FDA Approves Columvi for Large B-Cell Lymphomas

More than 40% of patients treated with the bispecific T-cell engager experienced complete remission.

June 19, 2023 By Food and Drug Administration (FDA)

FDA grants accelerated approval to glofitamab-gxbm for selected relapsed or refractory large B-cell lymphomas

On June 15, 2023, the Food and Drug Administration granted accelerated approval to glofitamab-gxbm (Columvi, Genentech, Inc.) for relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma, after two or more lines of systemic therapy.

View full prescribing information for Columvi.

Glofitamab-gxbm, a bispecific CD20-directed CD3 T-cell engager, was studied in trial NP30179 (NCT03075696), an open-label, multicenter, single-arm trial that included 132 patients for the evaluation of efficacy. Eighty percent of patients had relapsed or refractory DLBCL, NOS and 20% had LBCL arising from follicular lymphoma. Patients had received at least two prior lines of systemic therapy (median 3, range 2-7). The trial excluded patients with active or previous central nervous system lymphoma or disease.

The main efficacy outcome measures were objective response rate (ORR) and duration of response (DOR), determined by an Independent Review Committee using the 2014 Lugano criteria.

The ORR was 56% (95% CI: 47, 65) with 43% achieving complete responses. With an estimated median follow-up of 11.6 months among responders, the estimated median DOR was 18.4 months (95% CI: 11.4, not estimable). The 9-month Kaplan-Meier estimate for DOR was 68.5% (95% CI: 56.7, 80.3). The median time to response was 42 days.

The prescribing information includes a Boxed Warning for serious or fatal cytokine release syndrome (CRS). Other Warnings and Precautions include neurologic toxicity including Immune Effector Cell-Associated Neurotoxicity (ICANS), serious infections, and tumor flare. Among 145 patients with relapsed or refractory LBCL evaluated for safety, CRS occurred in 70% (Grade 3 or higher CRS, 4.1%), ICANS in 4.8%, serious infections in 16%, and tumor flare in 12%.

The most common (≥ 20%) adverse reactions, excluding laboratory terms, were CRS, musculoskeletal pain, rash, and fatigue. The most common (≥ 20%) Grade 3 to 4 laboratory abnormalities were decreases in lymphocyte counts, phosphate, neutrophil counts, and fibrinogen and increase in uric acid.

Following a single 1,000 mg dose of obinutuzumab on Cycle 1 Day 1 to deplete circulating and lymphoid tissue B cells, glofitamab-gxbm is administered by intravenous infusion according to a step-up dosing schedule (2.5 mg on Day 8 of Cycle 1 and 10 mg on Day 15 of Cycle 1), then 30 mg on Day 1 of each subsequent cycle for a maximum of 12 cycles. The cycle length is 21 days. Refer to the prescribing information for complete dosing information.

Glofitamab-gxbm should only be administered by a healthcare professional with appropriate medical support to manage severe reactions, including CRS. Because of the CRS risk, patients should be hospitalized during and for 24 hours after the first step up dose (2.5 mg on Day 8 of Cycle 1), and for the second step up dose (10 mg on Day 15 of Cycle 1) if any grade CRS occurs with the 2.5 mg dose. For subsequent doses, patients who experience Grade ≥ 2 CRS with their previous infusion should be hospitalized during and for 24 hours after the completion of the next infusion.

This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this review, FDA collaborated with Switzerland's Swissmedic, where the application is under review.

This review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment.

This application was granted priority review and fast track designation. FDA expedited programs are described in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

This announcement was published by the Food and Drug Administration on June 16, 2023.
