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® Panel: CLL/SLL/Hairy Cell Leukemia review the enclosed information for IMBRUVICA (ibrutinib) in patients with steroid-dependent/refractory chronic graft versus host disease (cGVHD) after failure of one or more lines of systemic therapy.

Specific Change: Updates to the IMBRUVICA Prescribing Information for your reference.

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 confirmatory trials
- 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: On August 2, 2017 the U.S. Food and Drug Administration approved updates to the IMBRUVICA® PI, please note the specific sections below. Please refer to the IMBRUVICA® PI for complete information about the use of IMBRUVICA® in its approved indications.

- Section 1 Indications and Usage
  - 1.6 Chronic Graft versus Host Disease
- Section 2 Dosage and Administration
  - 2.2 Dosage: Chronic Graft versus Host Disease
  - 2.3 Dose Modifications for Adverse Reactions
  - 2.4 Dose Modifications for Use with CYP3A Inhibitors
- Section 5 Warnings and Precautions
  - 5.2 Infections
5.3 Cytopenias

Section 6 Adverse Reactions

6.1 Clinical Trials Experience: Chronic Graft versus Host Disease
6.2 Postmarketing Experience

Section 7 Drug Interactions

7.1 Effect of CYP3A Inhibitors on Ibrutinib
7.2 Effect of CYP3A Inducers on Ibrutinib

Section 8 Use in Specific Populations

8.1 Pregnancy
8.6 Hepatic Impairment

Section 12 Clinical Pharmacology

12.2 Pharmacodynamics
12.3 Pharmacokinetics

Section 14 Clinical Studies

14.5 Chronic Graft versus Host Disease

The full prescribing information\(^1\) is submitted for your reference.


Sincerely,

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