

Submitted by:
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Dear NCCN Multiple Myeloma Guidelines Panel Members:

On behalf of Celgene Corporation, we respectfully request that the NCCN Guidelines Panel for Multiple Myeloma review recently published data on the use of POMALYST® (pomalidomide) in combination with cyclophosphamide and dexamethasone in patients with previously treated multiple myeloma (MM).

Specific Changes: Recommend an update to the guidelines regarding previously treated MM to reflect the results of a Phase II and retrospective study of the triplet combination of pomalidomide/cyclophosphamide/dexamethasone (PVD) in patients with relapsed/refractory MM (RRMM).

FDA Clearance: POMALYST is a thalidomide analogue indicated, in combination with dexamethasone, for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy (Celgene Corporation, 2015).

Rationale for Proposed Change:

The addition of triplet combinations to the treatment landscape for multiple myeloma has expanded the therapy options for patients with relapsed/refractory multiple myeloma (RRMM) in later lines of treatment. Despite tremendous progress, there continues to be an unmet medical need. Pomalidomide, cyclophosphamide and dexamethasone is an all oral triplet combination which potentially offers convenience to patients with RRMM.

The combination of pomalidomide, cyclophosphamide and dexamethasone (PomCyDex) in RRMM has been evaluated in 2 studies, including a prospective randomized multicenter Phase II study (Baz et al., 2016) and a single center retrospective study (Garderet et al., 2015).

The Phase II study compared the PomCyDex combination (pomalidomide 4 mg on Days 1-21, dexamethasone 40 mg weekly, cyclophosphamide 400 mg on Days 1, 8, 15 of a 28-day cycle) to pomalidomide and dexamethasone alone in 70 patients who were refractory to lenalidomide and had received ≥ 2 prior treatments (Baz et al., 2016). Compared with pomalidomide and dexamethasone alone, PomCyDex significantly improved response (overall response rate [ORR]; \geq partial response [PR], 64.7% vs. 38.9%; $P=.0355$). Progression-free survival (PFS; median 9.5 months vs. 4.4 months) and overall survival (OS; median, not reached vs. 16.8 months) also improved with the triplet combination, although the difference was not statistically significant. Patients on pomalidomide + dexamethasone who crossed over to PomCyDex at the time of progression (n=17) did not experience improved outcomes. There were no significant differences in AE reports between treatment arms; Grade 3 and 4 anemia, neutropenia and thrombocytopenia, respectively, were reported in 11%, 31% and 6% of pomalidomide + dexamethasone patients and 24%, 52% and 15% of PomCyDex patients.. The rate of febrile neutropenia was also similar between treatment groups (pomalidomide + dexamethasone, 11.4%; PomCyDex, 12.1%).

Similar outcomes were observed in a single center retrospective study of 20 RRMM patients who received PomCyDex until transplant or disease progression (Garderet et al., 2015). Response to combination treatment was 63%, with nearly half of patients (42%) responding after 1 cycle with a median time to response of 3 cycles. One year median PFS was 80.7% and 65% of patients were relapse-free. Toxicity was considered manageable and was mainly neutropenia (53%). Additionally, 1 case of pulmonary aspergillosis was reported.

The following enclosures are submitted in support of the above proposed changes: Baz et al., 2016; Garderet et al., 2015.

Your consideration of this submission is greatly appreciated.

Sincerely,



Eulena Horne, PharmD
Associate Director, Global Medical Information



Peg Squier
Vice President, US Medical Affairs

Cited References:

1. Baz RC, Martin TG 3rd, Lin H-Y, et al. Randomized multicenter phase II study of pomalidomide, cyclophosphamide, and dexamethasone in relapsed refractory myeloma. *Blood*. 2016; <http://www.ncbi.nlm.nih.gov/pubmed/26932802>.
2. Celgene Corporation. Pomalyst (pomalidomide) [Package Insert]. Summit, NJ: Celgene Corporation. <http://www.pomalyst.com/>.
3. Garderet L, Guelongo OOJ, Beohou E, et al. Pomalidomide, Cyclophosphamide and Dexamethasone for relapsed/refractory multiple myeloma: a retrospective single center experience [Poster]. Poster presented at: 57th Annual Meeting and Exposition of the American Society of Hematology (ASH); December 5-8, 2015; Orlando, FL, USA.