

December 21, 2017

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Date of request: December 21, 2017  
NCCN Guidelines® Panel: B-Cell Lymphomas

Dear NCCN:

Pharmacyclics LLC and Janssen Biotech, Inc. co-develop and co-commercialize IMBRUVICA® (ibrutinib) capsules. On behalf of Pharmacyclics LLC and Janssen Biotech, Inc., I respectfully request the NCCN Guidelines® - B-Cell Lymphomas Panel to review the enclosed information of IMBRUVICA (ibrutinib) for the treatment of mantle cell lymphoma (MCL).

Specific Change: Consider the available data on IMBRUVICA in patients with MCL for your updating purposes.

FDA Clearance:

IMBRUVICA® is a kinase inhibitor indicated for the treatment of adult patients with:

- Mantle cell lymphoma (MCL) who have received at least one prior therapy. Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL)
- Chronic lymphocytic leukemia (CLL)/Small lymphocytic lymphoma (SLL) with 17p deletion
- Waldenström's macroglobulinemia (WM)
- Marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy. Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy

Rationale: Conference proceedings from the 59<sup>th</sup> Annual Meeting of the American Society of Hematology (ASH) have reported on a updated pooled analysis of ibrutinib as a single-agent in patients with relapsed/refractory (R/R) MCL.

- **Rule et al (2017)**<sup>2,3</sup> presented updated results (median follow-up of 41.1 months) of a pooled analysis of baseline factors on response rates and survival outcomes in ibrutinib-treated patients with R/R MCL from international, open-label, phase 2, phase 3, and phase 3b studies (N=370) (PCYC-1104, MCL2001 [SPARK], MCL3001 [RAY], and CAN3001). Previously published results were described with median follow-up of 24 months from **Rule et al (2016)**.<sup>4</sup>

The following references are submitted with the full prescribing information<sup>1</sup> in support of the proposed change. We would like to acknowledge the contributions of the NCCN panel members who are also co-authors or co-contributors of these publications.

1. IMBRUVICA® (ibrutinib) [prescribing information]. Sunnyvale, CA: Pharmacyclics LLC; 2017.

2. Rule S, Dreyling M, Goy A, et al. Median 3.5-year follow-up of ibrutinib treatment in patients with relapsed/refractory mantle cell lymphoma: a pooled analysis [abstract]. *Blood*. 2017;129:Abstract 151. <https://ash.confex.com/ash/2017/webprogram/Paper107064.html>
3. Rule S. Median 3.5-year follow-up of ibrutinib treatment in patients with relapsed/refractory mantle cell lymphoma: a pooled analysis [oral presentation]. 59th Annual Meeting and Exposition of the American Society of Hematology; December 9-12, 2017; Atlanta, GA. Abstract 151.
4. Rule S, Dreyling M, Goy A, et al. Outcomes in 370 patients with mantle cell lymphoma treated with ibrutinib: a pooled analysis from three open-label studies. *Br J Haematol*. 2017. doi: <http://dx.doi.org/10.1111/bjh.14870>.

Sincerely,

A handwritten signature in black ink, appearing to read 'Alex Young', with a stylized, flowing script.

Alex Young, PharmD  
Manager, Scientific Communications  
Pharmacyclics LLC, an AbbVie Company