HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LUNSUMIO safely and effectively. See full prescribing information for LUNSUMIO.

LUNSUMIO™ (mosunetuzumab-axgb) injection, for intravenous use
Initial U.S. Approval: 2022

WARNING: CYTOKINE RELEASE SYNDROME
See full prescribing information for complete boxed warning.

Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving LUNSUMIO. Initiate treatment with the LUNSUMIO step-up dosing schedule to reduce the risk of CRS. Withhold LUNSUMIO until CRS resolves or permanently discontinue based on severity. (2.1, 2.4, 5.1)

----------RECENT MAJOR CHANGES----------

Warnings and Precautions (5.2)	11/2024
Warnings and Precautions (5.4)	11/2024

----------INDICATIONS AND USAGE----------

LUNSUMIO is a bispecific CD20-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1.1)

----------DOSAGE AND ADMINISTRATION----------

- Premedicate to reduce risk of cytokine release syndrome and infusion-related reactions. (2.3, 5.1)
- Administer only as an intravenous infusion. (2.1)
- Recommended dosage:
  - Cycle 1 Day 1 – 1 mg
  - Cycle 1 Day 8 – 2 mg
  - Cycle 1 Day 15 – 60 mg
  - Cycle 2 Day 1 – 60 mg
  - Cycle 3+ Day 1 – 30 mg

See Full Prescribing Information for instructions on preparation and administration. (2.5)

----------DOSAGE FORMS AND STRENGTHS----------

Injection:

- 1 mg/mL solution in a single-dose vial. (3)
- 30 mg/30 mL (1 mg/mL) solution in a single-dose vial. (3)

----------CONTRAINDICATIONS----------

None. (4)

----------WARNINGS AND PRECAUTIONS----------

- Neurologic Toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome: Can cause serious and life-threatening neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS). Monitor patients for signs and symptoms of neurologic toxicity during treatment; withhold or permanently discontinue based on severity. (5.2)
- Infections**:** Can cause serious or fatal infections. Monitor patients for signs and symptoms of infection, including opportunistic infections, and treat as needed. (5.3)
- Hemophagocytic Lymphohistiocytosis: Can cause serious or fatal reactions. For suspected cases, interrupt LUNSUMIO and evaluate and treat promptly. (5.4)
- Cytopenias: Monitor complete blood cell counts during treatment. (5.5)
- Tumor Flare: Can cause serious tumor flare reactions. Monitor patients at risk for complications of tumor flare. (5.6)
- Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception. (5.7, 8.1, 8.3)

----------ADVERSE REACTIONS----------

The most common adverse reactions (≥ 20%) are cytokine release syndrome, fatigue, rash, pyrexia, and headache.

The most common Grade 3 to 4 laboratory abnormalities (≥ 10%) are decreased lymphocyte count, decreased phosphate, increased glucose, decreased neutrophil count, increased uric acid, decreased white blood cell count, decreased hemoglobin, and decreased platelets. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------USE IN SPECIFIC POPULATIONS----------

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 11/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

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FULL PRESCRIBING INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME

Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving LUNSUMIO. Initiate treatment with the LUNSUMIO step-up dosing schedule to reduce the risk of CRS. Withhold LUNSUMIO until CRS resolves or permanently discontinue based on severity *[see Dosage and Administration (2.1 and 2.4) and Warnings and Precautions (5.1)]*.

1 INDICATIONS AND USAGE

1.1 Follicular Lymphoma

LUNSUMIO is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy.

This indication is approved under accelerated approval based on response rate *[see Clinical Studies (14.1)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosing Information

- Administer LUNSUMIO to well-hydrated patients.
- Premedicate before each dose in Cycle 1 and Cycle 2 *[see Dosage and Administration (2.3)]*.
- Administer only as an intravenous infusion through a dedicated infusion line. **Do not use an in-line filter to administer LUNSUMIO**. Drip chamber filters can be used to administer LUNSUMIO.
- LUNSUMIO should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as cytokine release syndrome and neurologic toxicity, including ICANS *[see Warnings and Precautions (5.1 and 5.2)]*.

2.2 Recommended Dosage

The recommended dosage for LUNSUMIO is presented in Table 1.

Administer for 8 cycles, unless patients experience unacceptable toxicity or disease progression.

For patients who achieve a complete response, no further treatment beyond 8 cycles is required. For patients who achieve a partial response or have stable disease in response to treatment with LUNSUMIO after 8 cycles, an additional 9 cycles of treatment (17 cycles total) should be administered, unless a patient experiences unacceptable toxicity or disease progression.

Table 1. Recommended LUNSUMIO Dose and Schedule (21-Day Treatment Cycles)

Day of Treatment		Dose of LUNSUMIO	Rate of Infusion
Cycle 1	Day 1	1 mg	Administer over a minimum of 4 hours.
	Day 8	2 mg	
	Day 15	60 mg	
Cycle 2	Day 1	60 mg	Administer over 2 hours if infusions from Cycle 1 were well-tolerated.
Cycles 3+	Day 1	30 mg	

Table 2. Recommendations for Restarting Therapy with LUNSUMIO After Dose Delay

Last Dose Administered	Time Since the Last Dose Administered	Action for Next Dose(s)
1 mg Cycle 1 Day 1	1 to 2 weeks	Administer 2 mg (Cycle 1 Day 8), then resume the planned treatment schedule.
	Greater than 2 weeks	Repeat 1 mg (Cycle 1 Day 1), then administer 2 mg (Cycle 1 Day 8) and resume the planned treatment schedule.
2 mg Cycle 1 Day 8	1 to 2 weeks	Administer 60 mg (Cycle 1 Day 15), then resume the planned treatment schedule.
	Greater than 2 weeks to less than 6 weeks	Repeat 2 mg (Cycle 1 Day 8), then administer 60 mg (Cycle 1 Day 15) and resume the planned treatment schedule.
	Greater than or equal to 6 weeks	Repeat 1 mg (Cycle 1 Day 1) and 2 mg (Cycle 1 Day 8), then administer 60 mg (Cycle 1 Day 15) and resume the planned treatment schedule.
60 mg Cycle 1 Day 15	1 week to less than 6 weeks	Administer 60 mg (Cycle 2 Day 1), then resume the planned treatment schedule.
	Greater than or equal to 6 weeks	Repeat 1 mg (Cycle 2 Day 1) and 2 mg (Cycle 2 Day 8), then administer 60 mg (Cycle 2 Day 15), followed by 30 mg (Cycle 3 Day 1) and then resume the planned treatment schedule.
60 mg Cycle 2 Day 1	3 weeks to less than 6 weeks	Administer 30 mg (Cycle 3 Day 1), then resume the planned treatment schedule.
	Greater than or equal to 6 weeks	Repeat 1 mg (Cycle 3 Day 1) and 2 mg (Cycle 3 Day 8), then administer 30 mg (Cycle 3 Day 15)*, followed by 30 mg (Cycle 4 Day 1) and then resume the planned treatment schedule.
30 mg Cycle 3 onwards	3 weeks to less than 6 weeks	Administer 30 mg, then resume the planned treatment schedule.
	Greater than or equal to 6 weeks	Repeat 1 mg on Day 1 and 2 mg on Day 8 during the next cycle, then administer 30 mg on Day 15*, followed by 30 mg on Day 1 of subsequent cycles.
* For the Day 1, Day 8, and Day 15 doses in the next cycle, administer premedication as per Table 3 for all patients		

2.3 Recommended Premedication and Prophylactic Medication

Premedication to reduce the risk of cytokine release syndrome and infusion-related reactions are outlined in Table 3 *[see Warnings and Precautions (5.1)]*.

Table 3. Premedication to be Administered to Patients Prior to LUNSUMIO Infusion

Treatment Cycle	Patients Requiring Premedication	Premedication	Dosage	Administration
Cycle 1 and Cycle 2	All patients	Corticosteroid	Dexamethasone 20 mg intravenous or methylprednisolone 80 mg intravenous	Complete at least 1 hour prior to infusion
		Antihistamine	Diphenhydramine hydrochloride 50 mg to 100 mg or equivalent oral or intravenous antihistamine	At least 30 minutes prior to infusion
		Antipyretic	Oral acetaminophen (500 mg to 1,000 mg)	At least 30 minutes prior to infusion
Cycles 3+	Patients who experienced any grade CRS with the previous dose	Corticosteroid	Dexamethasone 20 mg intravenous or methylprednisolone 80 mg intravenous	Complete at least 1 hour prior to infusion
		Antihistamine	Diphenhydramine hydrochloride 50 mg to 100 mg or equivalent oral or intravenous antihistamine	At least 30 minutes prior to infusion
		Antipyretic	Oral acetaminophen (500 mg to 1,000 mg)	At least 30 minutes prior to infusion

2.4 Dosage Modifications for Adverse Reactions

See Tables 4 and 5 for the recommended dosage modifications for adverse reactions of CRS and neurologic toxicity, including immune effector cell-associated neurotoxicity (ICANS). See Table 6 for the recommended dosage modifications for other adverse reactions following administration of LUNSUMIO.

Dosage Modifications for Cytokine Release Syndrome

Identify cytokine release syndrome (CRS) based on clinical presentation *[see Warnings and Precautions (5.1)]*. Evaluate for and treat other causes of fever, hypoxia, and hypotension.

If CRS is suspected, withhold LUNSUMIO until CRS resolves, manage according to the recommendations in Table 4 and per current practice guidelines. Administer supportive therapy for CRS, which may include intensive care for severe or life-threatening CRS.

Table 4. Recommendations for Management of Cytokine Release Syndrome

Grade[a]	Presenting Symptoms	Actions[b]
Grade 1	Fever ≥ 100.4°F (38°C)[c]	• Withhold current infusion of LUNSUMIO and manage per current practice guidelines. o If symptoms resolve, restart infusion at the same rate. • Ensure CRS symptoms are resolved for at least 72 hours prior to the next dose of LUNSUMIO.[d] • Administer premedication[e] prior to next dose of LUNSUMIO and monitor patient more frequently.

Grade[a]	Presenting Symptoms	Actions[b]
Grade 2	Fever ≥ 100.4°F (38°C)[c] with: Hypotension not requiring vasopressors and/or hypoxia requiring low-flow oxygen[f] by nasal cannula or blow-by.	• Withhold current infusion of LUNSUMIO and manage per current practice guidelines. ○ If symptoms resolve, restart infusion at 50% rate. • Ensure CRS symptoms are resolved for at least 72 hours prior to the next dose of LUNSUMIO.[d] • Administer premedication[e] prior to next dose of LUNSUMIO and consider infusing the next dose at 50% rate. • For the next dose of LUNSUMIO, monitor more frequently and consider hospitalization.
		Recurrent Grade 2 CRS • Manage per Grade 3 CRS.
Grade 3	Fever ≥ 100.4°F (38°C)[c] with: Hypotension requiring a vasopressor (with or without vasopressin) and/or hypoxia requiring high flow oxygen[f] by nasal cannula, face mask, non-rebreather mask, or Venturi mask.	• Withhold LUNSUMIO, manage per current practice guidelines and provide supportive therapy, which may include intensive care. • Ensure CRS symptoms are resolved for at least 72 hours prior to the next dose of LUNSUMIO.[d] • Administer premedication[e] prior to next dose of LUNSUMIO and infuse the next dose at 50% rate. • Hospitalize for the next dose of LUNSUMIO.
		Recurrent Grade 3 CRS • Permanently discontinue LUNSUMIO. • Manage CRS per current practice guidelines and provide supportive therapy, which may include intensive care.
Grade 4	Fever ≥ 100.4°F (38°C)[c] with: Hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring oxygen by positive pressure (e.g., CPAP, BiPAP, intubation and mechanical ventilation).	• Permanently discontinue LUNSUMIO. • Manage CRS per current practice guidelines and provide supportive therapy, which may include intensive care.

[a] Based on American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for CRS.
[b] If CRS is refractory to management, consider other causes including hemophagocytic lymphohistiocytosis *[see Warnings and Precautions (5.4)]*.
[c] Premedication may mask fever, therefore if clinical presentation is consistent with CRS, follow these management guidelines.
[d] Refer to Table 2 for information on restarting LUNSUMIO after dose delays *[see Dosage and Administration (2.2)]*.
[e] Refer to Table 3 for additional information on premedication.
[f] Low-flow oxygen defined as oxygen delivered at < 6 L/minute; high-flow oxygen defined as oxygen delivered at ≥ 6 L/minute.

Dosage Modifications for Neurologic Toxicity, including ICANS

Management recommendations for neurologic toxicity, including ICANS, is summarized in Table 5. At the first sign of neurologic toxicity, including ICANS, consider neurology evaluation and withholding of LUNSUMIO based on the type and severity of neurotoxicity. Rule out other causes of neurologic symptoms. Provide supportive therapy, which may include intensive care.

Table 5. Recommendations for Management of Neurologic Toxicity (including ICANS)

Adverse Reaction	Severity[1,2]	Actions
Neurologic Toxicity[1] (including ICANS[2])	Grade 1	• Continue LUNSUMIO and monitor neurologic toxicity symptoms. • If ICANS, manage per current practice guidelines.
	Grade 2	• Withhold LUNSUMIO until neurologic toxicity symptoms improve to Grade 1 or baseline for at least 72 hours.[3] • Provide supportive therapy, and consider neurologic evaluation. • If ICANS, manage per current practice guidelines.
	Grade 3	• Withhold LUNSUMIO until neurologic toxicity symptoms improve to Grade 1 or baseline for at least 72 hours.[3] • Provide supportive therapy, which may include intensive care, and consider neurology evaluation. • If ICANS, manage per current practice guidelines. • If recurrence of ICANS, permanently discontinue LUNSUMIO.
	Grade 4	• Permanently discontinue LUNSUMIO. • Provide supportive therapy, which may include intensive care, and consider neurology evaluation. • If ICANS, manage per current practice guidelines.

[1] Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.0.
[2] Based on American Society for Transplantation and Cellular Therapy (ASTCT) 2019 grading for ICANS.
[3] See Table 2 for recommendations on restarting LUNSUMIO after dose delays *[see Dosage and Administration (2.2)]*.

Table 6. Recommended Dosage Modification for Other Adverse Reactions

Adverse Reactions[1]	Severity[1]	Actions
Infections *[see Warnings and Precautions (5.3)]*	Grades 1 – 4	• Withhold LUNSUMIO in patients with active infection until the infection resolves.[2] • For Grade 4, consider permanent discontinuation of LUNSUMIO.
Neutropenia *[see Warnings and Precautions (5.4)]*	Absolute neutrophil count less than 0.5×10^9/L	• Withhold LUNSUMIO until absolute neutrophil count is 0.5×10^9/L or higher.[2]
Other Adverse Reactions *[see Warnings and Precautions (5.5) and Adverse Reactions (6.1)]*	Grade 3 or higher	• Withhold LUNSUMIO until the toxicity resolves to Grade 1 or baseline.[2]

[1] Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.0.
[2] See Table 2 for recommendations on restarting LUNSUMIO after dose delays *[see Dosage and Administration (2.2)]*.

2.5 Preparation and Administration

Preparation

Use aseptic technique to prepare LUNSUMIO.

- Inspect the vial visually for any particulate matter, prior to administration. Do not use if the solution is discolored, or cloudy, or if foreign particles are present.
- Determine the dose, the total volume of LUNSUMIO solution required, and the number of LUNSUMIO vials needed.

Dilution

1. Withdraw the volume from an infusion bag of 0.9% Sodium Chloride Injection, USP or 0.45% Sodium Chloride Injection, USP equal to the volume of the LUNSUMIO required for the patient's dose and discard. Only use infusion bags made of polyvinyl chloride (PVC) or polyolefin (PO) such as polyethylene (PE) and polypropylene.
2. Withdraw the required volume of LUNSUMIO from the vial using a sterile needle and syringe and dilute into the infusion bag of 0.9% Sodium Chloride Injection, USP or 0.45% Sodium Chloride Injection, USP according to Table 7. Discard any unused portion left in the vial.

Table 7. Dilution of LUNSUMIO

Dose of LUNSUMIO	**Volume of LUNSUMIO in 0.9% or 0.45% Sodium Chloride Solution**	**Size of Infusion Bag**
1 mg	1 mL	50 mL or 100 mL
2 mg	2 mL	50 mL or 100 mL
60 mg	60 mL	100 mL or 250 mL
30 mg	30 mL	50 mL, 100 mL, or 250 mL

3. Gently mix the intravenous bag by slowly inverting the bag. *Do not shake.*
4. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if visibly opaque particles, discoloration, or foreign particles are observed.
5. Apply the peel-off label from the package insert to the infusion bag.
6. Immediately use diluted LUNSUMIO infusion solution. If not used immediately, the diluted solution can be stored refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours and at ambient temperature 9°C to 30°C (48°F to 86°F) for up to 16 hours. Prior to administration, ensure the infusion solution comes to reach room temperature.

Administration

- Administer as an intravenous infusion only.
- **Do not use an in-line filter to administer LUNSUMIO**.
- Do not mix LUNSUMIO with, or administer through the same infusion line, as other medicinal products.
- No incompatibilities have been observed between LUNSUMIO and intravenous infusion bags with product contacting materials of polyvinyl chloride (PVC), or polyolefins (PO) such as polyethylene (PE) and polypropylene (PP). In addition, no incompatibilities have been observed with infusion sets or infusion aids with product contacting materials of PVC, PE, polyurethane (PUR), polybutadiene (PBD), silicone, acrylonitrile butadiene styrene (ABS), polycarbonate (PC), polyetherurethane (PEU),

fluorinated ethylene propylene (FEP), or polytetrafluorethylene (PTFE), or with drip chamber filter membrane composed of polyamide (PA).

3 DOSAGE FORMS AND STRENGTHS

LUNSUMIO is a sterile, colorless solution available as:

- Injection: 1 mg/mL mosunetuzumab-axgb of solution in a single-dose vial
- Injection: 30 mg/30 mL (1 mg/mL) mosunetuzumab-axgb of solution in a single-dose vial

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Cytokine Release Syndrome

LUNSUMIO can cause cytokine release syndrome (CRS), including serious or life-threatening reactions *[see Adverse Reactions (6.1)]*.

Cytokine release syndrome occurred in 39% of patients who received LUNSUMIO at the recommended dose in the clinical trial, with Grade 1 CRS occurring in 28%, Grade 2 in 15%, Grade 3 in 2%, and Grade 4 in 0.5% of patients. Recurrent CRS occurred in 11% of patients. Most patients experienced CRS following doses of 1 mg on Cycle 1 Day 1 (15%), 2 mg on Cycle 1 Day 8 (5%), and 60 mg on Cycle 1 Day 15 (33%). Five percent of patients experienced CRS after receiving 60 mg on Cycle 2 Day 1 with 1% of patients experiencing CRS following subsequent dosages of LUNSUMIO.

The median time to onset of CRS from the start of administration in Cycle 1 Day 1 was 5 hours (range: 1 hour to 3 days), Cycle 1 Day 8 was 28 hours (range: 5 hours to 3 days), Cycle 1 Day 15 was 25 hours (range: 0.1 hours to 16 days), and Cycle 2 Day 1 was 46 hours (range: 12 hours to 3 days). The median duration of CRS was 3 days (range: 1 to 29 days).

Clinical signs and symptoms of CRS included, but were not limited to, fever, chills, hypotension, tachycardia, hypoxia, and headache. Concurrent neurologic adverse reactions occurred in 6% of patients and included but were not limited to headache, confusional state, and anxiety.

Initiate therapy according to LUNSUMIO step-up dosing schedule to reduce the risk of CRS *[see Dosage and Administration (2.3)]*. Administer pretreatment medications to reduce the risk of CRS, ensure adequate hydration, and monitor patients following administration of LUNSUMIO accordingly.

At the first sign of CRS, immediately evaluate patients for hospitalization, manage per current practice guidelines and administer supportive care; withhold or permanently discontinue LUNSUMIO based on severity *[see Dosage and Administration (2.4)]*.

Patients who experience CRS (or other adverse reactions that impair consciousness) should be evaluated and advised not to drive and to refrain from operating heavy or potentially dangerous machinery until resolution.

5.2 Neurologic Toxicity, including Immune Effector Cell-Associated Neurotoxicity Syndrome

LUNSUMIO can cause serious and life-threatening neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS) *[see Adverse Reactions (6.1)].*

Neurologic toxicity occurred in 39% of patients who received LUNSUMIO at the recommended dose in the clinical trial, with Grade 3 neurologic toxicity occurring in 3% of patients. The most frequent neurologic toxicities were headache (21%), peripheral neuropathy (13%), dizziness (11%), and mental status changes (6%, including confusional state, disturbance in attention, cognitive disorder, delirium, encephalopathy, and somnolence). ICANS was reported in 1% of patients (Grade 1: 0.5%, Grade 2: 0.5%) who received LUNSUMIO at the recommended dose in the clinical trial.

Across a broader clinical trial population, ICANS or suspected ICANS occurred in 2.1% (20/949) of patients who received LUNSUMIO. The most frequent manifestations included confusional state and lethargy. Nineteen patients had Grade 1-2 events and 1 patient had a Grade 3 event. The majority of cases (75%) occurred during the first cycle of treatment. The median time to onset was 17 days (range: 1 to 48 days). In total, 87% of cases resolved after a median duration of 3 days (range: 1-20 days).

Coadministration of LUNSUMIO with other products that cause dizziness or mental status changes may increase the risk of neurologic toxicity.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient, consider neurology evaluation as appropriate, and provide supportive therapy based on severity; withhold or permanently discontinue LUNSUMIO based on severity and follow management recommendations *[see Dosage and Administration (2.4)]*.

Patients who experience neurologic toxicity such as tremors, dizziness, insomnia, severe neurotoxicity, or any other adverse reactions that impair consciousness should be evaluated, including potential neurology evaluation, and patients at increased risk should be advised not to drive and to refrain from operating heavy or potentially dangerous machinery until resolution.

5.3 Infections

LUNSUMIO can cause serious or fatal infections *[see Adverse Reactions (6.1)]*.

Among patients who received LUNSUMIO at the recommended dose in the clinical trial, serious infections, including opportunistic infections, occurred in 17%, with Grade 3 or 4 infections in 14%, and fatal infections in 0.9% of patients. The most common Grade 3 or greater infections were pneumonia, sepsis, and upper respiratory tract infection.

Monitor patients for signs and symptoms of infection prior to and during treatment with LUNSUMIO and treat appropriately. LUNSUMIO should not be administered in the presence of active infection. Caution should be exercised when considering the use of LUNSUMIO in patients with a history of recurring or chronic infections (e.g., chronic, active Epstein-Barr Virus), with underlying conditions that may predispose to infections or who have had significant prior immunosuppressive treatment. Administer prophylactic antimicrobials according to guidelines.

Withhold LUNSUMIO or consider permanent discontinuation of LUNSUMIO based on severity *[see Dosage and Administration (2.4)]*.

5.4 Hemophagocytic Lymphohistiocytosis

LUNSUMIO can cause fatal or serious hemophagocytic lymphohistiocytosis (HLH). HLH is a potentially life-threatening, hyperinflammatory syndrome that is independent of CRS. Common manifestations include fever, elevated ferritin, hemophagocytosis, cytopenias, coagulopathy, hepatitis, and splenomegaly.

Across a broader clinical trial population, HLH occurred in 0.5% (7/1536) of patients. Most cases (5/7) were identified within the first 28 days following initiation of LUNSUMIO, with 3 cases preceded by diagnosed or suspected CRS. Of the 7 cases of HLH, 6 had fatal outcomes, with 2 deaths from HLH alone and 4 deaths with concurrent unresolved HLH. Of the 7 cases of HLH, 4 occurred in the context of concurrent EBV and/or CMV infection.

Monitor for clinical signs and symptoms of HLH. Consider HLH when the presentation of CRS is atypical or prolonged, or when there are features of macrophage activation. For suspected HLH, interrupt LUNSUMIO and evaluate and treat promptly for HLH per current practice guidelines.

5.5 Cytopenias

LUNSUMIO can cause serious or severe cytopenias, including neutropenia, anemia, and thrombocytopenia *[see Adverse Reactions (6.1)]*.

Among patients who received the recommended dosage in the clinical trial, Grade 3 or 4 decreased neutrophils occurred in 38%, decreased hemoglobin in 19%, and decreased platelets in 12% of patients. Grade 4 decreased neutrophils occurred in 19% and decreased platelets in 5% of patients. Febrile neutropenia occurred in 2%.

Monitor complete blood counts throughout treatment. Based on the severity of cytopenias, temporarily withhold, or permanently discontinue LUNSUMIO. Consider prophylactic granulocyte colony-stimulating factor administration as applicable *[see Dosage and Administration (2.4)]*.

5.6 Tumor Flare

LUNSUMIO can cause serious or severe tumor flare *[see Adverse Reactions (6.1)]*.

Among patients who received LUNSUMIO at the recommended dosage in the clinical trial, tumor flare occurred in 4% of patients. Manifestations included new or worsening pleural effusions, localized pain and swelling at the sites of lymphoma lesions, and tumor inflammation.

Patients with bulky tumors or disease located in close proximity to airways or a vital organ should be monitored closely during initial therapy. Monitor for signs and symptoms of compression or obstruction due to mass effect secondary to tumor flare. If compression or obstruction develops, institute standard treatment of these complications.

5.7 Embryo-Fetal Toxicity

Based on its mechanism of action, LUNSUMIO may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with LUNSUMIO and for 3 months after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Cytokine Release Syndrome *[see Warnings and Precautions (5.1)]*
- Neurologic Toxicity, including Immune Effector Cell-associated Neurotoxicity Syndrome *[see Warnings and Precautions (5.2)]*
- Infections *[see Warnings and Precautions (5.3)]*
- Hemophagocytic Lymphohistiocytosis *[see Warnings and Precautions (5.4)]*
- Cytopenias *[see Warnings and Precautions (5.5)]*
- Tumor Flare *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The pooled safety population described in the WARNINGS AND PRECAUTIONS reflects exposure to LUNSUMIO as a single agent in GO29781 in 218 patients with hematologic malignancies in an open-label, multicenter, multi-cohort study. Patients received step-up doses of 1 mg on Cycle 1 Day 1 and 2 mg on Cycle 1 Day 8, followed by 60 mg on Cycle 1 Day 15, and 60 mg on Cycle 2 Day 1, then 30 mg every 3 weeks in subsequent cycles. A treatment cycle was 21 days. Among 218 patients who received LUNSUMIO, 52% were exposed for at least 8 cycles and 8% were exposed for 17 cycles.

In this pooled safety population, the most common (≥ 20%) adverse reactions were cytokine release syndrome (39%), fatigue (36%), rash (34%), pyrexia (24%), and headache (21%). The most common Grade 3 to 4 laboratory abnormalities (≥ 10%) were decreased lymphocyte count (92%), decreased phosphate (41%),

increased glucose (40%), decreased neutrophil count (38%), increased uric acid (15%), decreased white blood cell count (22%), decreased hemoglobin (19%), and decreased platelets (12%).

Relapsed or Refractory Follicular Lymphoma

GO29781

The safety of LUNSUMIO was evaluated in GO29781, an open-label, multicenter, multi-cohort study which included a cohort of 90 patients with relapsed or refractory follicular lymphoma (FL) *[see Clinical Studies (14)]*. In this cohort, patients with relapsed or refractory FL were required to have received at least two prior lines of systemic therapy, including an anti-CD20 monoclonal antibody and an alkylating agent. Patients received step-up doses of 1 mg on Cycle 1 Day 1 and 2 mg on Cycle 1 Day 8, followed by 60 mg on Cycle 1 Day 15 and 60 mg on Cycle 2 Day 1, then 30 mg every 3 weeks in subsequent cycles. A treatment cycle was 21 days. The median number of cycles was 8 (range: 1 – 17). In the relapsed or refractory FL cohort, 77% were exposed for at least 8 cycles and 12% were exposed for 17 cycles.

The median age of the patients who received LUNSUMIO in the relapsed or refractory FL cohort was 60 years (range: 29 to 90 years), 61% were male, 82% were White, 4% were Black or African American, 9% were Asian, and 8% were Hispanic or Latino.

Serious adverse reactions occurred in 47% of patients who received LUNSUMIO. Serious adverse reactions in ≥ 2% of patients included cytokine release syndrome, infection (including urinary tract infection, sepsis, pneumonia, EBV viremia, and COVID-19), renal insufficiency, pyrexia, and tumor flare.

Permanent discontinuation of LUNSUMIO due to an adverse reaction occurred in 3% of patients. Adverse reactions resulting in permanent discontinuation of LUNSUMIO included cytokine release syndrome and EBV viremia.

Dosage interruptions of LUNSUMIO due to an adverse reaction occurred in 37% of patients. Adverse reactions which required dosage interruption in ≥ 5% of patients included neutropenia, infection, and cytokine release syndrome.

Table 8 summarizes the adverse reactions in patients with relapsed or refractory FL in GO29781.

Table 8. Adverse Reactions (≥ 10%) in Patients with Relapsed or Refractory FL Who Received LUNSUMIO in GO29781

Adverse Reaction[1]	LUNSUMIO (N = 90)	
	All Grades (%)	Grade 3 or 4 (%)
Immune system disorders		
Cytokine release syndrome	44	2.2
General disorders and administration site conditions		
Fatigue[2]	42	0
Pyrexia	29	1.1[#]
Edema[3]	17	1.1
Chills	13	1.1[#]
Skin and subcutaneous tissue disorders		
Rash[4]	39	4.4[#]
Pruritus	21	0
Dry skin	16	0
Skin exfoliation	10	0
Nervous system		
Headache[5]	32	1.1[#]

Adverse Reaction[1]	LUNSUMIO (N = 90)	
	All Grades (%)	Grade 3 or 4 (%)
Peripheral neuropathy[6]	20	0
Dizziness[7]	12	0
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain[8]	28	1.1[#]
Arthralgia	11	0
Respiratory, thoracic, and mediastinal disorders		
Cough[9]	22	0
Dyspnea[10]	11	1.1[#]
Gastrointestinal disorders		
Diarrhea	17	0
Nausea	17	0
Abdominal pain[11]	12	1.1[#]
Infections		
Upper respiratory tract infection[12]	14	2.2[#]
Urinary tract infection[13]	10	1.1[#]
Psychiatric disorder		
Insomnia	12	0

[1] Adverse reactions were graded based on CTCAE Version 4.0, with the exception of CRS, which was graded per ASTCT 2019 criteria
[2] Fatigue includes fatigue, asthenia, and lethargy
[3] Edema includes edema, edema peripheral, peripheral swelling, face edema, swelling face, pulmonary edema, fluid overload, and fluid retention
[4] Rash includes rash, rash erythematous, exfoliative rash, rash macular, rash maculo-papular, rash papular, rash pruritic, rash pustular, erythema, palmar erythema, dermatitis, and dermatitis acneiform
[5] Headache includes headache and migraine
[6] Peripheral neuropathy includes peripheral neuropathy, peripheral sensory neuropathy, paresthesia, dysaesthesia, hypoaesthesia, burning sensation, and neuralgia
[7] Dizziness includes dizziness and vertigo
[8] Musculoskeletal pain includes musculoskeletal pain, back pain, myalgia, musculoskeletal chest pain, and neck pain
[9] Cough includes cough, productive cough, and upper airway cough syndrome
[10] Dyspnea includes dyspnea and dyspnea exertional
[11] Abdominal pain includes abdominal pain, lower abdominal pain, and abdominal discomfort
[12] Upper respiratory tract infection includes upper respiratory tract infection, nasopharyngitis, sinusitis, and rhinovirus infection
[13] Urinary tract infection includes urinary tract infection and acute pyelonephritis
[#] Only Grade 3 adverse reactions occurred

Clinically relevant adverse reactions in < 10% of patients who received LUNSUMIO included pneumonia, sepsis, COVID-19, EBV viremia, mental status changes, tumor lysis syndrome, renal insufficiency, anxiety, motor dysfunction (including ataxia, gait disturbance and tremor), tumor flare, and ICANS.

Table 9 summarizes the laboratory abnormalities in patients with relapsed or refractory FL in GO29781.

Table 9. Select Laboratory Abnormalities (≥ 20%) That Worsened from Baseline in Patients with Relapsed or Refractory FL Who Received LUNSUMIO in GO29781

Laboratory Abnormality	LUNSUMIO[1]	
	All Grades (%)	Grade 3 or 4 (%)
Hematology		
Lymphocyte count decreased	100	98
Hemoglobin decreased	68	12
White blood cells decreased	60	13
Neutrophils decreased	58	40
Platelets decreased	46	10
Chemistry		
Phosphate decreased	78	46
Glucose increased	42	42
Aspartate aminotransferase increased	39	4.4
Gamma-glutamyl transferase increased	34	9
Magnesium decreased	34	0
Potassium decreased	33	6
Alanine aminotransferase increased	32	7
Uric acid increased	22	22

[1] The denominator used to calculate the rate varied from 72 to 90 based on the number of patients with a baseline value and at least one post-treatment value.

7 DRUG INTERACTIONS

Effect of LUNSUMIO on CYP450 Substrates

LUNSUMIO causes release of cytokines *[see Clinical Pharmacology (12.2)]* that may suppress activity of CYP450 enzymes, resulting in increased exposure of CYP450 substrates. Increased exposure of CYP450 substrates is more likely to occur after the first dose of LUNSUMIO on Cycle 1 Day 1 and up to 14 days after the second 60 mg dose on Cycle 2 Day 1 and during and after CRS *[see Warnings and Precautions (5.1)]*. Monitor for toxicity or concentrations of drugs that are CYP450 substrates where minimal concentration changes may lead to serious adverse reactions. Consult the concomitant CYP450 substrate drug prescribing information for recommended dosage modification.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on the mechanism of action, LUNSUMIO may cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. There are no available data on the use of LUNSUMIO in pregnant women to evaluate for a drug-associated risk. No animal reproductive or developmental toxicity studies have been conducted with mosunetuzumab-axgb.

Mosunetuzumab-axgb causes T-cell activation and cytokine release; immune activation may compromise pregnancy maintenance. In addition, based on expression of CD20 on B-cells and the finding of B-cell depletion in non-pregnant animals, mosunetuzumab-axgb can cause B-cell lymphocytopenia in infants exposed to mosunetuzumab-axgb in-utero. Human immunoglobulin G (IgG) is known to cross the placenta; therefore, LUNSUMIO has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to the fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% – 4% and 15% – 20%, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of mosunetuzumab-axgb in human milk, the effect on the breastfed child, or milk production. Because human IgG is present in human milk, and there is potential for mosunetuzumab-axgb absorption leading to B-cell depletion, advise women not to breastfeed during treatment with LUNSUMIO and for 3 months after the last dose.

8.3 Females and Males of Reproductive Potential

LUNSUMIO may cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating LUNSUMIO.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with LUNSUMIO and for 3 months after the last dose.

8.4 Pediatric Use

The safety and efficacy of LUNSUMIO have not been established in pediatric patients.

8.5 Geriatric Use

Among the 90 patients with relapsed or refractory follicular lymphoma treated with LUNSUMIO, 33% were 65 years of age or older, and 8% were 75 years of age or older. There is an insufficient number of patients 65 years of age or older and 75 years of age or older to assess whether there are differences in safety or effectiveness in patients 65 years of age and older compared to younger adult patients.

11 DESCRIPTION

Mosunetuzumab-axgb is a bispecific CD20-directed CD3 T-cell engager. It is a humanized monoclonal anti-CD20xCD3 T-cell-dependent bispecific antibody of the immunoglobulin G1 (IgG1) isotype. Mosunetuzumab-axgb is produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology. The approximate molecular weight is 146 kDa.

LUNSUMIO (mosunetuzumab-axgb) injection is a sterile, preservative-free, colorless solution for intravenous use.

Each single-dose vial contains a 1 mL solution of mosunetuzumab-axgb (1 mg), acetic acid (0.4 mg), histidine (1.6 mg), methionine (1.5 mg), polysorbate 20 (0.6 mg), sucrose (82.1 mg), and Water for Injection, USP. The pH is 5.8.

Each single-dose vial contains a 30 mL solution of mosunetuzumab-axgb (30 mg), acetic acid (12.8 mg), histidine (46.6 mg), methionine (44.8 mg), polysorbate 20 (18 mg), sucrose (2,462.4 mg), and Water for Injection, USP. The pH is 5.8.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Mosunetuzumab-axgb is a T-cell engaging bispecific antibody that binds to the CD3 receptor expressed on the surface of T-cells and CD20 expressed on the surface of lymphoma cells and some healthy B-lineage cells.

In vitro, mosunetuzumab-axgb activated T-cells, caused the release of proinflammatory cytokines, and induced lysis of B-cells.

12.2 Pharmacodynamics

After administration of the recommended dosage of LUNSUMIO, peripheral B-cell counts decreased to undetectable levels (< 5 cells/microliter) in most patients (92%) by Cycle 2 Day 1 and the depletion was sustained at later cycles including at Cycle 4 and Cycle 8.

LUNSUMIO caused hypogammaglobulinemia (defined as IgG levels < 500 mg/dL). Among 67 patients with baseline IgG levels ≥ 500 mg/dL, 40% had their IgG level decreased to < 500 mg/dL after administration of the recommended dosage of LUNSUMIO.

Plasma concentrations of cytokines (IL-2, IL-6, IL-10, TNF-α, and IFN-γ) were measured, and transient elevation of cytokines were observed at doses of 0.4 mg and above. After administration of the recommended dosage of LUNSUMIO, the highest elevation of cytokines was observed within 24 hours after first dose on Cycle 1 Day 1 and after the first 60 mg dose on Cycle 1 Day 15. The elevated cytokine levels generally returned to baseline prior to the next infusion on Cycle 1 Day 8 and on Cycle 2 Day 1. Limited data is available in subsequent treatment cycles.

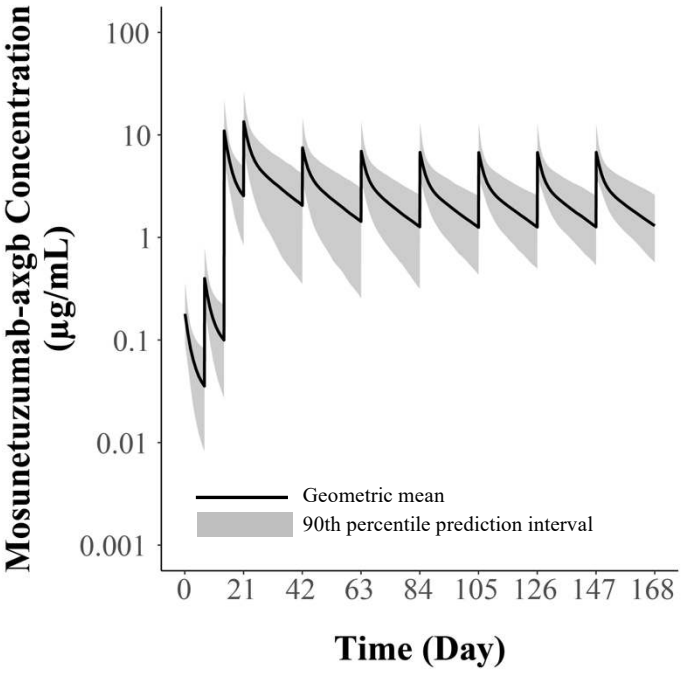
12.3 Pharmacokinetics

Mosunetuzumab-axgb PK exposure increased proportionally over a dose range from 0.2 mg to 60 mg (0.007 to 2 times the recommended treatment dosage). PK exposures are summarized for the recommended dosage of LUNSUMIO in Table 10 and Figure 1.

Table 10. Exposure Parameters of Mosunetuzumab-axgb

	AUC (day•µg/mL)[1]	C_{max} (µg/mL)[1]	C_{trough} (µg/mL)[1]
Cycle 1 (0 – 21 days)	35.2 (36.6)	11.1 (36.7)	2.57 (54.0)
Cycle 2 (21 – 42 days)	90.3 (48.5)	13.6 (37.7)	1.97 (83.1)
Steady state[2]	52.9 (40.7)	7.02 (37.9)	1.29 (59.9)
[1] Values are geometric mean with geometric CV% [2] Steady state values are approximated at Cycle 4 (63 – 84 days)			

Figure 1. Model-Predicted Mosunetuzumab Concentration Time Profile



Distribution

The mean (CV%) volume of distribution of mosunetuzumab-axgb was 5.49 L (31%).

Elimination

The steady-state geometric mean (CV%) terminal elimination half-life of mosunetuzumab-axgb was 16.1 (17.3%) days. The geometric mean (CV%) clearance at baseline and at steady state are 1.08 L/day (63%) and 0.584 L/day (18%), respectively.

Specific Populations

There were no clinically significant differences in the pharmacokinetics of mosunetuzumab-axgb based on age (19 to 96 years), sex, race (Asian and Non-Asian), ethnicity (Hispanic/Latino and not Hispanic/Latino), mild or moderate renal impairment (estimated Creatinine clearance [CrCL] by Cockcroft-Gault formula: 30 to 89 mL/min), or mild hepatic impairment (total bilirubin less than or equal to upper limit of normal [ULN] with AST greater than ULN or total bilirubin greater than 1 to 1.5 times ULN with any AST).

The effects of severe renal impairment (CrCL 15 to 29 mL/min) or moderate to severe hepatic impairment (total bilirubin greater than 1.5 times ULN with any AST) on the pharmacokinetics of mosunetuzumab-axgb are unknown.

Drug Interaction Studies

No clinical studies evaluating the drug interaction potential of mosunetuzumab-axgb have been conducted.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the study described below with the incidence of anti-drug antibodies in other studies, including those of mosunetuzumab-axgb.

During treatment in Study GO29781 (up to 12 months) *[see Clinical Studies (14)]*, using an enzyme-linked immunosorbent assay (ELISA), no patients (N = 418) treated with LUNSUMIO developed anti-mosunetuzumab-axgb antibodies. Based on these data, the clinical relevance of anti-mosunetuzumab-axgb antibodies could not be assessed.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity or genotoxicity studies have been conducted with mosunetuzumab-axgb.

No dedicated studies have been conducted to evaluate the effects of mosunetuzumab-axgb on fertility. No adverse effects on either male or female reproductive organs were identified in a 26-week repeat dose chronic toxicity study in sexually mature cynomolgus monkeys.

14 CLINICAL STUDIES

The efficacy of LUNSUMIO was evaluated in an open-label, multicenter, multi-cohort study (GO29781, NCT02500407) in patients with relapsed or refractory follicular lymphoma (FL) who had received at least two prior therapies, including an anti-CD20 monoclonal antibody and an alkylating agent. The study excluded patients with active infections, history of autoimmune disease, prior allogeneic transplant, or any history of CNS lymphoma or CNS disorders.

Patients received step-up doses of 1 mg on Cycle 1 Day 1 and 2 mg on Cycle 1 Day 8, followed by 60 mg on Cycle 1 Day 15, and 60 mg on Cycle 2 Day 1, then 30 mg every 3 weeks in subsequent cycles. A treatment cycle was 21 days. LUNSUMIO was administered for 8 cycles unless patients experienced progressive disease or unacceptable toxicity. After 8 cycles, patients with a complete response discontinued therapy; patients with a partial response or stable disease continued treatment up to 17 cycles, unless patients experienced progressive disease or unacceptable toxicity.

Among the 90 patients with relapsed or refractory FL, the median age was 60 years (range: 29 to 90 years), 33% were 65 years of age or older, 61% were male, 82% were White, 9% were Asian, 4% were Black or African

American, and 8% were Hispanic or Latino. A total of 77% of patients had Stage III-IV disease, 34% had bulky disease, and all patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. The median number of prior therapies was 3 (range: 2 to 10), with 38% receiving 2 prior therapies, 31% receiving 3 prior therapies, and 31% receiving more than 3 prior therapies.

Seventy-nine percent of patients were refractory to prior anti-CD20 monoclonal antibody therapy, 53% were refractory to both anti-CD20 monoclonal antibody and alkylator therapy, 9% received prior rituximab plus lenalidomide therapy, 21% received prior autologous stem cell transplant, and 3% received prior CAR T therapy. Fifty-two percent of patients had progression of disease within 24 months of first systemic therapy.

Efficacy was established on the basis of objective response rate (ORR) and duration of response (DOR) as assessed by an independent review facility according to standard criteria for NHL (Cheson 2007). The median follow-up for DOR was 14.9 months. The efficacy results are summarized in Table 11.

Table 11. Efficacy Results in Patients with Relapsed or Refractory FL

Response	**LUNSUMIO N = 90**
Objective response rate (ORR), n (%)	72 (80)
(95% CI)	(70, 88)
Complete response rate (CR), n (%)	54 (60)
(95% CI)	(49, 70)
Partial response rate (PR), n (%)	18 (20)
(95% CI)	(12, 30)
Duration of Response (DOR)	N = 72
Median DOR[1,2], months (95% CI)	22.8 (10, NR)
Rate of Continued Response[2]	
At 12 months, %	62
(95% CI)	(50, 74)
At 18 months, %	57
(95% CI)	(44, 70)

CI = confidence interval; NR = not reached
[1] DOR is defined as the time from the initial occurrence of a documented PR or CR until the patient experienced an event (documented disease progression or death due to any cause, whichever occurs first), among patients who achieved a PR or CR.
[2] Kaplan-Meier estimate.

The median time to first response was 1.4 months (range: 1.1 to 8.9).

16 HOW SUPPLIED/STORAGE AND HANDLING

LUNSUMIO (mosunetuzumab-axgb) injection is a sterile, colorless, preservative-free solution supplied as follows:

- One 1 mg/mL single-dose vial in a carton (NDC 50242-159-01)
- One 30 mg/30 mL (1 mg/mL) single-dose vial in a carton (NDC 50242-142-01).

Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light.
Do not freeze. Do not shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Cytokine Release Syndrome (CRS) – Discuss the signs and symptoms associated with CRS, including fever, chills, hypotension, tachycardia, hypoxia, and headache. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time. Advise patients who experience symptoms that impair

consciousness not to drive and refrain from operating heavy or potentially dangerous machinery until events resolve *[see Warnings and Precautions (5.1)]*.

Neurologic Toxicity, including ICANS – Discuss the signs and symptoms associated with neurologic toxicity, including ICANS, headache, peripheral neuropathy, dizziness, or mental status changes. Advise patients to immediately contact their healthcare provider if they experience any signs or symptoms of neurologic toxicity. Advise patients who experience neurologic toxicity that impairs consciousness to refrain from driving or operating heavy or potentially dangerous machinery until neurologic toxicity resolves *[see Warnings and Precautions (5.2)]*.

Infections – Discuss the signs or symptoms associated with infection *[see Warnings and Precautions (5.3)]*.

Hemophagocytic Lymphohistiocytosis (HLH) – Discuss the signs and symptoms associated with HLH, including fever, coagulopathy, cytopenias, and splenomegaly *[see Warnings and Precautions (5.4)]*.

Cytopenias – Discuss the signs and symptoms associated with cytopenias, including neutropenia and febrile neutropenia, anemia, and thrombocytopenia *[see Warnings and Precautions (5.5)]*.

Tumor Flare – Inform patients of the potential risk of tumor flare reaction and to report any signs and symptoms associated with this event to their healthcare provider for evaluation *[see Warnings and Precautions (5.6)]*.

Embryo-Fetal Toxicity – Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider if they are pregnant or become pregnant *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment with LUNSUMIO and for 3 months after the last dose *[see Use in Specific Populations (8.3)]*.

Lactation – Advise women not to breastfeed during treatment with LUNSUMIO and for 3 months after the last dose *[see Use in Specific Populations (8.2)]*.

Manufactured by:
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A Member of the Roche Group
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South San Francisco, CA 94080-4990

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MEDICATION GUIDE
LUNSUMIO™ (lun-SUM-mee-oh)
(mosunetuzumab-axgb)
injection, for intravenous infusion

What is the most important information I should know about LUNSUMIO?

LUNSUMIO may cause Cytokine Release Syndrome (CRS), a serious side effect that is common during treatment with LUNSUMIO, and can also be severe or life-threatening.

Get medical help right away if you develop any signs or symptoms of CRS at any time, including:

- fever of 100.4°F (38°C) or higher
- chills
- low blood pressure
- fast or irregular heartbeat
- tiredness or weakness
- difficulty breathing
- headache
- confusion
- feeling anxious
- dizziness or light-headedness
- nausea
- vomiting

Due to the risk of CRS, you will receive LUNSUMIO on a "step-up dosing schedule".

- The step-up dosing schedule is when you receive smaller "step-up" doses of LUNSUMIO on Day 1 and Day 8 of your first cycle of treatment.
- You will receive a higher dose of LUNSUMIO on Day 15 of your first cycle of treatment.
- If your dose of LUNSUMIO is delayed for any reason, you may need to repeat the "step-up dosing schedule."
- Before each dose in Cycle 1 and Cycle 2, you will receive medicines to help reduce your risk of CRS.
- See **"How will I receive LUNSUMIO?"** for more information about how you will receive LUNSUMIO.

Your healthcare provider will check you for CRS during treatment with LUNSUMIO and may treat you in a hospital if you develop signs and symptoms of CRS. Your healthcare provider may temporarily stop or completely stop your treatment with LUNSUMIO if you have severe side effects.

See **"What are the possible side effects of LUNSUMIO?"** for more information about side effects.

What is LUNSUMIO?

LUNSUMIO is a prescription medicine used to treat adults with follicular lymphoma whose cancer has come back or did not respond to previous treatment, and who have already received two or more treatments for their cancer.

It is not known if LUNSUMIO is safe and effective in children.

Before receiving LUNSUMIO, tell your healthcare provider about all of your medical conditions, including if you:

- have ever had an infusion reaction after receiving LUNSUMIO.
- have an infection or have had an infection in the past which lasted a long time or keeps coming back.
- have or had Epstein-Barr Virus.
- are pregnant or plan to become pregnant. LUNSUMIO may harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with LUNSUMIO.

  Females who are able to become pregnant:
  - your healthcare provider should do a pregnancy test before you start treatment with LUNSUMIO.
  - you should use an effective method of birth control (contraception) during your treatment and for 3 months after the last dose of LUNSUMIO.
- are breastfeeding or plan to breastfeed. It is not known if LUNSUMIO passes into your breast milk. Do not breastfeed during treatment and for 3 months after the last dose of LUNSUMIO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive LUNSUMIO?

- LUNSUMIO will be given to you by your healthcare provider by infusion through a needle placed in a vein (intravenous infusion).
- After you complete the weekly "step-up dosing schedule" in Cycle 1, LUNSUMIO is given every 21 days.
- After Cycle 1 and Cycle 2, your healthcare provider will decide if you need to continue to take other medicines to help reduce side effects from LUNSUMIO during future cycles.
- Your healthcare provider will decide how many treatment cycles you will receive of LUNSUMIO.

See **"What is the most important information I should know about LUNSUMIO?"** for more information about how you will receive LUNSUMIO.

What should I avoid while receiving LUNSUMIO?

Do not drive, operate heavy machinery, or do other dangerous activities if you develop dizziness, confusion, tremors, sleepiness, or any other symptoms that impair consciousness until your signs and symptoms go away. These may be signs and symptoms of CRS or neurologic problems.

See **"What is the most important information I should know about LUNSUMIO?"** and **"What are the possible side effects of LUNSUMIO?"** for more information about signs and symptoms of CRS and neurologic problems.

What are the possible side effects of LUNSUMIO?

LUNSUMIO may cause serious side effects, including:

See **"What is the most important information I should know about LUNSUMIO?"**

- **neurologic problems.** LUNSUMIO can cause serious and life-threatening neurologic problems. Your healthcare provider will check you for neurologic problems during treatment with LUNSUMIO. Your healthcare provider may also refer you to a healthcare provider who specializes in neurologic problems. Tell your healthcare provider right away if you develop any signs or symptoms of neurologic problems during or after treatment with LUNSUMIO, including:
  - headache
  - numbness and tingling of the arms, legs, hands, or feet
  - dizziness
  - confusion and disorientation
  - difficulty paying attention or understanding things
  - forgetting things or forgetting who or where you are
  - trouble speaking, reading, or writing
  - sleepiness or trouble sleeping
  - tremors
  - loss of consciousness
  - seizures
  - muscle problems or muscle weakness
  - loss of balance or trouble walking
  - tiredness
- **serious infections.** LUNSUMIO can cause serious infections that may lead to death. Your healthcare provider will check you for signs and symptoms of infection before and during treatment. Tell your healthcare provider right away if you develop any signs or symptoms of infection during treatment with LUNSUMIO, including:
  - fever of 100.4°F (38°C) or higher
  - cough
  - chest pain
  - tiredness
  - shortness of breath
  - painful rash
  - sore throat
  - pain during urination
  - feeling weak or generally unwell
- **hemophagocytic lymphohistiocytosis (HLH).** LUNSUMIO can cause overactivity of the immune system, a condition called hemophagocytic lymphohistiocytosis (HLH). HLH can be life-threatening and has led to death in people treated with LUNSUMIO. Your healthcare provider will check you for HLH especially if your CRS lasts longer than expected. Signs and symptoms of HLH include:
  - fever
  - enlarged spleen
  - easy bruising
  - low blood cell counts
  - liver problems
- **low blood cell counts.** Low blood cell counts are common during treatment with LUNSUMIO and can also be serious or severe.

  Your healthcare provider will check your blood cell counts during treatment with LUNSUMIO. LUNSUMIO can cause the following low blood cell counts:
  - **low white blood cell counts (neutropenia).** Low white blood cells can increase your risk for infection.
  - **low red blood cell counts (anemia).** Low red blood cells can cause tiredness and shortness of breath.
  - **low platelet counts (thrombocytopenia).** Low platelet counts can cause bruising or bleeding problems.

- **growth in your tumor or worsening of tumor related problems (tumor flare).** LUNSUMIO can cause serious or severe worsening of your tumor.

  Tell your healthcare provider if you develop any of these signs or symptoms of tumor flare during your treatment with LUNSUMIO:

  - chest pain
  - cough
  - trouble breathing
  - tender or swollen lymph nodes
  - pain or swelling at the site of the tumor

Your healthcare provider may temporarily stop or permanently stop treatment with LUNSUMIO if you develop severe side effects.

The most common side effects of LUNSUMIO include: tiredness, rash, fever, and headache.

The most common severe abnormal blood test results with LUNSUMIO include: decreased phosphate, increased glucose, and increased uric acid levels.

These are not all the possible side effects of LUNSUMIO.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of LUNSUMIO.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about LUNSUMIO that is written for health professionals.

What are the ingredients in LUNSUMIO?

Active ingredient: mosunetuzumab-axgb

Inactive ingredients: acetic acid, histidine, methionine, polysorbate 20, sucrose, and Water for Injection

Manufactured by: **Genentech, Inc.,** A Member of the Roche Group, 1 DNA Way, South San Francisco, CA 94080-4990

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For more information, call 1-844-832-3687 or go to www.LUNSUMIO.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 11/2024