



Submitted by:
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Date of request: March 21, 2019
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 ixazomib (NINLARO) in combination with cyclophosphamide-dexamethasone (ICd) for patients with multiple myeloma.

Specific Changes:

- Recommend inclusion of ICd as a Preferred Primary Therapy 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 and this combination is listed as a category 1 recommended therapy for previously treated multiple myeloma in the Multiple Myeloma NCCN Guidelines Version 2.2019. Ixazomib is not currently approved by the US FDA for use in newly diagnosed multiple myeloma nor in combination with cyclophosphamide and dexamethasone.

Rationale: The ICd combination has been studied in both patients with newly diagnosed multiple myeloma and those with relapsed/refractory multiple myeloma and exhibits high overall response rates and a favorable tolerability profile. The ICd combination provides a valuable option for patients for whom immunomodulatory drugs may not be preferred.

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

- Kumar SK et al., Phase 1/2 trial of ixazomib, cyclophosphamide and dexamethasone in patients with previously untreated symptomatic multiple myeloma Blood Cancer J. 2018 Jul 30;8(8):70.

- Dimopoulos MA, et al., All-oral ixazomib, cyclophosphamide, and dexamethasone for transplant-ineligible patients with newly diagnosed multiple myeloma, Eur J Cancer. 2019 Jan;106:89-98
- Kumar SK et al., Phase 2 study of all-oral ixazomib, cyclophosphamide and low-dose dexamethasone for relapsed/refractory multiple myeloma, Br J Haematol. 2019 Feb;184(4):536-546

Yours sincerely,

A handwritten signature in blue ink, appearing to read "Stephen J. Noga". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Stephen J. Noga, MD, Ph.D.
Vice President, U.S. Medical Affairs - Oncology