Dear NCCN,

Pharmacycics LLC and Janssen Biotech, Inc. co-develop and co-commercialize IMBRUVICA® (ibrutinib) capsules. On behalf of Pharmacycics LLC and Janssen Biotech, Inc., I respectfully request the NCCN Guidelines® - Non-Hodgkin’s Lymphomas Panel review the enclosed, updated information for inclusion of the following IMBRUVICA (ibrutinib) combination therapies for the treatment of patients with relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL).

**Specific Change:**
Recommend IMBRUVICA (ibrutinib) for the treatment of patients with R/R CLL for each of the following treatment options:
- Single-agent therapy: remain listed as Category 1
- Combination therapy with bendamustine and rituximab (BR): addition to currently listed options
- Combination therapy with ofatumumab: addition to currently listed options

**FDA Clearance:**
The U.S. Food and Drug Administration (FDA) approved IMBRUVICA (ibrutinib) for the treatment of patients with CLL who have received at least one prior therapy, CLL with 17p deletion, mantle cell lymphoma 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 of clinical benefit in confirmatory trials), and Waldenström’s macroglobulinemia.1

Ibrutinib is not currently approved by the FDA for R/R CLL in combination with BR or in combination with ofatumumab.

**Rationale:**
Recent, full publications are now available to support the use of ibrutinib in combination with other therapies for the treatment of patients with R/R CLL including a manuscript in *Lancet Oncology*, which, in addition to presentations at major congresses, reports results from the randomized Phase 3 HELIOS trial of ibrutinib + BR vs. placebo + BR (N=578 R/R CLL/small lymphocytic lymphoma [SLL] patients; CLL3001, NCT01611090), and a manuscript in *Blood*, which reports results from a Phase 1b/2 open-label study of ibrutinib + ofatumumab in patients with R/R CLL/SLL, prolymphocytic leukemia, or Richter’s transformation (N=71; PCYC-1109, NCT01217749).10

A supplemental New Drug Application (sNDA) was submitted to the FDA on November 13, 2015 for labeling considerations based on the Phase 3 HELIOS (CLL3001) data.11
The following references are submitted with the full Prescribing Information\(^1\) in support of the proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.


Sincerely,

Judy Wu, PharmD
Manager, Scientific Communications
Pharmacyclics LLC, an AbbVie Company