Submitted by:
Arpit Shah, PharmD
Sr. Manager, Global Medical Information
Celgene Corporation
86 Morris Ave
Summit, New Jersey 07901
Phone: 908-679-7870
Email: arpshah@celgene.com
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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 recently presented data regarding the use of REVLIMID® (lenalidomide) in combination with rituximab in previously untreated patients with follicular lymphoma.

Specific Changes:
We respectfully request updating the recommendation for the lenalidomide + rituximab combination treatment regimen to a Category 2A, preferred first-line therapy for follicular lymphoma (Grade 1-2).

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

Rationale:
In support of the proposed change, results from the phase III clinical study evaluating the efficacy and safety of lenalidomide plus rituximab (R^2) compared to rituximab plus chemotherapy (R-chemotherapy) followed by rituximab maintenance in patients with previously untreated follicular lymphoma (n=1030) are enclosed for your review. In the R^2 arm, patients received REVLIMID 20 mg on Days 2-22 every 28 days for up to 12 cycles; responding patients after 6 cycles then received REVLIMID 10 mg on Days 2-22 every 28 days for a total of 18 cycles. Rituximab 375 mg/m^2 was administered on Days 1, 8, 15, and 22 of Cycle 1, Day 1 of Cycles 2 to 6; responding patients continued with 375 mg/m^2 rituximab every 8 weeks for 12 cycles. Patients in the R-chemotherapy arm received one of the following: rituximab-CHOP (72%), rituximab-bendamustine (23%) or rituximab-CVP (5%); responding patients continued with 375 mg/m^2 rituximab every 8 weeks for 12 cycles.

Superiority for R^2 compared to R-chemotherapy was not met for the co-primary efficacy endpoints of complete response or unconfirmed complete response (CR/CRu) at 120 weeks and interim progression-free survival (PFS). An analysis of the data found 48% of patients in the R^2 arm and 53% of those receiving R-chemotherapy maintained CR/CRu 120 weeks after randomization (*P*=0.13), with a 3-year estimated interim PFS rate of 77% and 78% (*P*=0.48, HR [95% CI]: 1.10 [0.85-1.43]), respectively. Grade 3/4 neutropenia based on laboratory tests (32% vs 50%), Grade 3/4 febrile neutropenia (2% vs 7%) and Grade 3/4 cutaneous events (7% and 1%) were reported in the R^2 vs R-chemotherapy arms, respectively. Second primary malignancies were reported in 7% and 10% of patients in the R^2 and R-chemotherapy arms, respectively. Grade 5 treatment emergent adverse events were observed in 1% of each treatment arm.

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, Lymphoma Scientific Collaborations

Reference List:

1. Fowler NH, Morschhauser F, Feugier P, et al. RELEVANCE: Phase III Randomized study of lenalidomide plus rituximab (R^2) versus chemotherapy plus rituximab, followed by rituximab maintenance, in patients with previously untreated follicular lymphoma (FL) [Oral]. Presented at: 54th Annual Meeting of the American Society of Clinical Oncology (ASCO); June 1-5, 2018; Chicago, IL, USA.