NEW DRUG APPROVAL

Brand Name	Columvi™
Generic Name	glofitamab-gxbm
Drug Manufacturer	Genentech, Inc.,

Indications for Use

Columvi™ is a bispecific CD20-directed CD3 T-cell engager indicated for the treatment of adult patients with 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.

This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

New Drug Approval

Approval Date: June 15, 2023

Review Designation: N/A

Type of Review: Type 1 - Biologic License Application (BLA): 761309

Dispensing Restrictions: N/A

Therapeutic Class

Anti-CD20; Antineoplastic Agent, Anti-CD3; , Bispecific T Cell Engager; , Monoclonal Antibody

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Diffuse large B-cell lymphoma (DLBCL) is the most common histologic subtype of non-Hodgkin lymphoma (NHL), accounting for about one-third of patients with NHL. It is estimated that there will be approximately 25,000 new cases of DLBCL diagnosed in 2019 in the United States. About 30%–40% of patients with DLBCL relapse.

The diagnostic category of DLBCL is heterogeneous in terms of morphology, genetics, and biologic behavior. A number of clinicopathologic entities are now recognized in the 2017 World Health Organization (WHO) classification that are sufficiently distinct to be considered separate diagnostic categories:

- T cell/histiocyte-rich large B cell lymphoma.
- Primary DLBCL of the mediastinum, also called primary mediastinal (thymic) large B cell lymphoma.
- Intravascular large B cell lymphoma.
- Lymphomatoid granulomatosis, an Epstein-Barr virus positive large B cell lymphoma.
- Primary DLBCL of the central nervous system.
- Primary cutaneous DLBCL, leg type.
- DLBCL is associated with chronic inflammation.

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DLBCL is the most common lymphoma and accounts for approximately 25 percent of all NHLs in the developed world. In the United States and England, the incidence of DLBCL is approximately 7 cases per 100,000 persons per year. In Europe as a whole, the incidence is approximately 4.92 cases per 100,000 persons per year Incidence varies by ethnicity, with White Americans having higher rates than Black, Asian, and American Indian or Alaska Native individuals, in order of decreasing incidence By comparison, the incidence in Denmark is approximately 3 cases per 100,000 adults per year DLBCL appears to be a more frequent subtype of NHL in Central and South America, where it accounts for approximately 40 percent of NHLs.

Efficacy

Relapsed or Refractory DLBCL, NOS or LBCL Arising from Follicular Lymphoma

The efficacy of Columvi™ was evaluated in Study NP30179 (NCT03075696), an open-label, multicenter, multicohort, single-arm clinical trial that included patients with relapsed or refractory LBCL after two or more lines of systemic therapy. The trial required an ECOG performance status of 0 or 1, absolute neutrophil count ≥ 1,500/µL, platelet count ≥ 75,000/µL independent of transfusion, serum creatinine ≤ 1.5 x ULN or CLcr ≥ 50 mL/min, and hepatic transaminases ≤ 3 x ULN. The trial excluded patients with active or previous CNS lymphoma or CNS disease, acute infection, recent infection requiring intravenous antibiotics, or prior allogeneic HSCT.

Following pretreatment with obinutuzumab on Cycle 1 Day 1, patients received Columvi™ by intravenous infusion, starting with a 2.5 mg step-up dose on Cycle 1 Day 8, followed by a 10 mg step-up dose on Cycle 1 Day 15, then 30 mg on Cycle 2 Day 1 and on Day 1 of each subsequent cycle. The cycle length was 21 days. Columvi™ was administered for up to 12 cycles unless patients experienced progressive disease or unacceptable toxicity.

The efficacy population consists of 132 patients with de novo DLBCL, NOS (80%) or LBCL arising from follicular lymphoma (20%) who received at least one dose of Columvi™. The median age was 67 years (range: 21 to 90 years), 64% were male, 77% were White, 4.5% were Asian, 0.8% were Black or African American, 5% were Hispanic or Latino. The median number of prior lines of systemic therapy was 3 (range: 2 to 7). Most patients (83%) had refractory disease to the last therapy, 55% had primary refractory disease, 30% had received CAR-T cell therapy, and 19% had received autologous HSCT Efficacy was based on objective response rate (ORR) and duration of response (DOR), as determined by an Independent Review Committee (IRC) using the 2014 Lugano criteria. Efficacy results are summarized in Table 1. The median time to first response was 42 days (range: 31 to 178 days). Among responders, the estimated median follow-up for DOR was 11.6 months.

Safety

ADVERSE EVENTS

The most common (≥ 20%) adverse reactions, excluding laboratory abnormalities, are cytokine release syndrome, musculoskeletal pain, rash, and fatigue. The most common (≥ 20%) Grade 3 to 4 laboratory abnormalities are lymphocyte count decreased, phosphate decreased, neutrophil count decreased, uric acid increased, and fibrinogen decreased.

WARNINGS & PRECAUTIONS

Neurologic Toxicity: Can cause serious neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). Monitor for neurologic toxicity; withhold or permanently discontinue based on severity.

Serious Infections: Can cause serious or fatal infections. Monitor patients for signs and symptoms of infection and treat appropriately.

Tumor Flare: Can cause serious tumor flare reactions. Monitor patients at risk for complications of tumor flare.

Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception.

CONTRAINDICATIONS

None reported.

Clinical Pharmacology

MECHANISMS OF ACTION

Glofitamab-gxbm is a bispecific antibody that binds to CD20 expressed on the surface of B cells, and to CD3 receptor expressed on the surface of T cells. Glofitamab-gxbm causes T-cell activation and proliferation, secretion of cytokines, and the lysis of CD20-expressing B cells. Glofitamab-gxbm showed anti-tumor activity in vivo in mouse models of DLBCL.

Dose & Administration

ADULTS

Pretreat with a single 1,000 mg dose of obinutuzumab intravenously 7 days before initiation of Columvi™ (Cycle 1 Day 1).

Treatment Cycle[a]	Day	Dose of Columvi™	
Cycle 1	Day 1	Obinutuzumab 1,000 mg	
	Day 8	Step-up dose 1	2.5 mg
	Day 15	Step-up dose 2	10 mg
Cycle 2-12	Day 1	30 mg	

[a] Cycle = 21 days

PEDIATRICS

The safety and efficacy of Columvi™ in pediatric patients have not been established.

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

None

HEPATIC IMPAIRMENT

None

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injection:

- 2.5 mg/2.5 mL (1 mg/mL) in a single-dose vial.
- 10 mg/10 mL (1 mg/mL) in a single-dose vial.