NEW DRUG APPROVAL

Brand Name	Lunsumio™
Generic Name	mosunetuzumab-axgb
Drug Manufacturer	Genentech, Inc

New Drug Approval

FDA approval date: December 22, 2022

Review designation: N/A; Orphan

Type of review: Biologic License Application (BLA): 761263

Dispensing restriction: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Lymphoma is a type of blood cancer that develops when white blood cells called lymphocytes grow out of control. Lymphocytes are part of your immune system. They travel around your body in your lymphatic system, and blood, helping you fight infections. There are two types of lymphocyte: T lymphocytes (T cells) and B lymphocytes (B cells).

Lymphomas can be grouped as Hodgkin lymphomas or non-Hodgkin lymphomas (NHL), depending on the types of cell they contain. Follicular lymphoma (FL) is a common type of slow growing (low-grade) non-Hodgkin lymphoma that develops from B cells. It is called 'follicular' lymphoma because the abnormal B cells usually develop in clumps called 'follicles' inside lymph nodes.

Follicular lymphoma is one of the most common indolent non-Hodgkin lymphoma (NHL) subtype in Western countries. In 2016, an estimated 13,960 cases were diagnosed in the US, representing 12.4% of mature NHLs. For the latter part of the 20th century, NHL rates were rapidly increasing in Western countries and then stabilized around 2000. FL incidence in the US increased in the US from 1992-2001. Using data from the US Surveillance, Epidemiology and End Results (SEER) program, the age-adjusted incidence rate (using the US year 2000 as the standard population) for FL from 2000-2016 was 3.5 per 100,000 and was 1.2 times higher in men (3.9) than women (3.3). The incidence of FL increases sharply with age.

Efficacy

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.

Table 1. 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.

Safety

ADVERSE EVENTS

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.

WARNINGS & PRECAUTIONS

- **Neurologic Toxicity**: Can cause serious 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.
- **Infections**: Can cause serious or fatal infections. Monitor patients for signs and symptoms of infection, including opportunistic infections, and treat as needed.
- **Cytopenias**: Monitor complete blood cell counts during treatment.
- **Tumor Flare:** Can cause serious tumor flare reactions. Monitor patients at risk for complications of tumor flare.
- **Embryo-Fetal Toxicity**: May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception.

CONTRAINDICATIONS

None reported.

Clinical Pharmacology

MECHANISMS 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.

Dose & Administration

ADULTS

- Premedicate to reduce risk of cytokine release syndrome and infusion related reactions.
- Administer only as an intravenous infusion.
- 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

PEDIATRICS

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

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injection:

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