



Submitted by:

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Dear NCCN Non-Hodgkin's Lymphoma Guidelines Panel Members:

On behalf of Celgene Corporation, we respectfully request that the NCCN Guidelines Panel for Non-Hodgkin's Lymphoma (NHL) review recently presented data regarding the use of REVLIMID® (lenalidomide) in combination with rituximab as first line therapy in patients with follicular lymphoma (FL).

Specific Changes: Recommend the use of lenalidomide in combination with rituximab as a suggested treatment regimen for FL (Grade 1-2) as first line therapy. In addition, we respectfully request an update to the discussion (MS-76) surrounding first-line therapies for FL to reflect the recently presented results.

FDA Clearance: The FDA has not approved lenalidomide for the treatment of FL. Lenalidomide is indicated for the treatment of (Revlimid Prescribing Information):

- Patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib
- Multiple myeloma, in combination with dexamethasone, in patients who have received at least one prior therapy
- Patients with transfusion-dependent anemia due to low- or intermediate-1 risk myelodysplastic syndromes (MDS) associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities

Rationale:

A multi-center, single-arm, Phase II Alliance/Cancer and Leukemia Group B (CALGB) study of lenalidomide in combination with rituximab in previously untreated patients with Grade 1-3a FL was recently presented at the 12th *International Conference on Malignant Lymphoma* on June 20, 2013 (Martin et al. 2013b). This study evaluated lenalidomide 20 mg/day (with the potential to increase to 25 mg/day) on Days 1-21 of each 28-day cycle for 12 planned cycles plus rituximab 375 mg/m² weekly for 4 weeks during Cycle 1 and then on Day 1 of Cycles 4, 6, 8 and 10. Overall response was observed in 53 of 57 evaluable patients (93%) with 72% complete response (CR) and 21% partial response (PR). Neutropenia was the most commonly reported Grade 3/4 hematologic adverse event (AE; 20%) (Martin et al. 2013a). Non-hematologic AEs included Grade 2 thromboembolism (n=2) and Grade 3 rash (n=5), tumor lysis (n=2) and febrile neutropenia (n=1). There were no cases of Grade 4 non-hematologic AEs, second malignancies or tumor flare (Martin et al. 2013b).

This Alliance/CALGB study corroborated the findings of the single-center, single-arm, Phase II study of lenalidomide in combination with rituximab in patients with previously untreated, Stage III or IV indolent NHL, already described within the guidelines (Fowler et al. 2012).

Your consideration of this submission is greatly appreciated.

Please note that a copy of the recently presented data described above (Martin et al. 2013b) will be submitted separately as permission to distribute is obtained.

Sincerely,



Anjali Shah, PharmD
Sr. Manager, Global Medical Information



Ken Foon, MD
Vice President, Global Medical Affairs Disease Lead

Cited References:

1. Fowler NH, Neelapu SS, Hagemeister FB, et al. Lenalidomide and Rituximab for Untreated Indolent Lymphoma: Final Results of a Phase II Study [oral]. *Oral presented at: 54th Annual Meeting of the American Society of Hematology (ASH)* 2012; December 8-11; Atlanta, GA; USA.
2. Martin P, Jung S, Johnson J, et al. Calgb 50803 (Alliance): A phase 2 trial of lenalidomide plus rituximab in patients with previously untreated follicular lymphoma [abstract]. *Proceedings of the 12th Triennial International Conference on Malignant Lymphoma (ICML)* 2013a; June 19-22; Lugano, Switzerland: Abstract #063.
3. Martin P, Jung S, Johnson J, et al. Calgb 50803 (Alliance): A phase 2 trial of lenalidomide plus rituximab in patients with previously untreated follicular lymphoma [oral]. *Oral presented at: 12th Triennial International Conference on Malignant Lymphoma (ICML)* 2013b; June 19-22; Lugano, Switzerland.
4. Revlimid (lenalidomide) Prescribing Information. Summit, NJ: Celgene Corporation.
<http://www.revlimid.com/>