

**COLUMVI- glofitamab concentrate**  
**COLUMVI- glofitamab solution, concentrate**  
**Genentech, Inc.**

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use COLUMVI™ safely and effectively. See full prescribing information for COLUMVI.

**COLUMVI (glofitamab-gxbm) injection, for intravenous use**  
**Initial U.S. Approval: 2023**

**WARNING: CYTOKINE RELEASE SYNDROME**

*See full prescribing information for complete boxed warning*

**Cytokine Release Syndrome (CRS), including serious or fatal reactions, can occur in patients receiving COLUMVI. Premedicate before each dose, and initiate treatment with the COLUMVI step-up dosing schedule to reduce the risk of CRS. Withhold COLUMVI until CRS resolves or permanently discontinue based on severity. (2.1, 2.2, 2.3, 2.4, 5.1)**

----- **INDICATIONS AND USAGE** -----

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). (1)

----- **DOSAGE AND ADMINISTRATION** -----

- Pretreat with a single 1,000 mg dose of obinutuzumab intravenously 7 days before initiation of COLUMVI (Cycle 1 Day 1). (2.2)
- Administer premedications as recommended. (2.3)
- Administer only as an intravenous infusion. (2.1)
- Recommended dosage (2.2):

<b>Treatment Cycle*</b>	<b>Day</b>	<b>Dose of COLUMVI</b>	
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	

\* Cycle = 21 days

- Administer in a facility equipped to monitor and manage CRS. (2.1, 2.2)
- Patients should be hospitalized for the 2.5 mg step-up dose and for subsequent infusions as recommended. (2.1, 2.2)
- See Full Prescribing Information for instructions on preparation and administration. (2.5)

----- **DOSAGE FORMS AND STRENGTHS** -----

Injection:

- 2.5 mg/2.5 mL (1 mg/mL) in a single-dose vial. (3)
- 10 mg/10 mL (1 mg/mL) in a single-dose vial. (3)

----- **CONTRAINDICATIONS** -----

None. (4)

----- **WARNINGS AND 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. (5.2)

- **Serious Infections:** Can cause serious or fatal infections. Monitor patients for signs and symptoms of infection and treat appropriately. (5.3)
- **Tumor Flare:** Can cause serious tumor flare reactions. Monitor patients at risk for complications of tumor flare. (5.4)
- **Embryo-Fetal Toxicity:** May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception. (5.5, 8.1, 8.3)

#### -----ADVERSE REACTIONS-----

The most common ( $\geq 20\%$ ) adverse reactions, excluding laboratory abnormalities, are cytokine release syndrome, musculoskeletal pain, rash, and fatigue. The most common ( $\geq 20\%$ ) Grade 3 to 4 laboratory abnormalities are lymphocyte count decreased, phosphate decreased, neutrophil count decreased, uric acid increased, and fibrinogen decreased. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

#### -----USE IN SPECIFIC POPULATIONS-----

**Lactation:** Advise not to breastfeed. (8.2)

**See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.**

**Revised: 6/2023**

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## **FULL PRESCRIBING INFORMATION: CONTENTS\***

### **WARNING: CYTOKINE RELEASE SYNDROME**

#### **1 INDICATIONS AND USAGE**

#### **2 DOSAGE AND ADMINISTRATION**

2.1 Important Dosing Information

2.2 Recommended Dosage

2.3 Recommended Premedication and Prophylactic Medications

2.4 Dosage Modifications for Adverse Reactions

2.5 Preparation and Administration

#### **3 DOSAGE FORMS AND STRENGTHS**

#### **4 CONTRAINDICATIONS**

#### **5 WARNINGS AND PRECAUTIONS**

5.1 Cytokine Release Syndrome

5.2 Neurologic Toxicity

5.3 Serious Infections

5.4 Tumor Flare

5.5 Embryo-Fetal Toxicity

#### **6 ADVERSE REACTIONS**

6.1 Clinical Trials Experience

#### **7 DRUG INTERACTIONS**

#### **8 USE IN SPECIFIC POPULATIONS**

8.1 Pregnancy

8.2 Lactation

8.3 Females and Males of Reproductive Potential

8.4 Pediatric Use

8.5 Geriatric Use

#### **11 DESCRIPTION**

#### **12 CLINICAL PHARMACOLOGY**

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

12.6 Immunogenicity

### **13 NONCLINICAL TOXICOLOGY**

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

### **14 CLINICAL STUDIES**

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

### **16 HOW SUPPLIED/STORAGE AND HANDLING**

### **17 PATIENT COUNSELING INFORMATION**

\* Sections or subsections omitted from the full prescribing information are not listed.

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## **FULL PRESCRIBING INFORMATION**

### **WARNING: CYTOKINE RELEASE SYNDROME**

**Cytokine Release Syndrome (CRS), including serious or fatal reactions, can occur in patients receiving COLUMVI. Premedicate before each dose, and initiate treatment with the COLUMVI step-up dosing schedule to reduce the risk of CRS. Withhold COLUMVI until CRS resolves or permanently discontinue based on severity [see *Dosage and Administration (2.1, 2.2, 2.3, and 2.4)* and *Warnings and Precautions (5.1)*].**

## **1 INDICATIONS AND USAGE**

COLUMVI is 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 [see *Clinical Studies (14.1)*]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

## **2 DOSAGE AND ADMINISTRATION**

### **2.1 Important Dosing Information**

- Administer only as an intravenous infusion through a dedicated infusion line that includes a sterile 0.2-micron in-line filter.
- COLUMVI should only be administered by a healthcare professional with immediate access to appropriate medical support, including supportive medications to manage severe CRS [see *Dosage and Administration (2.4)*].
- Ensure adequate hydration before administering COLUMVI.
- Premedicate before each dose [see *Dosage and Administration (2.3)*].

- Following pretreatment with obinutuzumab, administer COLUMVI according to the step-up dosing schedule in Table 1 with appropriate premedication, including dexamethasone, to reduce the incidence and severity of CRS [see *Dosage and Administration (2.3)*].
- Due to the risk of CRS, patients should be hospitalized during and for 24 hours after completion of infusion of step-up dose 1 (2.5 mg on Cycle 1 Day 8) [see *Dosage and Administration (2.2)* and *Warnings and Precautions (5.1)*].
- 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 [see *Dosage and Administration (2.2)* and *Warnings and Precautions (5.1)*].
- For subsequent doses, patients who experienced Grade  $\geq 2$  CRS with their previous infusion should be hospitalized during and for 24 hours after the completion of the next COLUMVI infusion.

## 2.2 Recommended Dosage

### Pretreatment with Obinutuzumab

Pretreat all patients with a single 1,000 mg dose of obinutuzumab administered as an intravenous infusion on Cycle 1 Day 1, 7 days prior to initiation of COLUMVI (see Table 1) to deplete the circulating and lymphoid tissue B cells.

Obinutuzumab should be administered as an intravenous infusion at 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. Refer to the obinutuzumab prescribing information for complete dosing information.

### COLUMVI Step-up Dose Schedule

COLUMVI dosing begins with a step-up dose schedule. Following completion of pretreatment with obinutuzumab on Cycle 1 Day 1, administer COLUMVI as an intravenous infusion according to the step-up dose schedule in Table 1. Administer premedications for each dose of COLUMVI as described in Table 3 [see *Dosage and Administration (2.3)*].

**Table 1: COLUMVI Dosing Schedule (21-Day Treatment Cycles)**

Treatment cycle	Day	Dose of COLUMVI		Duration of infusion
<b>Cycle 1</b>	Day 1	Obinutuzumab*		
	Day 8	Step-up dose 1	2.5 mg	4 hours <sup>†</sup>
	Day 15	Step-up dose 2	10 mg	
<b>Cycle 2</b>	Day 1	30 mg		4 hours <sup>†</sup>
<b>Cycle 3 to 12</b>	Day 1	30 mg		2 hours <sup>‡</sup>

\* Refer to "Pretreatment with obinutuzumab" described above.

† For patients who experience CRS with their previous dose of COLUMVI, the time of infusion may be extended up to 8 hours.

‡ If the patient experienced CRS with the previous dose, the duration of infusion should be maintained at 4 hours.

Continue COLUMVI for a maximum of 12 cycles (inclusive of Cycle 1 step-up dosing) or until disease progression or unacceptable toxicity, whichever occurs first.

**Monitoring for Cytokine Release Syndrome [see Warnings and Precautions (5.1)]**

- Administer the COLUMVI infusions intravenously in a healthcare setting with immediate access to medical support to manage CRS, including severe CRS.
- For the first 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 COLUMVI 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  $\geq$  2 CRS with their previous infusion should be hospitalized during and for 24 hours after completion of the next COLUMVI infusion.
- For monitoring after delayed or missed doses of COLUMVI, follow the recommendations in Table 2.

**Delayed or Missed Doses**

If a dose of COLUMVI is delayed, restart therapy based on the recommendations made in Table 2, then resume the treatment schedule accordingly.

For repeat of the 2.5 mg dose patients should be hospitalized during and for 24 hours after completion of the COLUMVI infusion. For the repeat of the 10 mg dose, patients should be hospitalized during and for 24 hours after completion of the COLUMVI infusion if any grade CRS occurred during the most recent 2.5 mg dose.

**Table 2: Recommendations for Restarting COLUMVI After Dose Delay**

<b>Last Dose Administered</b>	<b>Time Since Last Dose Administered</b>	<b>Action for Next Dose(s)*</b>
Obinutuzumab pretreatment (Cycle 1 Day 1)	$\leq$ 2 weeks	<ul style="list-style-type: none"> <li>• Administer COLUMVI 2.5 mg (Cycle 1 Day 8)<sup>†</sup>, then resume the planned treatment schedule.</li> </ul>
	> 2 weeks	<ul style="list-style-type: none"> <li>• Repeat obinutuzumab 1,000 mg pretreatment (Cycle 1 Day 1).</li> <li>• Then administer COLUMVI 2.5 mg (Cycle 1 Day 8)<sup>†</sup> and resume the planned treatment schedule.</li> </ul>
COLUMVI 2.5 mg (Cycle 1 Day 8)	$\leq$ 2 weeks	<ul style="list-style-type: none"> <li>• Administer COLUMVI 10 mg (Cycle 1 Day 15)<sup>‡</sup>, then resume the planned treatment schedule.</li> </ul>
	> 2 to $\leq$ 4 weeks	<ul style="list-style-type: none"> <li>• Repeat COLUMVI 2.5 mg (Cycle 1 Day 8)<sup>†</sup>.</li> <li>• Then administer COLUMVI 10 mg (Cycle 1 Day 15)<sup>‡</sup> and resume the planned</li> </ul>

		treatment schedule.
	> 4 weeks	<ul style="list-style-type: none"> <li>Repeat obinutuzumab 1,000 mg pretreatment (Cycle 1 Day 1) and COLUMVI 2.5 mg (Cycle 1 Day 8)<sup>†</sup>.</li> <li>Then administer COLUMVI 10 mg (Cycle 1 Day 15)<sup>‡</sup> and resume the planned treatment schedule.</li> </ul>
COLUMVI 10 mg (Cycle 1 Day 15)	≤ 2 weeks	<ul style="list-style-type: none"> <li>Administer COLUMVI 30 mg (Cycle 2 Day 1), then resume the planned treatment schedule.</li> </ul>
	> 2 to ≤ 6 weeks	<ul style="list-style-type: none"> <li>Repeat COLUMVI 10 mg (Cycle 1 Day 15).<sup>‡</sup></li> <li>Then administer COLUMVI 30 mg (Cycle 2 Day 1) and resume the planned treatment schedule.</li> </ul>
	> 6 weeks	<ul style="list-style-type: none"> <li>Repeat obinutuzumab 1,000 mg pretreatment (Cycle 1 Day 1), COLUMVI 2.5 mg (Cycle 1 Day 8)<sup>†</sup>, and COLUMVI 10 mg (Cycle 1 Day 15)<sup>‡</sup>.</li> <li>Then administer COLUMVI 30 mg (Cycle 2 Day 1) and resume the planned treatment schedule.</li> </ul>
COLUMVI 30 mg (Cycle 2 onwards)	≤ 6 weeks	<ul style="list-style-type: none"> <li>Administer COLUMVI 30 mg, then resume the planned treatment schedule.</li> </ul>
	> 6 weeks	<ul style="list-style-type: none"> <li>Repeat the Cycle 1 regimen described in Table 1: obinutuzumab 1,000 mg pretreatment (Day 1), COLUMVI 2.5 mg (Day 8)<sup>†</sup>, and COLUMVI 10 mg (Day 15)<sup>‡</sup>.</li> <li>Then administer COLUMVI 30 mg (Day 1 of next cycle) and resume the planned treatment schedule.</li> </ul>

\* Administer premedication as per Table 3 for all patients.

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

‡ 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.

## 2.3 Recommended Premedication and Prophylactic Medications

### Premedication

Administer the following premedications to reduce the risk of CRS and infusion-related reactions [see *Warnings and Precautions (5.1)*].

**Table 3: Premedications to be Administered for COLUMVI Infusion**

<b>Day of Treatment Cycle</b>	<b>Patients requiring premedication</b>	<b>Premedication</b>	<b>Administration</b>
<b>Cycle 1, Day 8 and Day 15; Cycle 2; Cycle 3</b>	All patients	Dexamethasone 20 mg intravenously*	Completed at least 1 hour prior to COLUMVI infusion.
		Acetaminophen 500 mg to 1,000 mg orally	At least 30 minutes before COLUMVI infusion.
		Antihistamine (diphenhydramine 50 mg orally or intravenously or equivalent)	Completed at least 30 minutes before COLUMVI infusion.
<b>All subsequent infusions</b>	All patients	Acetaminophen 500 mg to 1,000 mg orally	At least 30 minutes before COLUMVI infusion.
		Antihistamine (diphenhydramine 50 mg orally or intravenously or equivalent)	Completed at least 30 minutes before COLUMVI infusion.
	Patients who experienced any grade CRS with the previous dose	Dexamethasone 20 mg intravenously*	Completed at least 1 hour prior to COLUMVI infusion.

\* If dexamethasone is not available, administer prednisone 100 mg, prednisolone 100 mg, or methylprednisolone 80 mg intravenously.

### Tumor Lysis Syndrome Prophylaxis

Before starting COLUMVI, administer anti-hyperuricemics to patients at risk of tumor lysis syndrome, ensure adequate hydration status, and monitor as appropriate [see *Adverse Reactions (6.1)*].

### Antiviral Prophylaxis

Before starting COLUMVI, consider initiation of antiviral prophylaxis to prevent herpes virus reactivation. Consider prophylaxis for cytomegalovirus infection in patients at increased risk [see *Warnings and Precautions (5.3)*].

### Pneumocystis jirovecii Pneumonia (PJP)

Consider PJP prophylaxis prior to starting COLUMVI in patients at increased risk [see *Warnings and Precautions (5.3)*].

## **2.4 Dosage Modifications for Adverse Reactions**

No dosage reduction for COLUMVI is recommended.

### Cytokine Release Syndrome

Identify CRS based on clinical presentation [see *Warnings and Precautions (5.1)*]. Evaluate for and treat other causes of fever, hypoxia, and hypotension.

If CRS is suspected, withhold COLUMVI and manage according to the recommendations in Table 4 and current practice guidelines. Administer supportive care for CRS, which may include intensive care for severe or life-threatening cases.

**Table 4: Recommendations for Management of Cytokine Release Syndrome**

Grade*	Presenting Symptoms	Actions
Grade 1	Temperature $\geq 100.4^{\circ}\text{F}$ ( $38^{\circ}\text{C}$ ) <sup>†</sup>	<ul style="list-style-type: none"> <li>• Withhold COLUMVI and manage per current practice guidelines.               <ul style="list-style-type: none"> <li>◦ If symptoms resolve, restart infusion at a slower rate.<sup>‡</sup></li> </ul> </li> <li>• Ensure CRS symptoms are resolved for at least 72 hours before next dose.<sup>§</sup></li> <li>• Consider slower infusion rate for next dose.</li> </ul>
Grade 2	Temperature $\geq 100.4^{\circ}\text{F}$ ( $38^{\circ}\text{C}$ ) <sup>†</sup> with: Hypotension not requiring vasopressors and/or Hypoxia requiring low-flow oxygen <sup>¶</sup> by nasal cannula or blow-by	<ul style="list-style-type: none"> <li>• Withhold COLUMVI and manage per current practice guidelines.               <ul style="list-style-type: none"> <li>◦ If symptoms resolve, restart infusion at a slower rate.<sup>‡</sup></li> </ul> </li> <li>• Ensure CRS symptoms are resolved for at least 72 hours before next dose.<sup>§</sup></li> <li>• For the next dose, consider a slower infusion rate, monitor more frequently, and consider hospitalization.</li> <li>• For recurrent Grade 2 CRS, manage per Grade 3 CRS.</li> </ul>
Grade 3	Temperature $\geq 100.4^{\circ}\text{F}$ ( $38^{\circ}\text{C}$ ) <sup>†</sup> with: Hypotension requiring vasopressor (with or without vasopressin) and/or Hypoxia requiring high-flow oxygen <sup>¶</sup> by nasal cannula, face mask, non-rebreather mask, or Venturi mask	<ul style="list-style-type: none"> <li>• Withhold COLUMVI and manage per current practice guidelines, which may include intensive care.</li> <li>• Ensure CRS symptoms are resolved for at least 72 hours before next dose.<sup>§</sup></li> <li>• Hospitalize for the next dose, monitor more frequently, and consider a slower infusion rate.<sup>‡</sup></li> <li>• For recurrent Grade 3 CRS, permanently discontinue COLUMVI.</li> </ul>
	Temperature $\geq 100.4^{\circ}\text{F}$ ( $38^{\circ}\text{C}$ ) <sup>†</sup> with: Hypotension requiring multiple vasopressors (excluding	<ul style="list-style-type: none"> <li>• Permanently discontinue COLUMVI</li> </ul>

Grade 4	vasopressors (excluding vasopressin) and/or Hypoxia requiring oxygen by positive pressure (e.g., CPAP, BiPAP, intubation, and mechanical ventilation)	and manage per current practice guidelines, which may include intensive care.
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- \* American Society for Transplantation and Cellular Therapy (ASTCT) 2019 consensus grading criteria.
- † Premedication may mask fever. Therefore if clinical presentation is consistent with CRS, follow these management guidelines.
- ‡ Duration of infusion may be extended up to 8 hours, as appropriate for that cycle (see Table 1).
- § Refer to Table 2 for information on restarting COLUMVI after dose delays [see *Dosage and Administration (2.2)*].
- ¶ Low-flow oxygen defined as oxygen delivered at < 6 L/minute, high-flow oxygen defined as oxygen delivered at ≥ 6 L/minute.

### Neurologic Toxicity, Including ICANS

Management recommendations for neurologic toxicity, including ICANS, is summarized in Table 5. At the first sign of neurologic toxicity, including ICANS, consider neurology evaluation and withholding COLUMVI based on the type and severity of neurotoxicity. Rule out other causes of neurologic symptoms. Provide supportive therapy, which may include intensive care.

**Table 5: Recommended Dosage Modification for Neurologic Toxicity (Including ICANS)**

Adverse Reaction	Severity <sup>*,†</sup>	Actions
	Grade 1	<ul style="list-style-type: none"> <li>• Continue COLUMVI and monitor neurologic toxicity symptoms.</li> <li>• If ICANS, manage per current practice guidelines.</li> </ul>
	Grade 2	<ul style="list-style-type: none"> <li>• Withhold COLUMVI until neurologic toxicity symptoms improve to Grade 1 or baseline.<sup>‡, §</sup></li> <li>• Provide supportive therapy, and consider neurologic evaluation.</li> <li>• If ICANS, manage per current practice guidelines.</li> </ul>
		<ul style="list-style-type: none"> <li>• Withhold COLUMVI until neurologic toxicity symptoms improve to Grade 1 or baseline for at least 7 days.<sup>§, ¶</sup></li> </ul>

Neurologic Toxicity* (including ICANS <sup>†</sup> ) [see <i>Warnings and Precautions</i> (5.2)]	Grade 3	<ul style="list-style-type: none"> <li>• For Grade 3 neurologic events lasting more than 7 days, consider permanently discontinuing COLUMVI.</li> <li>• Provide supportive therapy, and consider neurology evaluation.</li> <li>• If ICANS, manage per current practice guidelines.</li> </ul>
	Grade 4	<ul style="list-style-type: none"> <li>• Permanently discontinue COLUMVI.</li> <li>• Provide supportive therapy, which may include intensive care, and consider neurology evaluation.</li> <li>• If ICANS, manage per current practice guidelines.</li> </ul>

\* Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.

† Based on ASTCT 2019 grading for ICANS.

‡ Consider the type of neurologic toxicity before deciding to withhold COLUMVI.

§ See *Dosage and Administration* (2.2) on restarting COLUMVI after dose delays.

¶ Evaluate benefit-risk before restarting COLUMVI.

## Other Adverse Reactions

**Table 6: Recommended Dosage Modifications for Other Adverse Reactions**

<b>Adverse Reactions*</b>	<b>Severity*</b>	<b>Actions</b>
Infections [see <i>Warnings and Precautions</i> (5.3)]	Grades 1 - 4	<ul style="list-style-type: none"> <li>• Withhold COLUMVI in patients with active infection until the infection resolves.<sup>†</sup></li> <li>• For Grade 4, consider permanent discontinuation of COLUMVI.</li> </ul>
Tumor flare [see <i>Warnings and</i>	Grade 1	<ul style="list-style-type: none"> <li>• Monitor for signs and symptoms of compression or obstruction due to mass effect secondary to tumor flare.</li> </ul>
		<ul style="list-style-type: none"> <li>• Monitor for signs and symptoms of compression or obstruction</li> </ul>

<i>Precautions (5.4)]</i>	Grades 2 - 4	due to mass effect secondary to tumor flare, and institute appropriate treatment including antihistamine and corticosteroids. • Withhold COLUMVI until tumor flare resolves.†
Neutropenia	Absolute neutrophil count less than $0.5 \times 10^9/L$	• Withhold COLUMVI until absolute neutrophil count is $0.5 \times 10^9/L$ or higher.†
Thrombocytopenia	Platelet count less than $50 \times 10^9/L$	• Withhold COLUMVI until platelet count is $50 \times 10^9/L$ or higher.†
Other Adverse Reactions [see <i>Adverse Reactions (6.1)]</i>	Grade 3 or higher	• Withhold COLUMVI until the toxicity resolves to Grade 1 or baseline.†

\* Based on NCI CTCAE, version 4.03.

† See *Dosage and Administration (2.2)* on restarting COLUMVI after dose delays.

## 2.5 Preparation and Administration

### Preparation

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. COLUMVI is a colorless clear solution. Discard the vial if the solution is cloudy, discolored, or contains visible particles.
- Use aseptic technique when preparing the COLUMVI diluted solution for intravenous infusion.
- Determine the dose, total volume of COLUMVI solution, and the number of COLUMVI vials needed (see Table 7).

### Dilution

- Withdraw the volume of 0.9% Sodium Chloride Injection or 0.45% Sodium Chloride Injection from the infusion bag according to Table 7 and discard.
- Withdraw the required volume of COLUMVI from vial(s) using a sterile needle and syringe and dilute into the infusion bag of 0.9% Sodium Chloride Injection or 0.45% Sodium Chloride Injection according to Table 7 to a final concentration of 0.1 mg/mL to 0.6 mg/mL. Discard any unused portion left in the vial.

**Table 7: Dilution of COLUMVI for infusion**

<b>Dose of COLUMVI</b>	<b>Size of infusion bag</b>	<b>Volume of 0.9% Sodium Chloride Injection or 0.45% Sodium Chloride Injection to be withdrawn and discarded</b>	<b>Volume of COLUMVI to be added in the infusion bag</b>
2.5 mg	50 mL	27.5 mL	2.5 mL
10 mg	50 mL	10 mL	10 mL

10 mg	100 mL	10 mL	10 mL
30 mg	50 mL	30 mL	30 mL
	100 mL	30 mL	30 mL

- Gently invert infusion bag to mix the solution, in order to avoid excessive foaming. Do not shake.
- Immediately use diluted COLUMVI solution. If not used immediately, the diluted solution can be stored:
  - Refrigerated at 2°C to 8°C (36°F to 46°F) for up to 64 hours, or
  - At room temperature up to 25°C (77°F) for up to 4 hours.
  - Do not freeze the diluted infusion solution.
  - Discard diluted infusion solution if storage time exceeds these limits.

COLUMVI diluted with 0.9% Sodium Chloride Injection is compatible with intravenous infusion bags composed of polyvinyl chloride (PVC), polyethylene (PE), polypropylene (PP) or non-PVC polyolefin. When diluted with 0.45% Sodium Chloride Injection, COLUMVI is compatible with intravenous infusion bags composed of PVC.

No incompatibilities have been observed with infusion sets with product-contacting surfaces of polyurethane (PUR), PVC, or PE, and in-line filter membranes composed of polyethersulfone (PES) or polysulfone.

#### COLUMVI Administration

- Administer COLUMVI as an intravenous infusion only through a dedicated infusion line that includes a sterile 0.2-micron in-line filter.
- See Table 1 for duration of infusion. The maximum time for the administration of the diluted infusion solution may be extended up to 8 hours (see Table 4).
- Do not mix COLUMVI with other drugs.

### **3 DOSAGE FORMS AND STRENGTHS**

Injection:

- 2.5 mg/2.5 mL (1 mg/mL) clear, colorless solution in a single-dose vial.
- 10 mg/10 mL (1 mg/mL) clear, colorless solution in a single-dose vial.

### **4 CONTRAINDICATIONS**

None.

### **5 WARNINGS AND PRECAUTIONS**

#### **5.1 Cytokine Release Syndrome**

COLUMVI can cause serious and fatal cytokine release syndrome (CRS) [see *Adverse Reactions (6.1)*].

Among 145 patients who received COLUMVI, CRS occurred in 70%, with Grade 1 CRS developing in 52% of all patients, Grade 2 in 14%, Grade 3 in 2.8%, and Grade 4 in 1.4%. The most common manifestations of CRS included fever, tachycardia, hypotension,

chills, and hypoxia.

CRS occurred in 56% of patients after the 2.5 mg dose of COLUMVI, 35% after the 10 mg dose, 29% after the initial 30 mg target dose, and 2.8% after subsequent doses. With the first step-up dose of COLUMVI, the median time to onset of CRS (from the start of infusion) was 14 hours (range: 5 to 74 hours). CRS after any dose resolved in 98% of cases, with a median duration of CRS of 2 days (range: 1 to 14 days). Recurrent CRS occurred in 34% of all patients. CRS can first occur with the 10 mg dose; of 135 patients treated with the 10 mg dose of COLUMVI, 15 patients (11%) experienced their first CRS event with the 10 mg dose, of which 13 events were Grade 1, 1 event was Grade 2, and 1 event was Grade 3.

Administer COLUMVI in a facility equipped to monitor and manage CRS. Initiate therapy according to the COLUMVI step-up dosing schedule to reduce the risk of CRS, administer pretreatment medications, and ensure adequate hydration [*Dosage and Administration (2.3)*]. Patients should be hospitalized during and for 24 hours after completing infusion of the 2.5 mg step-up dose. Patients who experienced any grade CRS during the 2.5 mg step-up dose should be hospitalized during and for 24 hours after completion of the 10 mg step-up dose. For subsequent doses, patients who experienced Grade  $\geq 2$  CRS with the previous infusion should be hospitalized during and for 24 hours after the next COLUMVI infusion [*see Dosage and Administration (2.1 and 2.2)*].

At the first sign of CRS, immediately evaluate patients for hospitalization, manage per current practice guidelines, and administer supportive care; withhold or permanently discontinue COLUMVI based on severity [*see Dosage and Administration (2.4)*].

## **5.2 Neurologic Toxicity**

COLUMVI can cause serious and fatal neurologic toxicity, including Immune Effector Cell-Associated Neurotoxicity (ICANS) [*see Adverse Reactions (6.1)*].

Among 145 patients who received COLUMVI, the most frequent neurologic toxicities of any grade were headache (10%), peripheral neuropathy (8%), dizziness or vertigo (7%), and mental status changes (4.8%, including confusional state, cognitive disorder, disorientation, somnolence, and delirium). Grade 3 or higher neurologic adverse reactions occurred in 2.1% of patients and included somnolence, delirium, and myelitis. Cases of ICANS of any grade occurred in 4.8% of patients.

Coadministration of COLUMVI with other products that cause dizziness or mental status changes may increase the risk of neurologic toxicity. Optimize concomitant medications and hydration to avoid dizziness or mental status changes. Institute fall precautions as appropriate.

Monitor patients for signs and symptoms of neurologic toxicity, evaluate, and provide supportive therapy; withhold or permanently discontinue COLUMVI based on severity [*see Dosage and Administration (2.4)*].

Evaluate patients who experience neurologic toxicity such as tremors, dizziness, or adverse reactions that may impair cognition or consciousness promptly, including potential neurology evaluation. Advise affected patients to refrain from driving and/or engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, until the neurologic toxicity fully resolves.

### **5.3 Serious Infections**

COLUMVI can cause serious or fatal infections [see *Adverse Reactions (6.1)*].

Serious infections were reported in 16% of patients, including Grade 3 or 4 infections in 10%, and fatal infections in 4.8% of patients. Grade 3 or higher infections reported in  $\geq$  2% of patients were COVID-19 infection (6%), including COVID-19 pneumonia, and sepsis (4.1%). Febrile neutropenia occurred in 3.4% of patients.

COLUMVI should not be administered to patients with an active infection. Administer antimicrobial prophylaxis according to guidelines. Monitor patients before and during COLUMVI treatment for infection and treat appropriately. Withhold or consider permanent discontinuation of COLUMVI based on severity [see *Dosage and Administration (2.4)*].

### **5.4 Tumor Flare**

COLUMVI can cause serious tumor flare [see *Adverse Reactions (6.1)*]. Manifestations include localized pain and swelling at the sites of the lymphoma lesions and/or dyspnea from new pleural effusions.

Tumor flare was reported in 12% of patients who received COLUMVI, including Grade 2 tumor flare in 4.8% of patients and Grade 3 tumor flare in 2.8%. Recurrent tumor flare occurred in two (12%) of the affected patients. Most tumor flare events occurred during Cycle 1, with a median time to first onset of 2 days (range: 1 to 16 days) after the first dose of COLUMVI. The median duration was 3.5 days (range: 1 to 35 days).

Patients with bulky tumors or disease located in close proximity to airways or a vital organ should be monitored closely during initial therapy. Monitor for signs and symptoms of compression or obstruction due to mass effect secondary to tumor flare, and institute appropriate treatment. Withhold COLUMVI until tumor flare resolves [see *Dosage and Administration (2.4)*].

### **5.5 Embryo-Fetal Toxicity**

Based on its mechanism of action, COLUMVI may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with COLUMVI and for 1 month after the last dose [see *Use in Specific Populations (8.1, 8.3)*].

## **6 ADVERSE REACTIONS**

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Cytokine Release Syndrome [see *Warnings and Precautions (5.1)*]
- Neurologic Toxicity [see *Warnings and Precautions (5.2)*]
- Serious Infections [see *Warnings and Precautions (5.3)*]
- Tumor Flare [see *Warnings and Precautions (5.4)*]

### **6.1 Clinical Trials Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the

clinical trials of another drug and may not reflect the rates observed in practice.

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

### *Study NP30179*

The safety of COLUMVI was evaluated in Study NP30179, a multi-cohort, multicenter, single-arm clinical trial that included 154 adult patients with relapsed or refractory large B-cell lymphoma (LBCL) after two or more lines of systemic therapy [see *Clinical Studies (14.1)*]. The trial required an ECOG performance status of 0 or 1, absolute neutrophil count  $\geq 1,500/\mu\text{L}$ , platelet count  $\geq 75,000/\mu\text{L}$  independent of transfusion, serum creatinine  $\leq 1.5 \times$  upper limit of normal (ULN) or creatinine clearance (CLcr)  $\geq 50$  mL/min, and hepatic transaminases  $\leq 3 \times$  ULN. The trial excluded patients with active or previous central nervous system (CNS) lymphoma or CNS disease, acute infection, recent infection requiring intravenous antibiotics, or prior allogeneic hematopoietic stem cell transplantation (HSCT).

Patients received pretreatment with a single dose of obinutuzumab on Day 1 of Cycle 1 (seven days prior to start of COLUMVI). Following premedication, COLUMVI was administered by intravenous infusion according to the step-up dosing schedule with 2.5 mg on Day 8 of Cycle 1, and 10 mg on Day 15 of Cycle 1. Patients received the 30 mg COLUMVI dose by intravenous infusion on Day 1 of subsequent cycles for a maximum of 12 cycles (including step-up dosing). Each cycle was 21 days. Patients were hospitalized during and for 24 hours following completion of at least the first step-up dose.

Of the 154 patients who initiated study treatment, 145 received COLUMVI; nine patients (6%) did not receive COLUMVI due to infection, progressive disease, or patient decision. Patients received a median of 5 cycles of COLUMVI with 30% receiving all 12 cycles of COLUMVI.

Of patients who received COLUMVI, the median age was 66 years (range: 21 to 90 years); 66% were male; 77% were White, 4.8% were Asian, 1.4% were Black or African American, 6% were Hispanic or Latino. The main diagnoses were DLBCL, NOS and LBCL arising from follicular lymphoma.

Serious adverse reactions occurred in 48% of patients who received COLUMVI. Serious adverse reactions in  $\geq 2\%$  of patients included CRS, COVID-19 infection, sepsis, and tumor flare. Fatal adverse reactions occurred in 5% of patients from COVID-19 infection (3.4%), sepsis (1.4%), and delirium (0.6%).

Adverse reactions led to permanent discontinuation of COLUMVI in 7% of patients, including from infection, delirium, neutropenia, and CRS. Adverse reactions led to dose interruptions of COLUMVI in 19% of patients, most frequently ( $\geq 2\%$ ) from neutropenia and thrombocytopenia.

The most common ( $\geq 20\%$ ) adverse reactions, excluding laboratory terms, were CRS, musculoskeletal pain, rash, and fatigue. The most common Grade 3 to 4 laboratory abnormalities ( $\geq 20\%$ ) were lymphocyte count decreased, phosphate decreased, neutrophil count decreased, uric acid increased, and fibrinogen decreased.

Table 8 summarizes adverse reactions observed in Study NP30179.

### **Table 8: Select Adverse Reactions ( $\geq 10\%$ ) in Patients with**

**Relapsed or Refractory LBCL Who Received COLUMVI in Study  
NP30179**

Adverse Reactions	COLUMVI N=145	
	All grades (%)	Grade 3 or 4 (%)
<b>Immune system disorders</b>		
Cytokine release syndrome	70	4.1
<b>Musculoskeletal and connective tissue disorders</b>		
Musculoskeletal pain*	21	2.1
<b>General disorders</b>		
Fatigue†	20	1.4
Pyrexia	16	0
Edema‡	10	0
<b>Skin and subcutaneous tissue disorders</b>		
Rash§	20	1.4
<b>Gastrointestinal disorders</b>		
Constipation	14	0
Diarrhea	14	0
Nausea	10	0
Abdominal pain¶	10	0
<b>Neoplasms</b>		
Tumor flare	12	2.8
<b>Neurologic Disorders</b>		
Headache	10	0

The table includes a combination of grouped and ungrouped terms. Adverse reactions were graded using NCI CTCAE version 4.03, with the exception of CRS, which was graded per ASTCT consensus criteria in most cases.

\* Includes musculoskeletal pain, back pain, bone pain, flank pain, myalgia, neck pain, and pain in extremity.

† Includes fatigue and asthenia.

‡ Includes edema, edema peripheral, swelling face, and face edema.

§ Includes rash, rash pruritic, rash maculo-papular, dermatitis, dermatitis acneiform, dermatitis exfoliative, erythema, palmar erythema, pruritus, and rash erythematous.

¶ Includes abdominal pain, abdominal discomfort, and abdominal pain upper.

Clinically relevant adverse reactions occurring in < 10% of patients who received COLUMVI included infusion-related reaction, peripheral neuropathy, pneumonia, mental status changes, vomiting, tumor lysis syndrome, febrile neutropenia, upper respiratory tract infection, sepsis, herpes zoster infection, gastrointestinal hemorrhage, tremor, and myelitis.

Table 9 summarizes laboratory abnormalities in Study NP30179.

**Table 9: Select Laboratory Abnormalities (≥ 20%) That Worsened  
from Baseline in Patients with Relapsed or Refractory LBCL Who  
Received COLUMVI in Study NP30179**

Laboratory Abnormality	COLUMVI*	
	All Grades (%)	Grade 3 or 4 (%)
<b>Hematology</b>		
Lymphocytes decreased	90	83
Hemoglobin decreased	72	8
Neutrophils decreased	56	26 <sup>†</sup>
Platelets decreased	56	8
<b>Chemistry</b>		
Fibrinogen decreased	84	21
Phosphate decreased	69	28
Sodium decreased	49	7
Calcium decreased	48	2.1
Gamma-glutamyl transferase increased	33	9
Potassium decreased	32	6
Uric acid increased	23	23

\* The denominator used to calculate the rate varied from 137 to 145 based on the number of patients with a baseline value and at least one post-treatment value.

† Grade 4 neutrophil decrease occurred in 9% of patients.

## 7 DRUG INTERACTIONS

For certain CYP substrates where minimal concentration changes may lead to serious adverse reactions, monitor for toxicities or drug concentrations of such CYP substrates when coadministered with COLUMVI.

Glofitamab-gxbm causes the release of cytokines [see *Clinical Pharmacology (12.2)*] that may suppress the activity of CYP enzymes, resulting in increased exposure of CYP substrates. Increased exposure of CYP substrates is more likely to occur after the first dose of COLUMVI on Cycle 1 Day 8 and up to 14 days after the first 30 mg dose on Cycle 2 Day 1 and during and after CRS [see *Warnings and Precautions (5.1)*].

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Risk Summary

Based on its mechanism of action COLUMVI may cause fetal harm when administered to a pregnant woman [see *Clinical Pharmacology (12.1)*]. There are no available data on the use of COLUMVI in pregnant women to evaluate for a drug-associated risk. No animal reproductive and developmental toxicity studies have been conducted with glofitamab-gxbm.

Glofitamab-gxbm causes T-cell activation and cytokine release; immune activation may compromise pregnancy maintenance. In addition, based on expression of CD20 on B cells and the finding of B-cell depletion in non-pregnant animals, glofitamab-gxbm can cause B-cell lymphocytopenia in infants exposed to glofitamab-gxbm in-utero. Human

immunoglobulin G (IgG) is known to cross the placenta; therefore, COLUMVI has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to the fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

## **8.2 Lactation**

### Risk Summary

There are no data on the presence of glofitamab-gxbm in human milk or the effects on the breastfed child or milk production. Because human IgG is present in human milk, and there is potential for glofitamab-gxbm absorption leading to B-cell depletion, advise women not to breastfeed during treatment with COLUMVI and for 1 month after the last dose of COLUMVI.

## **8.3 Females and Males of Reproductive Potential**

COLUMVI may cause fetal harm when administered to a pregnant woman [see *Use in Specific Populations (8.1)*].

### Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating COLUMVI.

### Contraception

#### *Females*

Advise female patients of reproductive potential to use effective contraception during treatment with COLUMVI and for 1 month after the last dose of COLUMVI [see *Use in Specific Populations (8.1)*].

## **8.4 Pediatric Use**

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

## **8.5 Geriatric Use**

Of the 145 patients with relapsed or refractory LBCL who received COLUMVI in study NP30179, 55% were 65 years of age or older, and 23% were 75 years of age or older. There was a higher rate of fatal adverse reactions, primarily from COVID-19, in patients 65 years of age or older compared to younger patients [see *Adverse Reactions (6.1)*]. No overall differences in efficacy were observed between patients 65 years of age or older and younger patients.

## **11 DESCRIPTION**

Glofitamab-gxbm is a bispecific CD20-directed CD3 T-cell engager. It is a recombinant humanized anti-CD20 anti-CD3 $\epsilon$  bispecific immunoglobulin G1 (IgG1) monoclonal antibody produced in Chinese hamster ovary (CHO) cells. Glofitamab-gxbm has an approximate molecular weight of 197 kDa.

COLUMVI (glofitamab-gxbm) injection is a sterile, preservative-free, colorless, clear solution supplied in single-dose vials for intravenous infusion.

COLUMVI is supplied in 2.5 mg/2.5 mL and 10 mg/10 mL single-dose vials at a concentration of 1 mg/mL. Each mL of solution contains 1 mg glofitamab-gxbm, histidine (0.63 mg), histidine hydrochloride monohydrate (3.34 mg), methionine (1.49 mg), polysorbate 20 (0.5 mg), sucrose (82.15 mg), and Water for Injection, USP, at pH 5.5.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism 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.

### 12.2 Pharmacodynamics

#### Circulating B Cell Count

Peripheral B cell counts decreased to undetectable levels (< 5 cells/microliter) in 86.5% of patients by Cycle 1 Day 7 after obinutuzumab pretreatment of 1,000 mg on Cycle 1 Day 1, and in 88.2% of patients by Cycle 1 Day 10 after the first glofitamab-gxbm dose of 2.5 mg on Cycle 1 Day 8.

#### Cytokine Concentrations

Plasma concentrations of cytokines (IL-2, IL-6, IL-10, TNF- $\alpha$ , and IFN- $\gamma$ ) were measured and transient elevation of cytokines was observed at doses of 0.045 mg and above. After administration of the recommended dosage of COLUMVI, the highest elevation of cytokines was generally observed within 6 hours after the first glofitamab-gxbm dose of 2.5 mg on Cycle 1 Day 8. The elevated cytokine levels generally returned to baseline within 48 hours after the first 30 mg dose on Cycle 2 Day 1.

### 12.3 Pharmacokinetics

The pharmacokinetics of glofitamab-gxbm was determined following pretreatment with a single dose of obinutuzumab of 1,000 mg and the pharmacokinetic parameters are presented as geometric mean (CV%) unless otherwise specified. Glofitamab-gxbm exposure increased dose-proportionally over the dose range from 0.005 to 30 mg (0.000167 to 1 time the recommended treatment dosage). Glofitamab-gxbm exposure parameters are summarized in Table 10 for the approved recommended dosage of COLUMVI.

**Table 10: Exposure Parameters of Glofitamab-gxbm Following Pretreatment with a Single Dose of Obinutuzumab of 1,000 mg**

	<b>AUC<sub>tau</sub></b> <b>(day·mcg/mL)</b>	<b>C<sub>max</sub></b> <b>(mcg/mL)</b>	<b>C<sub>trough</sub></b> <b>(mcg/mL)</b>
--	-------------------------------------------------	-------------------------------------------	----------------------------------------------

First full 30 mg dose	44.5 (55%)	9.41 (27%)	0.52 (83%)
Steady state* 30 mg dose	48.6 (33%)	9.44 (26%)	0.59 (67%)

Data presented as geometric mean (CV%).  $AUC_{tau}$  = area under the concentration-time curve over one 21-day cycle;  $C_{max}$  = maximum glofitamab-gxbm concentration;  $C_{trough}$  = glofitamab-gxbm concentration prior to next dose; CV = geometric coefficient of variation.

\* Steady state values are approximated at Cycle 6 (week 18).

### Distribution

The glofitamab-gxbm total volume of distribution is 5.6 L (24%).

### Elimination

At steady state, the glofitamab-gxbm terminal half-life is 7.6 days (24%) and the clearance is 0.617 L/day (33%).

### *Metabolism*

Glofitamab-gxbm is expected to be metabolized into small peptides by catabolic pathways.

### Specific Populations

No clinically significant changes in the pharmacokinetics of glofitamab-gxbm were observed based on age (21 to 90 years), body weight (31 to 148 kg), sex, mild to moderate renal impairment (CLcr 30 to < 90 mL/min as estimated by Cockcroft-Gault formula) and mild hepatic impairment (total bilirubin > ULN to  $\leq 1.5 \times$  ULN or AST > ULN).

The effects of severe renal impairment (CLcr 15 to < 30 mL/min), end-stage renal disease (CLcr < 15 mL/min), or moderate to severe hepatic impairment (total bilirubin >  $1.5 \times$  ULN and any AST), and race/ethnicity on the pharmacokinetics of glofitamab-gxbm are unknown.

### Drug Interaction Studies

No clinical studies evaluating the drug interaction potential of glofitamab-gxbm have been conducted.

## **12.6 Immunogenicity**

The observed incidence of antidrug antibodies (ADA) is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of ADA in the study described below with the incidence of ADA in other studies, including those of glofitamab-gxbm.

During treatment in Study NP30179 (up to 9 months) [see *Clinical Studies (14.1)*], using an enzyme-linked immunosorbent assay (ELISA), the incidence of anti-glofitamab antibody formation was 1.1% (5/448) in patients treated with COLUMVI. Because of the low occurrence of ADAs, the effect of these antibodies on the pharmacokinetics, pharmacodynamics, safety, and/or effectiveness of glofitamab-gxbm is unknown.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity or genotoxicity studies have been conducted with glofitamab-gxbm. Fertility studies have not been conducted with glofitamab-gxbm.

## 14 CLINICAL STUDIES

### 14.1 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  $\geq 1,500/\mu\text{L}$ , platelet count  $\geq 75,000/\mu\text{L}$  independent of transfusion, serum creatinine  $\leq 1.5 \times \text{ULN}$  or CLcr  $\geq 50 \text{ mL/min}$ , and hepatic transaminases  $\leq 3 \times \text{ULN}$ . 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 11. 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.

**Table 11: IRC-Assessed Efficacy in Patients with Relapsed or Refractory DLBCL, NOS or LBCL Arising from Follicular Lymphoma**

Outcome per IRC	COLUMVI N=132
Overall Response Rate, n (%)	74 (56)

(95% CI)	(47, 65)
<b>Complete Response, n (%)</b> (95% CI)	57 (43) (35, 52)
<b>Partial Response, n (%)</b> (95% CI)	17 (13) (8, 20)
<b>Duration of Response*</b>	N = 74
Median DOR, months (95% CI)†	18.4 (11.4, NE)
9-month estimate, % (95% CI)†	68.5 (56.7, 80.3)

CI = confidence interval; NE = not estimable

\* From date of first response (PR or CR) until disease progression or death due to any cause.

† Kaplan-Meier estimate.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

COLUMVI (glofitamab-gxbm) injection is a sterile, preservative-free, colorless, clear solution for intravenous infusion.

COLUMVI is supplied as:

<b>Carton Contents</b>	<b>NDC</b>
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

Store refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

### Cytokine Release Syndrome

Inform patients of the risk of CRS. Advise patients to seek immediate medical attention if they experience signs and symptoms of CRS (fever, hypoxia, hypotension, chills and tachycardia) [see *Warnings and Precautions (5.1)*].

Provide patients with the Patient Wallet Card that they should carry with them at all times. This card describes symptoms of CRS which, if experienced, should prompt the patient to seek immediate medical attention.

### Neurologic Toxicity

Discuss the signs and symptoms associated with neurologic toxicity, including ICANS, headache, peripheral neuropathy, dizziness, or mental status changes. Advise patients to immediately contact their healthcare provider if they experience any signs or symptoms of neurologic toxicity. Advise patients who experience neurologic toxicity that impairs consciousness to refrain from driving or operating heavy or potentially

dangerous machinery until neurologic toxicity resolves [see *Warnings and Precautions (5.2)*].

### Serious Infections

Advise patients that COLUMVI can cause serious infections. Advise patients to notify their healthcare provider immediately if they develop any signs of infection (e.g., fever, chills, weakness) [see *Warnings and Precautions (5.3)*].

### Tumor Flare

Inform patients of the potential risk of tumor flare reaction and to report any signs and symptoms associated with this event (e.g., localized pain and swelling) to their healthcare provider for evaluation [see *Warnings and Precautions (5.4)*].

### Embryo-Fetal Toxicity

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider if they are pregnant or become pregnant. Advise females of reproductive potential to use effective contraception during treatment with COLUMVI and for 1 month after the last dose [see *Warnings and Precautions (5.5) and Use in Specific Populations (8.1, 8.3)*].

Advise women not to breastfeed while receiving treatment with COLUMVI and for 1 month after the last dose [see *Use in Specific Populations (8.2)*].

COLUMVI™ [glofitamab-gxbm]

Manufactured by:

**Genentech, Inc.**

A Member of the Roche Group

1 DNA Way

South San Francisco, CA 94080-4990

U.S. License No.: 1048

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**MEDICATION GUIDE**  
**COLUMVI™ (ko-loom-vee)**  
**(glofitamab-gxbm)**  
**injection, for intravenous infusion**

**What is the most important information I should know about COLUMVI?**

**COLUMVI can cause Cytokine Release Syndrome (CRS)**, a serious side effect that is common during treatment with COLUMVI, and can also be serious and lead to death.

• **Call your healthcare provider or get emergency medical help right away if you develop any signs or symptoms of CRS, including:**

- fever of 100.4°F (38°C) or higher
- chills or shaking
- fast or irregular heartbeat
- dizziness or light-headedness
- trouble breathing
- shortness of breath

- **Due to the risk of CRS, you will receive COLUMVI on a "step-up dosing schedule".**
  - A single dose of a medicine called obinutuzumab will be given to you on the first day of your first treatment cycle (Day 1 of Cycle 1).
  - You will start the COLUMVI step-up dosing schedule a week after the obinutuzumab dose. The step-up dosing schedule is when you receive smaller "step-up" doses of COLUMVI on Day 8 and Day 15 of Cycle 1. This is to help reduce your risk of CRS. You should be hospitalized during your infusion and for 24 hours after receiving the first step-up dose on Day 8. You should be hospitalized during your infusion and for 24 hours after receiving the second step-up dose on Day 15 if you experienced CRS during the first step-up dose.
  - You will receive your first full dose of COLUMVI a week after the second step-up dose (this will be Day 1 of Cycle 2).
  - If your dose of COLUMVI is delayed for any reason, you may need to repeat the "step-up dosing schedule".
  - If you had more than mild CRS with your previous dose of COLUMVI, you should be hospitalized during and for 24 hours after receiving your next dose of COLUMVI.
  - Before each dose of COLUMVI, you will receive medicines to help reduce your risk of CRS and infusion-related reactions.
  - See "**How will I receive COLUMVI?**" for more information about how you will receive COLUMVI.
- Your healthcare provider will monitor you for CRS during treatment with COLUMVI and may treat you in a hospital if you develop signs and symptoms of CRS. Your healthcare provider may temporarily stop or completely stop your treatment with COLUMVI if you have severe side effects.
- **Carry the COLUMVI Patient Wallet Card with you at all times and show it to all of your healthcare providers.** The COLUMVI Patient Wallet Card lists the signs and symptoms of CRS you should get emergency medical help for right away.

See "**What are the possible side effects of COLUMVI?**" for more information about side effects.

### **What is COLUMVI?**

COLUMVI is a prescription medicine used to treat adults with certain types of diffuse large B-cell lymphoma (DLBCL) or large B-cell lymphoma (LBCL) that has come back (relapsed) or that did not respond to previous treatment (refractory), and who have received 2 or more prior treatments for their cancer.

It is not known if COLUMVI is safe and effective in children.

### **Before receiving COLUMVI, tell your healthcare provider about all of your medical conditions, including if you:**

- have an infection
- have kidney problems
- are pregnant or plan to become pregnant. COLUMVI may harm your unborn baby.

#### **Females who are able to become pregnant:**

- Your healthcare provider should do a pregnancy test before you start treatment with COLUMVI.
- You should use effective birth control (contraception) during treatment and for 1 month after your last dose of COLUMVI. Talk to your healthcare provider about what birth control method is right for you during this time.

- Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with COLUMVI.
- are breastfeeding or plan to breastfeed. It is not known if COLUMVI passes into your breastmilk. Do not breastfeed during treatment and for 1 month after your last dose of COLUMVI.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

### **How will I receive COLUMVI?**

- COLUMVI will be given to you by your healthcare provider by infusion through a needle placed in your vein (intravenous infusion).
- Your COLUMVI treatment schedule is divided into cycles that are 21 days (3 weeks) long.
- On Day 1 of Cycle 1, your healthcare provider will give you a single dose of a medicine called obinutuzumab by intravenous infusion. You will then receive COLUMVI on Day 8 and Day 15 of Cycle 1. Starting with Cycle 2, you will receive COLUMVI 1 time every three weeks.

Your healthcare provider will decide how many treatment cycles you will receive of COLUMVI. See "**What is the most important information I should know about COLUMVI?**" for more information about how you will receive COLUMVI.

### **What should I avoid while receiving COLUMVI?**

**Do not** drive, operate heavy machinery, or do other dangerous activities if you develop dizziness, confusion, shaking (tremors), sleepiness, or any other symptoms that impair consciousness until your signs and symptoms go away. These may be signs and symptoms of neurologic problems.

See "**What are the possible side effects of COLUMVI?**" for more information about signs and symptoms of neurologic problems.

### **What are the possible side effects of COLUMVI?**

**COLUMVI may cause serious side effects, including:**

- **Cytokine Release Syndrome.** See "**What is the most important information I should know about COLUMVI?**"
- **Neurologic problems.** COLUMVI can cause serious neurologic problems that may lead to death. Your healthcare provider will monitor you for neurologic problems during treatment with COLUMVI. Your healthcare provider may also refer you to a healthcare provider who specializes in neurologic problems. Tell your healthcare provider right away if you develop any signs or symptoms of neurologic problems, including:
  - headache
  - confusion and disorientation
  - difficulty paying attention or understanding things
  - trouble speaking
  - sleepiness
  - memory problems
  - numbness, tingling, or weakness of the hands or feet
  - dizziness
  - shaking (tremors)
- **Serious infections.** COLUMVI can cause serious infections that may lead to death. Your healthcare provider will monitor you for signs and symptoms of infection and treat you as needed. Tell your healthcare provider right away if you develop any signs

of infection, including: fever, chills, weakness, cough, shortness of breath, or sore throat.

- **Growth in your tumor or worsening of tumor related problems (tumor flare).** Tell your healthcare provider if you get any of these signs or symptoms of tumor flare:
  - tender or swollen lymph nodes
  - pain or swelling at the site of the tumor
  - chest pain
  - cough
  - trouble breathing

Your healthcare provider may temporarily stop or completely stop treatment with COLUMVI if you develop certain side effects.

**The most common side effects of COLUMVI include:** CRS, muscle and bone pain, rash, and tiredness.

**The most common severe abnormal lab test results with COLUMVI include:** decreased white blood cells, decreased phosphate (an electrolyte), increased uric acid levels, and decreased fibrinogen (a protein that helps with blood clotting).

These are not all the possible side effects of COLUMVI.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**General information about the safe and effective use of COLUMVI.**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your healthcare provider or pharmacist for information about COLUMVI that is written for health professionals.

**What are the ingredients in COLUMVI?**

**Active ingredient:** glofitamab-gxbm

**Inactive ingredients:** histidine, histidine hydrochloride monohydrate, methionine, polysorbate 20, sucrose, and Water for injection.

Manufactured by: **Genentech, Inc.**, A Member of the Roche Group, 1 DNA Way, South San Francisco, CA 94080-4990

U.S. License No.: 1048

For more information, go to [www.COLUMVI.com](http://www.COLUMVI.com) or call 1-877-436-3683.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Issued: 6/2023

**PRINCIPAL DISPLAY PANEL - 10 mg/10 mL Vial Carton**

NDC 50242-127-01

Columvi™

(glofitamab-gxbm)

Injection

10 mg/10 mL

(1 mg/mL)

For Intravenous Infusion

After Dilution.

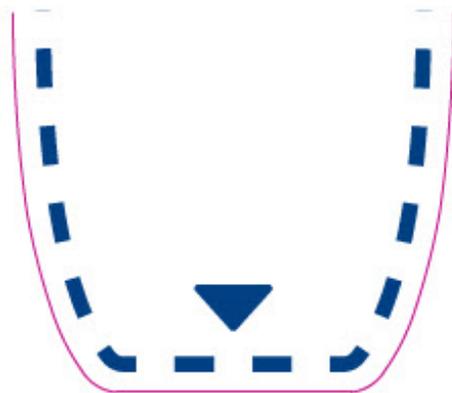
Single-Dose Vial.  
Discard Unused Portion.

ATTENTION: Dispense the enclosed  
Medication Guide to each patient.

Rx only

1 vial  
Genentech

10252990



NDC 50242-127-01

**Columvi**<sup>TM</sup>

(glofitamab-gxbm)  
Injection

**10 mg/10 mL**  
**(1 mg/mL)**

**For Intravenous Infusion  
After Dilution.**

**Single-Dose Vial.**  
**Discard Unused Portion.**

**ATTENTION:** Dispense the enclosed  
Medication Guide to each patient.

1 vial

**R<sub>x</sub> only**  
**Genentech**

10252990

**PRINCIPAL DISPLAY PANEL - 2.5 mg/2.5 mL Vial Carton**

NDC 50242-125-01

Columvi™

(glofitamab-gxbm)  
Injection

2.5 mg/2.5 mL  
(1 mg/mL)

For Intravenous Infusion  
After Dilution.

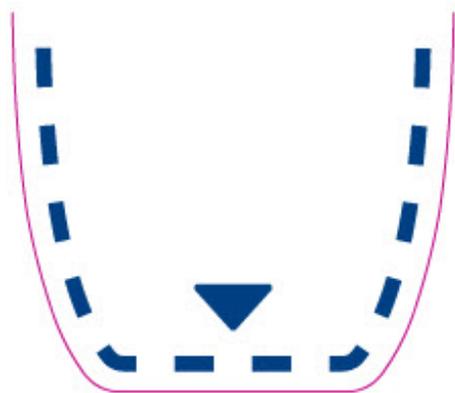
Single-Dose Vial.  
Discard Unused Portion.

ATTENTION: Dispense the enclosed  
Medication Guide to each patient.

Rx only

1 vial  
Genentech

10252987



NDC 50242-125-01

**Columvi**<sup>TM</sup>

(glofitamab-gxbm)  
Injection

**2.5 mg/2.5 mL**  
**(1 mg/mL)**

**For Intravenous Infusion  
After Dilution.**

**Single-Dose Vial.**  
**Discard Unused Portion.**

**ATTENTION:** Dispense the enclosed  
Medication Guide to each patient.

1 vial

**R<sub>x</sub> only**  
**Genentech**

10252987

## COLUMVI

glofitamab concentrate

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:50242-127
<b>Route of Administration</b>	INTRAVENOUS		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
<b>GLOFITAMAB</b> (UNII: 06P3KLK2J8) (GLOFITAMAB - UNII:06P3KLK2J8)	GLOFITAMAB	10 mg in 10 mL

### Inactive Ingredients

Ingredient Name	Strength
<b>HISTIDINE</b> (UNII: 4QD397987E)	6.3 mg in 10 mL
<b>HISTIDINE MONOHYDROCHLORIDE MONOHYDRATE</b> (UNII: X573657P6P)	33.4 mg in 10 mL
<b>METHIONINE</b> (UNII: AE28F7PNPL)	14.9 mg in 10 mL
<b>SUCROSE</b> (UNII: C151H8M554)	821.5 mg in 10 mL
<b>POLYSORBATE 20</b> (UNII: 7T1F30V5YH)	5 mg in 10 mL

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50242-127-01	1 in 1 CARTON	06/15/2023	
1		10 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761309	06/15/2023	

## COLUMVI

glofitamab solution, concentrate

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:50242-125
<b>Route of Administration</b>	INTRAVENOUS		

Active Ingredient/Active Moiety				
Ingredient Name		Basis of Strength	Strength	
GLOFITAMAB (UNII: 06P3KCLK2J8) (GLOFITAMAB - UNII:06P3KCLK2J8)		GLOFITAMAB	2.5 mg in 2.5 mL	
Inactive Ingredients				
Ingredient Name			Strength	
HISTIDINE (UNII: 4QD397987E)			1.6 mg in 2.5 mL	
HISTIDINE MONOHYDROCHLORIDE MONOHYDRATE (UNII: X573657P6P)			8.4 mg in 2.5 mL	
METHIONINE (UNII: AE28F7PNPL)			3.7 mg in 2.5 mL	
SUCROSE (UNII: C151H8M554)			205.4 mg in 2.5 mL	
POLYSORBATE 20 (UNII: 7T1F30V5YH)			1.25 mg in 2.5 mL	
WATER (UNII: 059QF0K00R)				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50242-125-01	1 in 1 CARTON	06/15/2023	
1		2.5 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		
Marketing Information				
Marketing Category	Application Number or Monograph Citation		Marketing Start Date	Marketing End Date
BLA	BLA761309		06/15/2023	

**Labeler** - Genentech, Inc. (080129000)

### Establishment

Name	Address	ID/FEI	Business Operations
Roche Diagnostics GmbH		323105205	API MANUFACTURE(50242-125, 50242-127) , ANALYSIS(50242-125, 50242-127)

### Establishment

Name	Address	ID/FEI	Business Operations
Genentech, Inc.		080129000	ANALYSIS(50242-125, 50242-127) , MANUFACTURE(50242-125, 50242-127) , PACK(50242-125, 50242-127)

### Establishment

Name	Address	ID/FEI	Business Operations
Genentech, Inc.		146373191	ANALYSIS(50242-125, 50242-127)

### Establishment

Name	Address	ID/FEI	Business Operations
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Roche Diagnostics GmbH		315028860	ANALYSIS(50242-125, 50242-127)
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## Establishment

Name	Address	ID/FEI	Business Operations
F. Hoffmann-La Roche Ltd.		485244961	LABEL(50242-125, 50242-127) , PACK(50242-125, 50242-127)

Revised: 6/2023

Genentech, Inc.