenia (50% and 13%) and leukopenia (7% and 2%), respectively. Grade 5 TEAEs were reported in 2 patients in each arm. At the time of analysis, 16 and 26 deaths were reported in the R^2 and control arms, respectively.

A copy of the phase III data presentation and the REVLIMID Prescribing Information are enclosed for your review. Your consideration of this submission is greatly appreciated.

Sincerely,

Arpit Shah, PharmD
Sr. Manager, Global Medical Information

Kenneth Foon, MD
Vice President, Global Medical Affairs, Lymphoma

Reference List:

1. Leonard JP, Trneny M, Izutsu K, et al. AUGMENT: A Phase III Randomized Study of Lenalidomide Plus Rituximab (R^2) vs Rituximab/Placebo in Patients with Relapsed/Refractory Indolent Non-Hodgkin Lymphoma [Oral]. Presented at: 60th Annual Meeting & Exposition of the American Society of Hematology (ASH); December 1-4, 2018; San Diego, CA, USA.