Direct Healthcare Professional Communication

September 2025

Polatuzumab Vedotin (Polivy), Identified Risk: Severe Infusion Site Extravasation Events - Update to Warning and Precautions

Dear Healthcare professional,

Roche Products Saudi Arabia in agreement with The Saudi Food and Drug Authority [SFDA] would like to inform you of the following:

Summary

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

- **A comprehensive analysis of the data available across the polatuzumab vedotin program has identified cases that provided sufficient evidence of a causal association of infusion site extravasation events with polatuzumab vedotin.**

- **Monitor venous access and infusion site; stop infusion immediately if extravasation is suspected and manage per guidance. Be aware of infusion site extravasation.**

Background on the safety concern

- Polatuzumab vedotin is an antibody-drug conjugate composed of the anti-mitotic agent monomethyl auristatin E (MMAE) covalently conjugated to a CD79b-directed monoclonal antibody (recombinant humanized immunoglobulin G1 [IgG1], produced in Chinese Hamster Ovary cells by recombinant DNA technology).

- Therapeutic indications:
    - Polivy in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) is indicated for the treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL).
    - Polivy in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant.

- 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 [1]

- As of 09 June 2025, an estimated cumulative total of 96,261 patients have received polatuzumab vedotin across postmarketing setting 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 polatuzumab vedotin, with no alternate explanations. These cases included one literature case [2] (index case), one from Non-Interventional Study/Non-Interventional Program (NIS/NIP), one from a non-Roche clinical study and one unsolicited postmarketing report.

- Based upon the totality of evidence, known class effect of infusion site extravasation event associated with similar-in-class drugs such as enfortumab vedotin and brentuximab vedotin, infusion site extravasation event is considered as associated with polatuzumab vedotin.

Recommendations for Healthcare Professionals

- 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.
- 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.

The Warnings and Precautions section of the product labels will be updated to reflect this risk. This DHPC (Dear Healthcare Professional Communication) has been disseminated in advance of the label updates to make you aware of the identified risk and to facilitate prompt management of the risk.

References

1. Fidalgo, J. P., Fabregat, L. G., & ESMO Guidelines Working Group. (2012). Management of chemotherapy extravasation: ESMO–EONS clinical practice guidelines. Annals of oncology, 23, vii167-vii173.
2. Sushila A. Toulmin, Hana I. Nazir, Jeremy S. Abramson, Jacob D. Soumerai & Esther E. Freeman (2025) Polatuzumab vedotin extravasation injury: a case report, Leukemia & Lymphoma, 66:6, 1169-1171, DOI: 10.1080/10428194.2025.2456092

CALL FOR REPORTING

Healthcare professionals should report any adverse events, which are suspected to be associated with the use of Polivy®, in accordance with the requirements via the national spontaneous reporting systems to:

The National Pharmacovigilance Centre (NPC)
Land Line: 19999.
Web-page: http://ade.sfda.gov.sa
Email: npc.drug@sfda.gov.sa

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COMPANY CONTACT POINT

Should you have any questions regarding the use of Polivy®, please feel free to contact us at *jeddah.medinfo@roche.com*

This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA)

Yours sincerely,

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