

Submitted by:
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NCCN Guidelines Panel: Multiple Myeloma Panel

On behalf of Amgen Inc., I respectfully request the NCCN Multiple Myeloma panel members to review the enclosed data on the use of Kyprolis[®] (carfilzomib) in combination with dexamethasone with once weekly dosing in a phase 1/2 study in relapsed/refractory multiple myeloma (RRMM) patients.

FDA Approval: Kyprolis[®] (carfilzomib) for Injection is approved by the US FDA:

- in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy.
- as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

Carfilzomib is not currently approved by the US FDA for once weekly dosing at 70 mg/m² in patients with RRMM.

Rationale: The final analysis from a phase 1/2 trial were recently published and presented on December 3, 2016 at the 58th American Society of Hematology Annual Meeting and Exposition and provides supportive data in RRMM for once weekly dosing in combination with dexamethasone.

In a phase 1/2 trial (N = 116), once-weekly carfilzomib with dexamethasone was evaluated to determine the maximum tolerated dose (MTD) along with safety and tolerability. During the phase 1 portion of the study, patients received either carfilzomib at 45, 56, 70, or 80 mg/m². The MTD of carfilzomib in combination with dexamethasone at once-weekly dosing was 70 mg/m². The 70 mg/m² dosage was used in the phase 2 portion of the study to evaluate safety and efficacy as determined by overall response rate (ORR). The most common adverse events (AEs) occurring in at least 20% of all patients during the phase 2 portion of the study were fatigue (52%), nausea (35%), insomnia (31% and headache (28%). The most common grade 3 or higher AEs occurring in at least 3% of all patients were fatigue (11%), pneumonia (6%), acute kidney injury (7%), and hypertension (8%). The ORR for the phase 1/2 at 70 mg/m² once weekly dosing (n = 104) was 77% (95% CI, 68-85) and 12.5% in complete response or greater (≥ CR). At the final analysis of the study at 13.6 months, the median progression-free survival (PFS) was 16.2 months. (95% CI, 10.2-21.0).²

Supporting Documentation: The following have been submitted in support of this request:

1. Berenson JR, et al. CHAMPION-1: A phase 1/2 study of once-weekly carfilzomib and dexamethasone for relapsed or refractory multiple myeloma. *Blood*. 2016 June 30; 127(26):3360-8.

2. Berdeja JG, et al. Once-Weekly Carfilzomib With Dexamethasone Demonstrated Promising Safety and Efficacy in Patients With Relapsed or Refractory Multiple Myeloma Regardless of Age and Prior Bortezomib Exposure. Presented at: the 58th American Society of Hematology Annual Meeting and Exposition; December 3-6; San Diego, CA.

Sincerely,

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