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NCCN Guidelines® Panel: Non-Hodgkin's Lymphomas

Dear NCCN,

Pharmacyclics, Inc. and Janssen Biotech, Inc. co-develop and co-commercialize IMBRUVICA™ (ibrutinib) capsules. On behalf of Pharmacyclics Inc. and Janssen Biotech, Inc., I respectfully request the NCCN Guidelines® - Non-Hodgkin's Lymphomas Panel review the enclosed data for inclusion of IMBRUVICA™ (ibrutinib) for the treatment of patients with the activated B cell-like (ABC) subtype of relapsed/refractory (RR) diffuse large B-cell lymphoma (DLBCL).

Specific Change:

Recommend IMBRUVICA™ (ibrutinib) for the treatment of patients with the ABC subtype of RR DLBCL.

FDA Clearance:

The FDA has approved IMBRUVICA™ (ibrutinib) for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. This indication is based on overall response rate. An improvement in survival or disease-related symptoms has not been established.

Rationale:

An ongoing phase 2, multicenter, open-label study (PCYC-1106, N=70) evaluated the safety and efficacy of ibrutinib 560 mg orally once daily in patients with RR DLBCL, of which 29 patients had the ABC subtype. The ABC subtype demonstrated an overall response rate of 41%, with a complete response of 17% and a partial response of 24%. The median overall survival in the ABC subtype was 9.76 months. Safety endpoints were not reported specifically for the ABC subtype; however, for the total study population grade 3 or higher hematologic adverse events (AEs) with an incidence between >3% and <10% included: decreased lymphocyte count, neutropenia, thrombocytopenia, and anemia. Grade 3 or greater non-hematologic AEs in >3% and <10% of patients included: fatigue, hyponatremia, pneumonia, dehydration, pleural effusion, and sepsis.[1, 2]

The following study publications are submitted with the Full Prescribing Information.[3] We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

1) deVos S, Wilson WH, Gerecitano J, et al. The bruton's tyrosine kinase (BTK) inhibitor, ibrutinib (PCI-32765), has preferential activity in the activated B cell-like (ABC) subtype of relapsed/refractory (R/R) DLBCL: interim phase 2 results [abstract]. *Hematol J*. 2013;98(suppl 1):490:S1180.

2) deVos S, Wilson WH, Gerecitano J, et al. The bruton's tyrosine kinase (BTK) inhibitor, ibrutinib (PCI-32765), has preferential activity in the activated B cell-like (ABC) subtype of relapsed/refractory (R/R) DLBCL: interim phase 2 results. Data presented at the *18th Congress of the European Hematology Association*, June 13-16,2013. Stockholm, Sweden.

3) IMBRUVICA™ (ibrutinib) capsules [package insert]. Sunnyvale, CA: Pharmacyclics, Inc.

Sincerely,

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Therapeutic Manager, Oncology Medical Information
Janssen Scientific Affairs, LLC