Dear NCCN Multiple Myeloma Guidelines Panel Members:

On behalf of Celgene Corporation, we respectfully request the NCCN Guidelines Panel for Multiple Myeloma review updated data regarding the use of POMALYST® (pomalidomide) in combination with dexamethasone and carfilzomib in patients with relapsed/refractory multiple myeloma (RRMM). This is in follow-up to earlier data submitted to the panel for consideration on April 8, 2016.

Specific Changes: Recommend an update to the guidelines regarding previously treated MM to reflect results from two Phase I/II studies of the triplet combination pomalidomide/dexamethasone/carfilzomib (PdC) in patients with RRMM (see enclosed prior submission dated April 8, 2016). Updated results from one of the two studies were orally presented at the American Society of Clinical Oncology 2016 meeting and are described below for your consideration (Rosenbaum et al., 2016).

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:
In the updated Phase Ib/II study, a total of 56 patients were enrolled in the overall population with relapsed MM or RRMM after ≥1 prior therapy and had received prior lenalidomide. Of the 56 in the overall population, 46 patients were included in the primary study population who were PI-naïve or -sensitive with LEN-refractory disease for 2nd line or LEN-refractory/exposure for 3rd line or later (Rosenbaum et al., 2016). As the MTD was not reached in the Phase I portion, the enrollment for Phase II at the time of reporting was at Dose Level 3 (carfilzomib 20/27 mg/m², pomalidomide 4 mg and dexamethasone 40/20 mg weekly for cycles 1-4/5-8). In the overall (n=54) vs. primary (n=44) population, respectively, ORR (≥PR) was 65% vs. 61% after Cycle 1 and 72% vs. 73% after Cycle 4 (≥VGPR, 30% vs. 23%; CR/nCR, 4% vs. 2%; CBR [≥MR], 80% vs. 82%). Best response in the overall (n=55) vs. primary (n=45) population, respectively, was ORR (≥PR) of 84% vs. 84% (≥VGPR, 47% vs. 44%; CR/nCR, 16% vs. 13%; CBR [≥MR], 93% vs. 96%). After a median 17.9 months follow-up, median PFS was 12.9 months (12 month PFS, 53%; 24 month PFS, 22%) and median OS was not reached (12 month OS, 91%; 24 month OS, 78%) for all 56 enrolled patients; outcomes were similar in the primary study population. As of reporting, 21 patients remained on treatment and Phase II enrollment was ongoing.

Hematologic AEs (Grade 3/4) included neutropenia (21%) and thrombocytopenia (7%), and non-hematologic toxicities (all grades) were fatigue (60%), infection (56%), and gastrointestinal (49%).

The following enclosures are submitted in support of the above proposed changes: Rosenbaum et al., 2016, Shah et al., 2013; Shah et al., 2015. The previous submission, with an earlier presentation of the Rosenblum data dated April 8, 2016 is also enclosed for your reference.
List of Abbreviations:

AE: Adverse Event; CBR: Clinical Benefit Rate; CR: Complete Response; LEN: lenalidomide; MTD: Maximum Tolerated Dose; MR: Minor Response; nCR: Near Complete Response; ORR: Overall Response Rate; OS: Overall Survival; PFS: Progression-Free Survival; PI: Proteasome Inhibitor; PR: Partial Response; RR: Relapsed/Refractory; VGPR: Very Good Partial Response

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:


Enclosures: Rosenbaum et al., 2014; Rosenbaum et al. 2016; Shah et al., 2013; Shah et al., 2015; Previous NCCN submission 2016APR08