



Submitted by:

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Date of Request: June 5, 2012

Dear NCCN Non-Hodgkin's Lymphoma Guidelines Panel:

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 in patients with recurrent follicular lymphoma.

Specific Changes: Recommend the use of lenalidomide (with or without rituximab) as a suggested treatment regimen in the guidelines for follicular lymphoma (grade 1-2) as second line and subsequent therapy with a *Category 2A* recommendation. In addition, we respectfully request an update to the discussion surrounding second-line therapies for relapsed or progressive disease for follicular lymphoma on page MS-50, and patients with relapsed/refractory Diffuse Large B-Cell Lymphoma who are not eligible for high dose therapy/autologous stem cell rescue on pages MS-59 and MS-60 of the NHL Clinical Practice Guidelines to reflect the recently presented results.

FDA Clearance: The FDA has not approved lenalidomide for the treatment of follicular lymphoma. Lenalidomide is indicated for the treatment of:

- 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 randomized, Phase II Cancer and Leukemia Group B (CALGB) study of lenalidomide in combination with rituximab in patients with recurrent follicular lymphoma was recently presented at the 48th Annual Meeting of the American Society of Clinical Oncology (ASCO) on June 2, 2012. This study evaluated lenalidomide alone (cycle 1: 15 mg/day; cycles 2-12: 20-25 mg/day) or lenalidomide (cycle 1: 15 mg/day; cycles 2-12: 20-25 mg/day) with rituximab (cycle 1: 375 mg/m² weekly for 4 weeks). Both treatment arms demonstrated significant efficacy; higher overall response rates (ORR) were observed in patients treated with the combination of lenalidomide with rituximab (72.7% ORR; 36.4% complete response [CR]) compared with lenalidomide monotherapy (51.1% ORR; 13.3% CR). The incidence of Grade 3 and 4 adverse events was similar for both arms (Leonard et al. 2012b; Leonard et al. 2012a).

Results from an additional study on lenalidomide in combination with rituximab in relapsed/refractory indolent NHL were also presented at the *11th International Conference on Malignant Lymphoma (ICML)* meeting in June, 2011 (Dutia et al. 2011a; Dutia et al. 2011b).

The following are enclosed for your review (permissions obtained where applicable):

1. Leonard JP, Jung S, Johnson J, et al. CALGB 50401: A randomized trial of lenalidomide alone versus lenalidomide plus rituximab in patients with recurrent follicular lymphoma [oral presentation]. *Proceedings of the 48th Annual Meeting of the American Society of Clinical Oncology (ASCO) 2012*; June 1-5; Chicago, IL; USA.
2. Dutia M, DeRoock I, Reed-Pease C, et al. Lenalidomide plus rituximab leads to a high rate of durable responses in patients with relapsed/ refractory indolent non-Hodgkin's lymphoma [poster]. *Poster presented at: 11th Triennial International Conference on Malignant Lymphoma (ICML) 2011*; June 15-18; Lugano, Switzerland.

Your consideration of this submission is greatly appreciated.

Sincerely,



Anjali Shah, PharmD
Sr. Manager, Global Medical Information



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

Cited References:

1. Dutia M, DeRoock I, Reed-Pease C, et al. Lenalidomide plus rituximab leads to a high rate of durable responses in patients with relapsed/ refractory indolent non-Hodgkin's lymphoma [abstract]. *Proceedings of the 11th Triennial International Conference on Malignant Lymphoma (ICML) 2011a*; June 15-18; Lugano, Switzerland: Abstract #306.
2. Dutia M, DeRoock I, Reed-Pease C, et al. Lenalidomide plus rituximab leads to a high rate of durable responses in patients with relapsed/ refractory indolent non-Hodgkin's lymphoma [poster]. *Poster presented at: 11th Triennial International Conference on Malignant Lymphoma (ICML) 2011b*; June 15-18; Lugano, Switzerland.
3. Leonard J, Jung SH, Johnson JL, et al. CALGB 50401: A randomized trial of lenalidomide alone versus lenalidomide plus rituximab in patients with recurrent follicular lymphoma [oral]. *Oral presented at: 48th Annual Meeting of the American Society of Clinical Oncology (ASCO) 2012a*; June 1-5; Chicago, IL; USA.

4. Leonard J, Jung SH, Johnson JL, et al. CALGB 50401: A randomized trial of lenalidomide alone versus lenalidomide plus rituximab in patients with recurrent follicular lymphoma [abstract]. *Proceedings of the 48th Annual Meeting of the American Society of Clinical Oncology (ASCO) 2012b*; June 1-5; Chicago, IL; USA: Abstract #8000.
http://abstract.asco.org/AbstView_114_93509.html