



August 2024

Subject: New and Updated Important Safety Information with the Use of LUNSUMIO® (mosunetuzumab-axgb): HLH and ICANS

Dear Healthcare Provider:

The purpose of this letter is to inform you of important safety information for LUNSUMIO, which is under accelerated approval and indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy [Please see US Prescribing Information for more details].

Serious Risks With Use of LUNSUMIO

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 adverse events, including fatal cases, have been reported on the LUNSUMIO clinical trial and compassionate use programs, observed in the context of disease progression and infections. The incidence of HLH on clinical trials and the compassionate use program is 0.3% (7 cases/2234 patients). HLH may resemble severe Cytokine Release Syndrome (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.

Neurologic toxicity including ICANS

 ICANS is a clinical and neuropsychiatric syndrome that can occur following administration of T cell engaging therapies. Neurologic toxicity including ICANS have been reported in patients receiving LUNSUMIO. A recent cumulative analysis showed adverse events consistent with ICANS (Lee 2019) at a rate of 1.9% (23 cases/1219 patients) including severe or life-threatening in 0.3% (4 cases/1219 patients) across LUNSUMIO clinical trials and the compassionate use program (see section 5.2 of the USPI). Manifestations of ICANS reported in patients receiving LUNSUMIO included confusional state, delirium, disturbance in attention and cognitive disorder, disorientation, lethargy, memory impairment, and encephalopathy. The majority of cases of ICANS occurred during Cycle 1 of treatment but can also happen after Cycle 1. ICANS can occur in the setting of CRS, or independent of CRS.

Updates to the Prescribing Information are planned.

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

Prescriber Action (see section 2.4 of the USPI)

- For any case of suspected HLH, interrupt LUNSUMIO and treat per current practice guidelines (e.g., institutional guidelines or ASTCT expert consensus guidelines (Hines et al. 2023)). Expert consultation is recommended if HLH is suspected.
- For any case of suspected neurotoxicity, including ICANS, monitor neurologic toxicity symptoms, interrupt LUNSUMIO as appropriate based on severity, consider neurology consultation and evaluation, and consider treatment per current practice guidelines (e.g., Crombie et al. 2024).

Reporting Adverse Events / Product Complaints and Company Contact

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

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

Sincerely,

Toby Patterson, MBBS Senior Vice President Head of U.S. Medical Affairs