

Up Close with Glofitamab

This section provides an overview of glofitamab-gxbm (COLUMVI™).

-  Indications
-  Dosing and Administration
-  CRS
-  Neurotoxicity (including ICANS)
-  Other Toxicities

Indications



FDA-Approved Indications

Glofitamab is a **bispecific CD20-directed CD3 T-cell engager** indicated for the treatment of

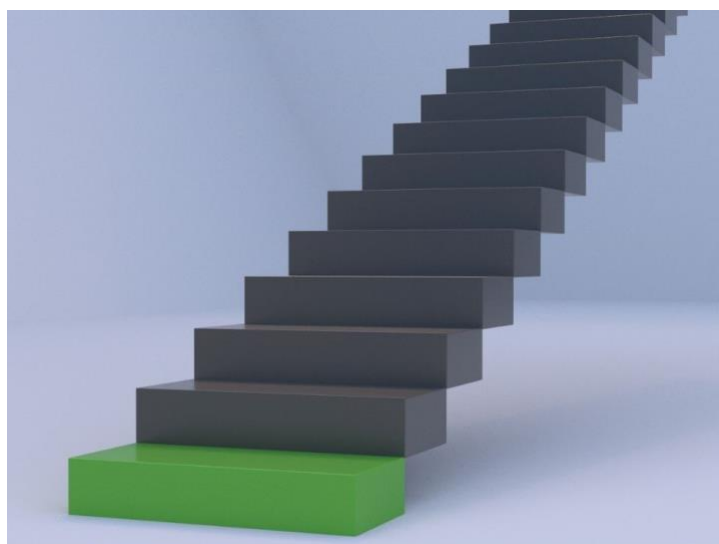
- Adult patients with **relapsed or refractory Diffuse Large B-Cell Lymphoma (DLBCL)**, not otherwise specified (NOS), or **Large B-Cell Lymphoma (LBCL)** arising from follicular lymphoma, **after 2 or more lines of systemic therapy**.

Note: These indications are approved under accelerated approval based on response rate and durability of response. Continued approval may be contingent upon verification of clinical benefit in confirmatory trials.

Guideline-Recommended Indications

- Glofitamab is recommended for **second line therapy for relapsed or refractory DLBCL when used in combination with gemcitabine and oxaliplatin**. This regimen may be used in ≤ 12 months or ≥ 12 months of relapsed disease.

Dosing and Administration



Glofitamab is administered **intravenously (IV) as a 21-day cycle** for a maximum of 12 cycles, or until disease progression unacceptable toxicity. To reduce the risk of cytokine release syndrome, glofitamab as a **unique step-up dosing** schedule as shown below.

Prior to glofitamab administration, all patients must receive obinutuzumab. Obinutuzumab is used prior to glofitamab to deplete circulating and lymphoid tissue B-cells. The recommended dose of obinutuzumab is as followed:

- 1000 mg of obinutuzumab as a single intravenous dose (Cycle 1 Day 1)

Glofitamab 2 Step-Up Dosing Schedule			
Treatment Cycles		Dose of Glofitamab / Route	Duration of Infusion
Cycle 1	Day 1	Obinutuzumab ¹ IV	4 hours ²
	Day 8	2.5 mg ^a IV	
	Day 15	10 mg IV	
Cycle 2	Day 1	30 mg IV	4 hours ²
Cycles 3 to 12	Day 1	30 mg IV	2 hours ³

¹Refer to obinutuzumab dosing as described above
²Patients who experience CRS with their previous dose of glofitamab, may extend their infusion time up to 8 hours
³Patients who experience CRS with the previous dose of glofitamab, should have their infusion duration maintained at 4 hours
^aAll patients are required to be hospitalized during the first step-up dose (2.5 mg Cycle 1 Day 8) and for 24 hours following completion

Recommendations for Restarting Therapy with Glofitamab after Dosage Delay				
Patient's Treatment History		Last Dose Administered	Time Elapsed since Last Dose	Recommended Next Actions
Medication	Cycle 1			
Obinutuzumab (pretreatment)	Day 1	1000 mg	≤ 2 weeks	Administer glofitamab 2.5 mg (Cycle 1 Day 8) ^b , then resume with treatment plan as scheduled.
			> 2 weeks	Repeat obinutuzumab pretreatment. Then administer glofitamab 2.5 mg (Cycle 1 Day 8) ^b , and resume treatment plan as scheduled.
Glofitamab	Day 8	2.5 mg	≤ 2 weeks	Administer glofitamab 10 mg (Cycle 1 Day 15) ^c , then resume treatment plan as scheduled.
			> 2 to ≤ 4 weeks	Repeat glofitamab 2.5 mg (Cycle 1 Day 8) ^b , then administer glofitamab 10 mg (Cycle 1 Day 15) ^c . Upon completion, resume treatment plan as scheduled.
			> 4 weeks	Repeat obinutuzumab pretreatment (Cycle 1 Day 1). Then administer glofitamab 2.5 mg (Cycle 1 Day 8) ^b and glofitamab 10 mg (Cycle 1 Day 15) ^c . Upon completion, resume treatment plan as scheduled.
	Day 15	10 mg	≤ 2 weeks	Administer glofitamab 30 mg (Cycle 2 Day 1) and resume treatment plan as scheduled.
			> 2 to ≤ 6 weeks	Readminister glofitamab 10 mg (Cycle 1 Day 15) ^c . Then administer glofitamab 30 mg (Cycle 2 Day 1) and resume treatment plan as scheduled.
			> 6 weeks	Repeat obinutuzumab pretreatment (Cycle 1 Day 1), glofitamab 2.5 mg (Cycle 1 Day 8) ^b and glofitamab 10 mg (Cycle 1 Day 15) ^c . Then administer glofitamab 30 mg (Cycle 2 Day 1) and resume treatment plan as scheduled.
Medication	Cycle 2+			
Glofitamab	Day 1	30 mg	≤ 6 weeks	Administer glofitamab 30 mg (Cycle 2 Day 1), then resume treatment plan as scheduled.
			> 6 weeks	Repeat Cycle 1 regimen as described above: obinutuzumab 1,000 mg pretreatment (Day 1), glofitamab 2.5 mg (Day 8) ^b , and glofitamab 10 mg (Day 15) ^c . Then administer glofitamab 30 mg (Day 1 of next cycle) and resume treatment plan as scheduled.

^aRefer to obinuztumab dosing as described above

^bPatients who experience CRS with their previous dose of glofitamab, may extend their infusion time up to 8 hours

^cPatients who experience CRS with the previous dose of glofitamab, should have their infusion duration maintained at 4 hours

Recommended Pre-Medications for Glofitamab Infusion			
Day of Treatment Cycle	Patients Requiring Medications	Pre-Medication(s) / Route	Administration
Cycle 1 (Day 8, 15) Cycle 2 (Day 1) Cycle 3 (Day 1)	All patients	Dexamethasone 20 mg* IV	Complete ≥1 hour prior to infusion.
		Diphenhydramine HCl 50 mg or equivalent antihistamine IV / PO	Complete ≥30 minutes prior to infusion
		Acetaminophen 500 mg to 1000 mg PO	Complete ≥30 minutes prior to infusion
Subsequent Cycles	All patients	Acetaminophen 500 mg to 1000 mg PO	Complete ≥30 minutes prior to infusion
		Diphenhydramine HCl 50 mg to 100 mg or equivalent antihistamine IV / PO	Administer orally or intravenously and complete at least 30 minutes prior to infusion.
	Patients who experienced any grade CRS with a previous dose	Dexamethasone 20 mg* IV	Complete ≥1 hour prior to infusion
PO, orally *If dexamethasone is unavailable, it is appropriate to administer prednisone 100 mg, prednisolone 100 mg, or methylprednisolone 80 mg intravenously			

Tumor Lysis Syndrome (TLS) Prophylaxis

- Before initiating glofitamab, **patients who are at risk for TLS should be administered anti-hyperuricemics.**
- Carefully monitor for adequate hydration status and appropriate care.

⚠ CRS



What is it? Cytokine release syndrome (CRS) is a systemic inflammatory response that can occur when the immune system is activated and releases large amounts of cytokines—proteins that help regulate immune responses.

- **Signs and symptoms:** pyrexia, hypotension, hypoxia, dyspnea, chills, and tachycardia.
- CRS is frequently graded using the [American Society for Transplantation and Cellular Therapy \(ASTCT\) consensus criteria](#).

Why it matters. CRS occurred in **70% of patients** in the clinical trial, NP30179.

- **Most CRS events** occurred during **Cycle 1**, with the **highest events** occurring on the initiation of glofitamab (**Cycle 1 Day 8**).
 - All events were **primarily Grade 1 or 2**, however due to the significantly increased risk of CRS, **all patients are required to be hospitalized during the first step-up dose (2.5 mg Cycle 1 Day 8) and for 24 hours following completion**.
- The **median time to onset of CRS** across all doses was **14 hours** following the initial step-up dose of glofitamab (range: 5 to 74 hours) post-administration.
- The **median duration** of CRS was **2 days** (range: 1 to 14 days) and resolved in 98% of cases.
- Additionally, any patient that experiences
 - **CRS during Cycle 1**, regardless of the grade, **should be hospitalized during and for 24 hours following completion of the second step-up dose** of glofitamab (10 mg on Cycle 1 Day 15).
 - **Grade ≥ 2 CRS during or following subsequent doses** of glofitamab (Day 1 of Cycle 2+) **should be hospitalized during and for 24 hours following completion** of infusion.

The bottom line. CRS was primarily low-grade, predictable, and manageable.

🧠 Neurotoxicity (including ICANS)



What is it? Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) is characterized by various neurological symptoms resulting from the activation of the immune system and the resultant inflammatory processes.

- **Signs and symptoms:** encephalopathy, headaches, seizures, aphasia, motor deficits, ataxia, and tremor.
- ICANS is frequently graded using the [ASTCT consensus criteria](#).

Why it matters. ICANS of any grade occurred in **4.8%** of patients in the clinical trial. However, the more common neurological toxicities associated with glofitamab were dizziness/vertigo, confusion, peripheral neuropathy, and headache.

- ICANS resolved in most cases and lasted a few days.
- Care teams should **monitor patients for any signs and symptoms of neurological toxicity**, including headache, peripheral neuropathy, vertigo/dizziness and confusional state.
 - Coadministration of any other neurologically acting agents may increase the risk of neurotoxicity.
 - Consider **withholding or permanently discontinuing** glofitamab **based on severity** of ICANS.

The bottom line. ICANS was uncommon and primarily low-grade.

Other Toxicities



Glofitamab may cause other adverse reactions such as **infections, tumor flares, or embryo-fetal toxicity**.

Why it matters. In addition to the risks of CRS and neurotoxicity (including ICANS), care teams need to be on the lookout for other **glofitamab**-associated toxicities.

Infections. Glofitamab can cause serious and fatal infections.

- **Serious infections**, including opportunistic infections, occurred in **16% of patients**, with **Grade 3 or 4 infections in 10%**, and **fatal infections in 4.8%**.
 - The most common serious infections reported were pneumonia, sepsis, and increased risk of COVID-19 acquired infections.

The bottom line. Care teams should **monitor patients for signs of infection before and during treatment**; treat appropriately.

- Avoid administration in patients with active infections; withhold or discontinue glofitamab based on severity.
- Consider providing *Pneumocystis jirovecii pneumonia* (PJP), herpes virus, and cytomegalovirus prophylaxis before starting glofitamab for those who may be at increased risk.

Cytopenias. Glofitamab may cause cytopenias, including thrombocytopenia and neutropenia.

- In the clinical trial, **neutropenia and thrombocytopenia** occurred in **56% of patients** whereas **febrile neutropenia** occurred in **3.4% of patients**.

The bottom line. Care teams should **monitor complete blood counts throughout treatment**.

- **Withhold or discontinue** glofitamab **based on severity of the cytopenia**.
 - Neutropenia (ANC < 0.5 x 10⁹/L) and/or
 - Thrombocytopenia (platelets < 50 x 10⁹/L)
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Embryo-Fetal Toxicity. Glofitamab may cause fetal harm when administered to a pregnant woman.

- Advise **females of reproductive potential** to use effective contraception **during treatment and for 1 month after the last dose**.
 - Verify pregnancy status before initiating glofitamab.
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Use in Specific Populations.

- **Lactation:** Human immunoglobulin-G (IgG) is present in human milk, and therefore there is a potential for glofitamab absorption leading to B-cell depletion. Advise women not to breastfeed during treatment and for 1 month after the last dose.
- **Geriatric Use** (in NP3071):
 - No overall difference identified in efficacy of glofitamab use in patients 65 years of age or older when compared to younger patients.
 - Higher rate of fatal adverse reactions, mainly infections, including COVID-19, in patients ≥ 65 years old compared to younger adults.
- **Pediatric Use:** At this time, no safety and effectiveness data has been established in pediatric patients.

Updated: 5/16/2025

References

1. [Glofitamab \(COLUMVI™\) \[package insert\]. Genentech, Inc. San Francisco, CA. 2023.](#)
2. [Lee DW, Santomaso BD, Locke FL, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biol Blood Marrow Transplant*. 2019;25\(4\):625-638. doi:10.1016/j.bbmt.2018.12.758.](#)
3. [Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma. *N Engl J Med*. 2022;387\(24\):2220-2231. doi:10.1056/NEJMoa2205183.](#)
4. [NCCN Clinical Practice Guidelines in Oncology \(NCCN Guidelines®\) for B-Cell Lymphomas V2.2025. National Comprehensive Cancer Network, Inc. 2025. Accessed March 4, 2025.](#)