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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 from the phase II 2012-0277 study on the use of ixazomib plus lenalidomide as maintenance following autologous stem cell transplant in patients with newly diagnosed multiple myeloma.

Specific Changes:

- Recommend inclusion of ixazomib plus lenalidomide as a suggested Category 2A Regimen for Maintenance Post-Transplant in Newly Diagnosed 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 3.2020. Ixazomib is not currently approved by the US FDA for maintenance in multiple myeloma.

Rationale: The phase II 2012-0277 trial treated 64 multiple myeloma patients with ixazomib plus lenalidomide maintenance until progression following autologous stem cell transplant. As of September 2017, patients received a median of 30 cycles (range, 1-55). Forty-five percent of patients had an improvement in their best overall response from post-transplant baseline, resulting in a \geq VGPR rate of 90%. At a median follow-up of 38.2 months, the median PFS had not been reached and the estimated 2-year PFS was 81%. Seventy-five percent of patients had peripheral neuropathy (PN) at enrollment; PN reported in the trial included 34% grade 1 and 9% grade 3. The rate of second primary malignancies was 5% (1 patient with breast DCIS and 2 with squamous skin cell cancer).

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

- Patel KK, et al. Update on a Phase II Study of Ixazomib with Lenalidomide as Maintenance Therapy Following Autologous Stem Cell Transplant in Patients with Newly Diagnosed Multiple Myeloma. Blood (2017) 130 (Supplement 1): 437.

Yours sincerely,

A handwritten signature in dark ink, appearing to read "Stephen J. Noga", with a stylized flourish at the end.

Stephen J. Noga, MD, Ph.D.

Vice President, U.S. Medical Affairs - Oncology