Genentech
A Member of the Roche Group

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Subject: New Safety Information with the Use of POLIVY® (polatuzumab vedotin-piiq): Severe Infusion Site Extravasation Events

Dear Health Care Provider:

The purpose of this letter is to inform you of new safety information for POLIVY, a CD79b-directed antibody and microtubule inhibitor conjugate indicated in combination with a rituximab product, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adult patients who have previously untreated diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) or high-grade B-cell lymphoma (HGBL) and who have an International Prognostic Index score of 2 or greater. It is also indicated in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory DLBCL, NOS, after at least two prior therapies [Please see U.S. Prescribing Information for more details].

Risk of Severe Infusion Site Extravasation Events with the Use of POLIVY®

- Infusion site extravasation (including severe events) is a new identified risk for POLIVY. Health care professionals need to be aware of the full range of signs and symptoms of infusion site extravasation and the appropriate medical attention.

Background on the Safety Concern

- Infusion site extravasation refers to the unintended leakage of a drug or fluids from the vascular system into the paravenous space, which can potentially lead to surrounding skin and soft tissue damage due to toxic effects of the infused drug.
- The signs and symptoms of infusion site extravasation events may range from sensation of burning, tingling, pain, discomfort, swelling and redness at site of injection, which may progress to more severe events like blistering, necrosis, ulceration, and tissue damage such as cellulitis. The onset of these events can occur early, within hours to days, or may be delayed, appearing weeks after the incident of extravasation (Fidalgo et al. 2012).
- As of 9 June 2025, an estimated cumulative total of 96,261 patients have received POLIVY across postmarketing and clinical settings. A cumulative analysis of the data available retrieved a total of 31 cases reporting an event of infusion site extravasation, with a crude reporting rate of 0.03% (31/96,261). Among these 31 cases, four cases of infusion site extravasation events were assessed with sufficient evidence suggesting a probable causal association

between infusion site extravasation events and POLIVY, with no alternate explanations.
- Based upon the totality of evidence and the known class effect of infusion site extravasation event associated with similar-in-class drugs, infusion site extravasation event is considered as associated with POLIVY.

Updates to the Prescribing Information are planned. The benefit-risk profile of POLIVY in the approved indications remains favorable.

Prescriber Action

Counsel patients about the risks and benefits of POLIVY, including the risk of infusion site extravasation events.

To minimize the risk of infusion site extravasation events:
- Ensure adequate venous access prior to initiating the infusion.
- The infusion site should be closely monitored throughout administration for signs of extravasation.
- If extravasation is suspected, the infusion should be stopped immediately.
- The needle should be withdrawn following a brief aspiration. The affected limb should be elevated, and appropriate symptomatic management may be initiated, as required, in accordance with institutional guidelines.
- If the symptoms are mild, the remaining dose can be administered in the other limb after ensuring adequate venous access prior to initiating the infusion. Alternatively, if the symptoms are moderate to severe, the infusion may be reinitiated after resolution of events, at the discretion of the treating physician.

Reporting Adverse Events / Product Complaints and Company Contact

Health Care Providers should report any adverse events suspected to be associated with the use of POLIVY 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 POLIVY to Genentech at (800) 334-0290.

Should you have any questions about the information in this letter or the safe and effective use of POLIVY, 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 POLIVY. Please refer to the enclosed full prescribing information.

Sincerely,

Beatriz Perez

Beatriz Perez Sanz, M.D.
Interim Head of U.S. Medical