09-J4000-60

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Reviewed: 08/14/24

Revised: 03/15/25

Subject: Glofitamab-gxbm (Columvi) IV Infusion

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DESCRIPTION:

Diffuse large B-cell lymphoma (DLBCL) is the most common histologic subtype of non-Hodgkin lymphoma (NHL) and accounts for approximately one-third of NHL patients. The highest incidence of DLBCL is among patients equal to or older than 65 years of age; however, it can present in pediatric patients. The clinical presentation typically consists of swollen or enlarged lymph nodes, unexplained weight loss (greater than 10% body weight in prior 6 months), night sweats, and fever (greater than 100.4 degrees F for greater than or equal to 3 days).

DLBCL are generally aggressive, but potentially curable in the majority of patients. Initial treatment for DLBCL includes combination chemotherapy plus rituximab such as R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) or Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, and prednisone). This can lead to survival rates of approximately 70%, 60%, and 45% at 3, 5, and 10 years, respectively, after diagnosis. Unfortunately, about 30 to 40 percent of patients with DLBCL relapse. Therefore, second line therapies may include bendamustine with rituximab, brentuximab vedotin (Adcetris) for CD30+ tumors, CEPP (cyclophosphamide, etoposide, prednisone, procarbazine, rituximab), CEOP (cyclophosphamide, etoposide, vincristine, prednisone , rituximab), GDP (gemcitabine, dexamethasone, carboplatin, with rituximab), lenalidomide (Revlimid) with rituximab, and ibrutinib (Imbruvica). If relapse occurs in less than 12 months or for primary refractory disease, anti-CD19 chimeric antigen receptor (CAR) T-cell therapy may be considered.

On June 15, 2023, the FDA granted accelerated approval to glofitamab-gxbm (Columvi) 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. Glofitamab-gxbm (Columvi) 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

The efficacy and safety of glofitamab-gxbm (Columvi) was evaluated in Phase 2 of a Phase 1-to-2, open-label, multicenter, multicohort, single-arm clinical trial. Patients 18 years of age or older who had

histologically confirmed DLBCL (not otherwise specified), transformed follicular lymphoma, high-grade B-cell lymphoma, or primary mediastinal large B-cell lymphoma and an Eastern Cooperative Oncology Group performance-status score of 0 or 1 (on a 5-point scale, with higher numbers indicating greater disability) were enrolled. All patients had disease that had relapsed after, or was refractory to, at least two previous lines of therapy including at least one anti-CD20 antibody-containing regimen and at least one anthracycline-containing regimen. Patients were administered pretreatment with obinutuzumab 1000 mg intravenously 7 days before the first dose of glofitamab (Columvi). Glofitamab (Columvi) was then administered intravenously as step-up doses on day 8 (2.5 mg) and day 15 (10 mg) of cycle 1, followed by a dose of 30 mg on day 1 of cycles 2 through 12 (cycles lasted 21 days). Patients were treated for 12 cycles or until the occurrence of disease progression or an unacceptable level of toxic effects. The primary end point was complete response according to assessment by an independent review committee. Secondary end points included duration of response, survival, and safety. Of the 155 patients who were enrolled, 154 received at least one dose of any study treatment (obinutuzumab or glofitamab). At a median follow-up of 12.6 months, 39% (95% confidence interval [CI], 32 to 48) of the patients had a complete response according to independent review. The median time to a complete response was 42 days (95% confidence interval [CI], 42 to 44) and the duration of CR was not reached (95% confidence interval [CI], 16.8 month to not reached). Objective response (OR) was observed in 52% of patients, with a median duration of 18.4 months (95% confidence interval [CI], 13.7 to not reached). The 6-month progression-free survival (PFS) was 46%, and 12-month PFS was 37% with a median PFS of 4.9 months (95% confidence interval [CI], 3.4 to 8.1 months). Discontinuation of glofitamab due to adverse events occurred in 3% of the patients. The most common adverse event was cytokine release syndrome (63%), and the most common Grade 3 or 4 adverse event was neutropenia (27%). Adverse events of Grade 3 or higher occurred in 62% of the patients, with Grade 3 or higher CRS in 4% and Grade 3 or higher neurologic events in 3%.

The NCCN compendia also lists glofitamab-gxbm (Columvi) as a third-line option for HIV-related B-cell lymphoma (e.g., diffuse large B-cell lymphoma, primary effusion lymphoma, HHV8-positive DLBCL, not otherwise specified), diffuse large B-cell lymphoma, including DLBCL transformed from indolent lymphoma, high-grade B-cell lymphoma, including high-grade B-cell lymphoma, NOS and high-grade B-cell lymphomas with translocation of *MYC* and *BCL2* and/or *BCL6* (double-/triple-hit lymphoma), and monomorphic post-transplant lymphoproliferative disorder (PTLD) (B-cell type).

POSITION STATEMENT:

Administration of glofitamab-gxbm (Columvi) **meets the definition of medical necessity** when **ANY** of the following are met ("1" or "2"):

1. **ALL** of the following ("a" to "d"):
    a. Member has a confirmed diagnosis of **ANY** of the following ("i" to "iv") - *medical record documentation confirming the patient's diagnosis and complete treatment history must be submitted*:
        i. HIV-related B-cell lymphoma that includes any of the following subtypes:
            - Diffuse large B-cell lymphoma (DLBCL)
            - Primary effusion lymphoma

- HHV8-positive DLBCL, not otherwise specified (NOS)

ii. Diffuse large B-cell lymphoma (DLBCL) [including DLBCL transformed from indolent lymphoma]

iii. High-grade B-cell lymphoma [includes high-grade B-cell lymphoma, NOS and high-grade B-cell lymphomas with translocation of *MYC* and *BCL2* and/or *BCL6* (double-/triple-hit lymphoma)]

iv. Monomorphic post-transplant lymphoproliferative disorder (PTLD) (B-cell type)

b. Glofitamab-gxbm (Columvi) will be used as either second-line or subsequent therapy

c. Glofitamab-gxbm (Columvi) will be used as a single-agent therapy or in combination with gemcitabine and oxaliplatin

d. Dosage of glofitamab-gxbm (Columvi) does not exceed the following:

i. Cycle 1: 2.5 mg IV on Day 8 (Step-up dose 1) 10 mg IV on Day 15 (Step-up dose 2)

ii. Cycles 2-12: 30 mg IV on Day 1 for 12 total cycles

2. Member has another FDA-approved or NCCN-supported diagnosis, and **ALL** of the following criteria are met ("a", "b", and "c"):

a. **EITHER** of the following ("i" or "ii"):

i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert), **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)

ii. Indication **AND** usage are recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

b. Glofitamab-gxbm (Columvi) is used in a treatment regimen in accordance with the FDA-approved prescribing information or applicable NCCN guideline recommendation for the diagnosis

c. Dosage of glofitamab-gxbm (Columvi) does not exceed the maximum recommended in the FDA-approved prescribing information or the maximum recommended by the applicable NCCN guidelines for the diagnosis

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Glofitamab-gxbm (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.

- Obinutuzumab 1000 mg should be administered intravenously 7 days before the first dose of glofitamab (Columvi) [Cycle 1 Day 1] at an infusion rate of 50 mg/hour. The rate of infusion can be escalated in 50 mg/hour increments every 30 minutes to a maximum of 400 mg/hour.
- Glofitamab (Columvi) is administered intravenously as step-up doses on day 8 (2.5 mg) and day 15 (10 mg) of cycle 1, followed by a dose of 30 mg on day 1 of cycles 2 through 12 (cycles lasted 21 days).
- Premedication with dexamethasone 20 mg intravenously (or prednisone 100 mg, prednisolone 100 mg, or methylprednisolone 80 mg intravenously), acetaminophen 500 to 1,000 mg orally, and an antihistamine (diphenhydramine 50 mg orally or intravenously or equivalent) is recommended to prevent and/or minimize the Cytokine Release Syndrome (CRS).
- Administration of glofitamab (Columvi) should occur in a facility equipped to monitor and manage CRS with patients being hospitalized for the 2.5 mg step-up dose and for subsequent infusions as recommended. For the first glofitamab (Columvi) step-up dose (2.5 mg on Cycle 1 Day 8), patients should be hospitalized during and for 24 hours after completion of the infusion. Patients who experienced any grade CRS during step-up dose 1 should be hospitalized during and for 24 hours after completion of step-up dose 2 (10 mg on Cycle 1 Day 15). CRS with step-up dose 2 can occur in patients who did not experience CRS with step-up dose 1. For subsequent infusions (30 mg on Day 1 of Cycle 2 or subsequent cycles), patients who experienced Grade ≥ 2 CRS with their previous infusion should be hospitalized during and for 24 hours after completion of the next glofitamab (Columvi) infusion.
- Before starting glofitamab (Columvi), administer anti-hyperuricemics to patients at risk of tumor lysis syndrome, ensure adequate hydration status, and monitor as appropriate.
- Prior to starting glofitamab (Columvi), consider initiation of antiviral prophylaxis to prevent herpes virus reactivation, prophylaxis for cytomegalovirus infection in patients at increased risk, and PJP prophylaxis in patients at increased risk.
- Administer glofitamab (Columvi), only as an intravenous infusion through a dedicated infusion line that includes a sterile 0.2- micron in-line filter.
- The recommended duration of infusion for glofitamab (Columvi) for Cycles 1 and 2 is 4 hours; the duration of infusion may be reduced to 2 hours for Cycles 3 through 12.

Dose Adjustments

- The effect of renal or hepatic impairment on the pharmacokinetics of glofitamab-gxbm (Columvi) is unknown.
- For patients who experience CRS with the 4-hour duration of infusion, the time of infusion may be extended up to 8 hours.
- For patients who experienced CRS with the 2-hour duration of infusion, the duration of infusion should be maintained at 4 hours.
- Recommendations for restarting glofitamab (Columvi) after dose delay are listed below:

Last Dose Administered	Time Since Last Dose Administered	Action for Next Dose(s)[a]
Obinutuzumab pretreatment (Cycle 1 Day 1)	≤ 2 weeks	• Administer glofitamab (Columvi) 2.5 mg (Cycle 1 Day 8)[b], then resume the planned treatment schedule.
	> 2 weeks	• Repeat obinutuzumab 1,000 mg pretreatment (Cycle 1 Day 1). • Then administer glofitamab (Columvi) 2.5 mg (Cycle 1 Day 8)[b] and resume the planned treatment schedule.
Glofitamab (Columvi) 2.5 mg (Cycle 1 Day 8)	≤ 2 weeks	• Administer glofitamab (Columvi) 10 mg (Cycle 1 Day 15)[c], then resume the planned treatment schedule.
	> 2 to ≤ 4 weeks	• Repeat glofitamab (Columvi) 2.5 mg (Cycle 1 Day 8)[b]. • Then administer glofitamab (Columvi) 10 mg (Cycle 1 Day 15)[c] and resume the planned treatment schedule.
	> 4 weeks	• Repeat obinutuzumab 1,000 mg pretreatment (Cycle 1 Day 1) and glofitamab (Columvi) 2.5 mg (Cycle 1 Day 8)[b]. • Then administer glofitamab (Columvi) 10 mg (Cycle 1 Day 15)c and resume the planned treatment schedule.
Glofitamab (Columvi) 10 mg (Cycle 1 Day 15)	≤ 2 weeks	• Administer glofitamab (Columvi) 30 mg (Cycle 2 Day 1), then resume the planned treatment schedule.
	> 2 to ≤ 6 weeks	• Repeat glofitamab (Columvi) 10 mg (Cycle 1 Day 15)[c] • Then administer glofitamab (Columvi) 30 mg (Cycle 2 Day 1) and resume the planned treatment schedule.
	> 6 weeks	• Repeat obinutuzumab 1,000 mg pretreatment (Cycle 1 Day 1), glofitamab (Columvi) 2.5 mg (Cycle 1 Day 8)[b], and

		glofitamab (Columvi) 10 mg (Cycle 1 Day 15)[c]. • Then administer glofitamab (Columvi) 30 mg (Cycle 2 Day 1) and resume the planned treatment schedule.
Glofitamab (Columvi) 30 mg (Cycle 2 onwards)	≤ 6 weeks	• Administer glofitamab (Columvi) 30 mg, then resume the planned treatment schedule.
	> 6 weeks	• Repeat the standard dosing schedule: obinutuzumab 1,000 mg pretreatment (Day 1), glofitamab (Columvi) 2.5 mg (Day 8)[b] , and glofitamab (Columvi) 10 mg (Day 15)[c]. • Then administer glofitamab (Columvi) 30 mg (Day 1 of next cycle) and resume the planned treatment schedule

[a] Administer premedication for all patients.

[b] Patients should be hospitalized during and for 24 hours after completing infusion of the 2.5 mg dose.

[c] Patients should be hospitalized during and for 24 hours after completing infusion of the 10 mg dose if CRS occurred during the most recent 2.5 mg dose.

Drug Availability

- Glofitamab-gxbm (Columvi) injection is a sterile, preservative-free, colorless, clear solution for intravenous infusion.
- Glofitamab-gxbm (Columvi) is supplied as:
  - One 2.5 mg/2.5 mL (1 mg/mL) single-dose vial (NDC 50242-125-01)
  - One 10 mg/10 mL (1 mg/mL) single-dose vial (NDC 50242-127-01)

PRECAUTIONS:

Boxed Warning

- Cytokine Release Syndrome (CRS), including serious or fatal reactions, can occur in patients receiving glofitamab-gxbm (Columvi). Premedicate before each dose, and initiate treatment with the step-up dosing schedule to reduce the risk of CRS. Withhold glofitamab-gxbm (Columvi) until CRS resolves or permanently discontinue based on severity.

Contraindications

- None

Precautions/Warnings

- **Neurologic Toxicity:** Glofitamab-gxbm (Columvi) 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:** Glofitamab-gxbm (Columvi) can cause serious or fatal infections. Monitor patients for signs and symptoms of infection and treat appropriately.
- **Tumor Flare:** Glofitamab-gxbm (Columvi) can cause serious tumor flare reactions. Monitor patients at risk for complications of tumor flare.
- **Embryo-Fetal Toxicity:** Glofitamab-gxbm (Columvi) may cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9286	Injection, glofitamab-gxbm, 2.5 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

B20	Human immunodeficiency virus [HIV] disease [for AIDS-related B-cell lymphomas only and only used in combination with C83.30-C83.39, C83.80-C83.89, or C85.80-C85.89]
C83.30 – C83.38	Diffuse large B-cell lymphoma
C83.390	Primary central nervous system lymphoma
C83.398	Diffuse large B-cell lymphoma of other extranodal and solid organ sites
C83.80 – C83.89	Other non-follicular lymphoma
C83.90 – C83.99	Non-follicular (diffuse) lymphoma, unspecified
C85.10 – C85.19	Unspecified B-cell lymphoma
C85.80 – C85.89	Other specified types of non-Hodgkin lymphoma
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 08/14/24.

GUIDELINE UPDATE INFORMATION:

09/15/23	New Medical Coverage Guideline – Glofitamab-gxbm as a third-line or subsequent monotherapy for HIV-related B-cell lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphoma, and monomorphic post-transplant lymphoproliferative disorder.
01/01/24	Revision: Added HCPCS code J9286 and deleted code J9999.
09/15/24	Review and revision to guideline consisting of updating references.
10/01/24	Revision: Updating ICD-10 billing codes.
03/15/25	Revision to guideline consisting of updating the position statement to add new 1 and 2A NCCN recommendations for second-line or subsequent therapy and use in combination with gemcitabine and oxaliplatin.