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September 9, 2019

Submission Request

National Comprehensive Cancer Network

RE: Evidence in support of Sandoz biosimilar filgrastim, Zarxio® (filgrastim-sndz) injection, as primary prophylaxis against febrile neutropenia in patients with non-Hodgkin's Lymphoma receiving R-CHOP chemotherapy and no additional risk factors

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NCCN Panel:	Hematopoietic Growth Factors

Dear Panel Members,

Sandoz respectfully requests the NCCN Hematopoietic Growth Factors Panel to review the attached data for ZARXIO® (filgrastim-sndz), a biosimilar filgrastim, for inclusion as a recommendation for primary prophylaxis against febrile neutropenia in patients with non-Hodgkin's Lymphoma receiving R-CHOP chemotherapy and no additional risk factors. Currently, the recommendation for patients who are receiving chemotherapy regimens at intermediate-risk for febrile neutropenia with no additional risk factors (i.e., 10-20% risk) is to observe for the first cycle and provide secondary prophylaxis with a myeloid growth factor if the patient experiences a febrile neutropenia episode or a dose-limiting neutropenic event following a previous chemotherapy cycle.

On March 6, 2015, ZARXIO was the first biosimilar G-CSF approved in the US following the FDA biosimilar approval pathway. ZARXIO is approved for five of the labeled indications for Neupogen®, one of which is to "decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever." Biosimilars such as ZARXIO were developed to address the critical need for a lower cost alternative to current available therapies and allow more patients access to care with important biologics.

G-CSFs, including ZARXIO, have been an important tool to manage the risks of chemotherapy-induced neutropenia for many years, and primary prophylaxis is recommended by the NCCN guidelines for patients with a ≥20% risk of developing febrile neutropenia. A patient's probability of experiencing febrile neutropenia is based on regimen-risk alone (e.g., high-risk) or based on both regimen- and patient-related risk factors (e.g., intermediate risk regimen plus one or more patient-related risk factors).

It is important to note that historically, the risk threshold for primary prophylaxis was much higher than it is today; primary prophylaxis with a G-CSF was recommended for patients at ≥40% risk of developing febrile neutropenia.[1] Economic models based on real-world evidence and measures of total healthcare resource utilization demonstrated the cost-effectiveness of filgrastim; these provided the data necessary to lower this risk threshold to its current value of 20%.[2]

Accordingly, Sandoz has published a similar economic model based on real-world evidence in patients with non-Hodgkin's Lymphoma receiving R-CHOP therapy who have an intermediate risk (10-20%) of developing febrile neutropenia (FN) to estimate the cost-effectiveness over a lifetime horizon of ZARXIO

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as primary prophylaxis against FN compared to ZARXIO as secondary prophylaxis. This is the first known model to focus on intermediate risk patients to compare two treatment strategies, primary and secondary prophylaxis, using the G-CSF biosimilar. The analysis estimated the incremental cost-effectiveness of ZARXIO as primary prophylaxis compared to ZARXIO as secondary prophylaxis to be $50,676 per FN event avoided, $41,761 per life year gained, and $46,207 per quality-adjusted life year gained. Our conclusion is that ZARXIO as primary prophylaxis is cost-effective versus ZARXIO as secondary prophylaxis using a $50,000 per QALY willingness-to-pay threshold. This data has been published in abstract form (Abstract #107) and was presented at the 2019 American Society of Clinical Oncology Quality Care Symposium in September 2019.[3]

If adopted, a recommendation to use ZARXIO as primary prophylaxis has the potential to lead to better population-based outcomes such as fewer FN events and additional life-years gained. We appreciate the opportunity to provide this information for consideration by the NCCN Hematopoietic Growth Factors Panel. If you have any questions or require additional information, please do not hesitate to contact me at (609) 578-7058 or via e-mail at kim.campbell@sandoz.com. Thank you for your consideration.

Literature in Support:

1. Calhoun EA, et al. Granulocyte colony--stimulating factor for chemotherapy-induced neutropenia in patients with small cell lung cancer: the 40% rule revisited. Pharmacoeconomics. 2005;23(8):767-75.
2. Lyman GH, Kuderer NM. The economics of the colony-stimulating factors in the prevention and treatment of febrile neutropenia. Crit Rev Oncol Hematol. 2004 May;50(2):129-46.
3. Lyman GH, et al. A cost-effectiveness analysis of primary prophylaxis (PP) versus secondary prophylaxis (SP) with biosimilar myeloid growth factors (MGFs) for preventing chemotherapy-induced febrile neutropenia (FN) in non-Hodgkin lymphoma (NHL) patients at intermediate risk. *J Clin Oncol*. 2019; 37(27 Suppl): abstr 107.

Sincerely,

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Enclosures: Copies of referenced literature, abstract, and poster.