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Subject: New Important Safety Information with the Use of COLUMVI® (glofitamab-gxbm): Hemophagocytic Lymphohistiocytosis

Dear Health Care Provider:

The purpose of this letter is to inform you of important safety information for COLUMVI, which is under accelerated approval and 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.

Serious Risk of Hemophagocytic Lymphohistiocytosis with the Use of COLUMVI®

- Hemophagocytic lymphohistiocytosis (HLH) is a severe hyperinflammatory syndrome driven by pathologic activation of cytotoxic T-lymphocytes and macrophages ultimately leading to cytokine storm and organ damage if not treated appropriately. In adults, infections and malignancies are common triggers for HLH, and lymphomas represent the most common trigger for malignancy-associated HLH, with an incidence of 1-20% in lymphoma patients (Wang et al. 2017). HLH secondary to T cell engaging therapies, also described as Immune Effector Cell-associated HLH like Syndrome (IEC-HS), is an emergent toxicity associated with life-threatening complications, where early detection and management is essential. HLH, including fatal cases, have been reported in COLUMVI clinical trials, compassionate use program, investigator-initiated studies, and marketing experience. HLH may resemble severe CRS with respect to clinical signs and symptoms, but may differ by presenting with a delayed onset, rapid increases in serum ferritin, and differences in cytokine profile. While symptoms may overlap with CRS, emergent treatment recommendations for HLH are distinct from those of CRS.

Updates to the Prescribing Information are planned.

The benefit-risk profile of COLUMVI in the approved indication remains favorable.

Prescriber Action
For any case of suspected HLH, interrupt COLUMVI and treat per current practice guidelines (e.g., institutional guidelines or expert consensus guidelines [Hines et al. 2023]). Expert consultation is recommended if HLH is suspected.

Reporting Adverse Events / Product Complaints and Company Contact
Health Care Providers should report any adverse events suspected to be associated with the use of COLUMVI to Genentech at 1-888-835-2555. Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088) or online (www.fda.gov/medwatch).

Please report any product complaint suspected to be associated with the use of COLUMVI to Genentech at (800) 334-0290.

Should you have any questions about the information in this letter or the safe and effective use of COLUMVI, please feel free to contact us at: Genentech Medical Information/Communications Department at (800) 821-8590.

This letter is not intended as a complete description of the benefits and risks related to the use of COLUMVI. Please refer to the enclosed full prescribing information.

Sincerely,

Charlotte Owens, M.D., FACOG
Head of U.S. Medical

References:

Hines et al. Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis-Like Syndrome. Transplant Cell Ther. 2023 Jul;29(7):438.e1-438.e16. doi: 10.1016/j.jtct.2023.03.006. Epub 2023 Mar 9. PMID: 36906275; PMCID: PMC10330221.

Wang H, Xiong L, Tang W, Zhou Y, Li F. A systematic review of malignancy- associated hemophagocytic lymphohistiocytosis that needs more attentions. Oncotarget. 2017 Jul 14;8(35):59977-59985. doi: 10.18632/oncotarget.19230. PMID: 28938698; PMCID: PMC5601794.