



Submitted by:
Kim Lee, PharmD
Director, Global Medical Information
Celgene Corporation
86 Morris Avenue
Summit, NJ 07901
Phone: 908-219-0777
Email: kilee@celgene.com
Date of Request: March 30, 2018

Dear NCCN Multiple Myeloma Guidelines Panel Members:

On behalf of Celgene Corporation, we respectfully request the NCCN Guidelines Panel for Multiple Myeloma review recently presented data regarding the use of POMALYST® (pomalidomide) and dexamethasone (Pd) plus or minus daratumumab (DPd) sequentially following a lenalidomide-based regimen in patients with relapsed/refractory multiple myeloma (rrMM).

Specific Changes: We request an update to the Guidelines surrounding the use of Pd and DPd in patients with Previously Treated Multiple Myeloma to include information from two recent presentations from the MM-014 trial in which patients received Pd or DPd immediately after failing a lenalidomide-based regimen (Siegel et al., 2017b) (Siegel et al., 2017a).

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).

DARZALEX® (daratumumab) is indicated in combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor (Janssen Biotech).

Rationale for Proposed Change: The open-label, multicenter, international, Phase II study (MM-014) evaluated both Pd (Cohort A, n=56) and DPd (Cohort B, n=40) in patients with rrMM sequentially following a lenalidomide-based treatment failure (Siegel et al., 2017b) (Siegel et al., 2017a). Interim results found that patients included in the study had a median overall response rate (ORR) of 33.9% and 72.5% when treated with Pd or DPd, respectively, after progressing on their last lenalidomide-based therapy (were relapsed or refractory).

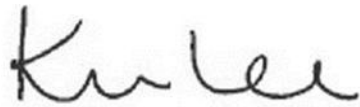
In Cohort A (n=56), patients received Pd in the third line. After a median follow up of 19.0 months (range, 0.6-39.4), the primary endpoint of ORR by IMWG criteria was 33.9%, including 14.3% who achieved ≥VGPR; median PFS was 9.6 months and median OS has not yet been reached. Common (≥10%) Grade 3/4 adverse events included anemia (25%), infections and infestations (25%), pneumonia

(14%), fatigue (14%) and neutropenia (11%).

In Cohort B (n=40), patients received DPd in the second or third line. After a median follow up of 6.8 months (range, 0.5-12.7), the primary endpoint of ORR by IMWG criteria was 72.5%, including 25.0% who achieved \geq VGPR. Common ($\geq 10\%$) Grade 3/4 adverse events included neutropenia (70%), infections and infestations (30%), thrombocytopenia (25%) and anemia (20%). Infusion-related reactions occurred in 15 (38%) patients and two patients experienced either a DVT or PE.

Copies of the MM-014 poster presentations are attached for your review. Your consideration of this submission is greatly appreciated.

Sincerely,



Kim Lee, PharmD
Director, Global Medical Information



Thorsten Sperber, MSc
Executive Director, US Medical Affairs

REFERENCES

1. Celgene Corporation. Pomalyst (pomalidomide) [Package Insert]. Summit, NJ: Celgene Corporation. <http://www.pomalyst.com/>.
2. Janssen Biotech. Darzalex® [Package Insert]. Horsham, PA: Janssen Biotech. https://www.janssenmd.com/pdf/darzalex/darzalex_pi.pdf. Accessed on March 30, 2018.
3. Siegel DS, Schiller GJ, Samaras C, et al. Safety and Efficacy of Pomalidomide + Low-Dose Dexamethasone + Daratumumab as Second-or Third-Line Therapy in Patients With Relapsed and/or Refractory Multiple Myeloma After Lenalidomide-Based Treatment Failure [Poster]. Poster presented at: 59th Annual Meeting and Exposition of the American Society of Hematology (ASH); December 9-12, 2017a; Atlanta, GA, USA.
4. Siegel DS, Schiller GJ, Song KW, et al. Pomalidomide + Low-Dose Dexamethasone Safety and Efficacy in Patients With Relapsed and/or Refractory Multiple Myeloma Previously Treated With a Proteasome Inhibitor and in Whom Last Prior Therapy With Lenalidomide Failed [Poster]. Poster presented at: 59th Annual Meeting and Exposition of the American Society of Hematology (ASH); December 9-12, 2017b; Atlanta, GA, USA.