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 presented data on the use of POMALYST® (pomalidomide) in combination with dexamethasone and ixazomib in patients with previously treated multiple myeloma (MM).

Specific Changes: Recommend an update to the guidelines regarding previously treated MM to reflect results from the Phase I/II study of the triplet combination of pomalidomide/dexamethasone/ixazomib described herein.

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 RRMM in later lines of treatment. Despite tremendous progress, there continues to be an unmet medical need in the treatment of RRMM. Pomalidomide, ixazomib and dexamethasone is an all oral triplet combination which potentially offers convenience to patients with RRMM.

The triplet combination of pomalidomide, dexamethasone and ixazomib has demonstrated activity in a Phase I/II study in 22 MM patients who were refractory to lenalidomide- and proteasome inhibitor-based therapy (Voorhees et al., 2015). Pomalidomide 2-4 mg on Days 1-21 and ixazomib 3-4 mg on Days 1, 8 and 15 were administered in a standard 3+3 dose escalation with dexamethasone 40 mg (20 mg if >75 years) on Days 1, 8, 15 and 22 in 28-day cycles. Response was achieved in approximately half the patient population (overall response rate [ORR], 55%), with a median time to response of 1.9 months. Response among cytogenetically high risk patients (ORR, 46%), patients refractory to sequential lenalidomide and proteasome inhibitor (57%) and patients refractory to combination lenalidomide and proteasome inhibitor (50%) were similar to the overall study population; response was achieved among all (ORR, 100%) standard risk cytogenetics patients. Responses were observed at all dose levels evaluated and reported as durable. Adverse events (AEs), at least possibly treatment-related, included Grade 3/4 hematologic toxicities (decreased white blood cell, 5 events; neutropenia, 9 events; lymphopenia, 6 events; anemia, 2 events; thrombocytopenia, 4 events) and 1 pulmonary embolism (PE) was reported.

A copy of this Phase I/II study recently presented at the American Society of Hematology Annual Meeting is enclosed for your review.

Your consideration of this submission is greatly appreciated.

Sincerely,

Eulena Horne, PharmD
Assoc Director, Global Medical Information

Peg Squier
Vice President, US Medical Affairs

Cited References:

1. Celgene Corporation. Pomalyst (pomalidomide) [Package Insert]. Summit, NJ: Celgene Corporation. http://www.pomalyst.com/.
2. Voorhees PM, Mulkey F, Hassoun H, et al. Alliance A061202. a Phase I/II Study of Pomalidomide, Dexamethasone and Ixazomib Versus Pomalidomide and Dexamethasone for Patients with Multiple Myeloma Refractory to Lenalidomide and Proteasome Inhibitor Based Therapy: Phase I Results [Oral]. Oral presented at: 57th Annual Meeting and Exposition of the American Society of Hematology (ASH); December 5-8, 2015; Orlando, FL, USA.