

## Direct Healthcare Professional Communication (DHPC)

**Date: 19 Nov 2025**

**Subject: Important Safety Information Regarding Yescarta® (axicabtagene ciloleucel) and Risk of Cerebral Edema in Primary Mediastinal B Cell Lymphoma (PMBCL)**

**Dear Health Care Provider,**

The marketing authorisation holder (MAH) Gilead Sciences Ireland UC, (hereafter referred to as Gilead), in agreement with the Saudi Food and Drug Authority (SFDA), would like to inform you of important safety information regarding the possible risk of cerebral edema, which may progress rapidly with potentially fatal outcomes in patients with primary mediastinal B cell lymphoma (PMBCL) treated with Yescarta® (axicabtagene ciloleucel). Cerebral edema is a known risk of CAR-T therapy and is described in the Yescarta Prescribing Information.

**Risk of Cerebral Edema:**

- Patients with PMBCL may be at increased risk for developing cerebral edema, which can be fatal. The underlying mechanism of this risk is not known and may involve disease biology, anatomical location (large mediastinal mass), prior therapy, and/or other factors.
- The cerebral edema reporting rate to Gilead/Kite in PMBCL is 1.4% (0.9% fatal) compared with 0.2% (0.1% fatal) in Diffuse Large B Cell Lymphoma (DLBCL). The cerebral edema reporting rate in US and EU patient registry studies was consistent at 1.7% (0.8% fatal) in PMBCL and 0.7% (0.2% fatal) in DLBCL.
- Cerebral edema may evolve as a manifestation of Immune-Effector Cell Associated Neurotoxicity Syndrome (ICANS) but does not follow a predictable clinical course and in some cases has occurred after only mild neurologic symptoms.
- The etiology of cerebral edema, independent of CAR-T therapy, is not fully understood; risk factors include and are not limited to: Superior vena cava (SVC) syndrome, sepsis or other systemic infections, kidney disease, hyponatremia, and brain radiation therapy.

**Prescriber Action:**

- Consider increasing the frequency of monitoring for ICANS in PMBCL patients during the first 7-14 days of Yescarta therapy, because cerebral edema can develop rapidly following mild neurological symptoms.
- Promptly initiate treatment for ICANS per applicable guidelines. Initiate prompt evaluation (e.g., neuroimaging) and consultation (e.g., neurosurgery) if cerebral edema is suspected.
- Published case reports have suggested intrathecal therapy may be useful for the management of ICANS (see references). Clinical status and contraindications for lumbar puncture should be appropriately considered.

## **Reporting Adverse Events:**

Health care providers and patients are encouraged to report adverse events in patients taking Yescarta to Kite at [Drugsafety.KSA@gilead.com](mailto:Drugsafety.KSA@gilead.com). You are encouraged to report negative side effects of prescription drugs to the National Pharmacovigilance Centre (NPC) unified number: 19999 or email:  [npc.drug@sfda.gov.sa](mailto: npc.drug@sfda.gov.sa).

You may also contact our medical information department at [askgileadME@gilead.com](mailto:askgileadME@gilead.com) if you have any questions about the information contained in this letter or the safe and effective use of Yescarta. This letter is not intended as a complete description of the benefits and risks related to the use of Yescarta. Please refer to the full prescribing information enclosed.

**Yours faithfully,**

Mohannad Alghamdi  
Head of Patient Safety & QPPV of Gilead/Kite

Signed by Mohannad Alghamdi  
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 November 19, 2025 | 8:25:53 AM PST  
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## **References**

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### **Intrathecal Therapy for ICANS**

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