



Submitted by:  
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**Date of request: April 23, 2018**  
**NCCN Guidelines Panel: Multiple Myeloma**

On behalf of Takeda Pharmaceutical Company Limited, we respectfully request the NCCN Multiple Myeloma Panel to review the enclosed data on the use of oral ixazomib (NINLARO) in combination with cyclophosphamide and dexamethasone (ICd) as both first-line therapy for transplant-ineligible patients with multiple myeloma as well as therapy for patients with relapsed/refractory multiple myeloma.

**Specific Changes:**

- Recommend inclusion of ICd as a suggested Category 2A Preferred Regimen for both Primary Therapy for Non-Transplant Candidates and Therapy for Previously Treated Multiple Myeloma.

**FDA Clearance:** Ixazomib in combination with lenalidomide and dexamethasone is approved by the US FDA for the treatment of patients with multiple myeloma who have received at least one prior therapy. Ixazomib is not currently approved by the US FDA for the treatment of newly diagnosed patients with multiple myeloma nor in combination with cyclophosphamide and dexamethasone.

**Rationale:** Final data from studies of ixazomib in combination with cyclophosphamide and dexamethasone show promising activity and safety. Inclusion of the ICd regimen in the NCCN recommendations would be beneficial to patients with both newly diagnosed and relapsed/refractory multiple myeloma for whom an immunomodulatory-based regimen may not be appropriate.

The following publications are submitted in support of these proposed changes. We would like to acknowledge the contributions of NCCN panel members who are also co-authors of some of these publications.

1. Dimopoulos MA, et al. An open-label, phase 2 study to evaluate the oral combination of ixazomib, cyclophosphamide and dexamethasone in transplant-ineligible patients with newly diagnosed multiple myeloma. *Haematologica* 2017;102(s2):111 (abstract P338); data from poster presentation at the 2017 Annual Congress of EHA.
2. Lacy M, et al. Phase 1/2 trial of ixazomib, cyclophosphamide, and dexamethasone for newly diagnosed multiple myeloma (NDMM). *Journal of Clinical Oncology* 2016;34:15\_suppl, 8002-8002; data from oral presentation at the 2016 Annual Meeting of ASCO



3. Kumar S, et al. Phase 2 Study of the All-Oral Combination of Ixazomib Plus Cyclophosphamide and Low-Dose Dexamethasone (ICd) in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM). International Myeloma Workshop 2017; abstract PS-235 (d); data from poster presentation at the 16th International Myeloma Workshop in 2017

Yours sincerely,

A handwritten signature in black ink, appearing to read "Stephen J. Noga".

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