

June 3, 2016

Submission Request  
National Comprehensive Cancer Network

**RE: Clinical Evidence in Support of Arzerra® (ofatumumab) in Chronic Lymphocytic Leukemia**

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Date of request: xxxxx  
NCCN Guidelines Panel: Non-Hodgkin's Lymphoma (CLL/SLL)

To Whom It May Concern:

As the NCCN Non-Hodgkin's Lymphoma Panel reviews the NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines) for Non-Hodgkin's Lymphoma v.2.2016 and the associated Drugs & Biologics Compendium™, we have enclosed data relating to treatment with Arzerra® (ofatumumab). This information is highlighted below:

- Data to support the use of ofatumumab in combination with ibrutinib in patients with relapsed/refractory CLL

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**Arzerra (ofatumumab) for the treatment of CLL**

This request is for the Panel to consider the addition of the combination of ofatumumab and ibrutinib as a treatment option in CLL/SLL subsection of the Non-Hodgkin's Lymphoma Guidelines and the associated NCCN Drugs & Biologics Compendium.

Based on the Phase I/II study that included 66 patients with relapsed/refractory CLL/SLL, ofatumumab was studied in combination with ibrutinib in three treatment schema. Ofatumumab combined with ibrutinib in patients with relapsed/refractory CLL had an overall response rate (ORR) of 83% with a median time to response of <3 months in all groups. Most frequent adverse events of any grade were diarrhea (70%), infusion-related reaction (45%), and peripheral sensory neuropathy (44%); no dose-limiting toxicities (DLTs) were identified.<sup>1</sup>

**Specific changes recommended for the Guidelines and Compendium**

Please add ofatumumab in combination with ibrutinib as a treatment option for patients with relapsed/refractory CLL.

**FDA status**

Ofatumumab is approved for the treatment of relapsed CLL in patients with two previous lines of therapy and CLL refractory to fludarabine and alemtuzamab. Ofatumumab is not currently approved in combination with ibrutinib.

**Rationale for recommended change**

Based on Phase I/II data, the ORR of ofatumumab in combination with ibrutinib in relapsed/refractory CLL was 83% with a median time to response of <3 months with no DLTs identified, demonstrating a shorter time to response and more durable responses than either agent alone.

\* \* \* \* \*

**Literature support**

1. Jaglowski SM, Jones JA, Nagar V. Safety and activity of BTK inhibitor ibrutinib combined with ofatumumab in chronic lymphocytic leukemia: a phase 1b/2 study. *Blood*. 2015;126(7):842-850.

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We appreciate the opportunity to provide this additional information for consideration by the NCCN NHL Panel. If you have any questions or require additional information, please do not hesitate to contact me at 1-862-778-5494 or via e-mail at [Neilda.baron@novartis.com](mailto:Neilda.baron@novartis.com). Thank you for your time and consideration.

Sincerely,

Neilda Baron, MD  
Executive Director, Medical Information Oncology  
Novartis Pharmaceuticals Corporation

Enclosure: Copy of referenced primary literature