Mosunetuzumab-axgb (LUNSUMIO)
National Drug Mini-monograph
November 2024

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Bispecific CD20-directed CD3 T-cell engager
Indication Under Review[1]	Relapsed or refractory follicular lymphoma (FL) after 2 or more lines of therapy (LOT) Accelerated approval based on response rate. Contingent upon verification and description in a confirmatory trial.
Dosage Regimen	C#1 Day 1 – 1mg IV over at least 4 hours Day 8 – 2mg IV Day 15 – 60mg IV C#2 Day 1 – 60mg IV over 2 hours if C#1 doses are tolerated C#3+ Day 1 – 30mg IV
Dosage Forms Under Review	1mg/ml solution SDV 30mg/30ml solution SDV

EFFICACY CONSIDERATIONS

Trial	**NCT02500407**
Design	Single-arm, multicenter, phase 2
Population	N=90; Follicular lymphoma (grade 1-3a), ECOG PS 0-1, s/p ≥ 2 LOT (including anti-CD20 mab and alkylating agent)
Demographics	mAge 60 yrs (53-67); male 61%; White 82%, Asian 9%, Black 4%; Hispanic or Latino 8%ECOG PS 0 59%; bulky disease 34%; Stage III-IV disease 77%; median LOT 3 (3-10); prior ASCT 21%; prior CAR T-cell 3%
Intervention	C#1 Day 1 – mosunetuzumab 1mg IV over at least 4 hours Day 8 – 2mg IV Day 15 – 60mg IV C#2 Day 1 – 60mg IV over 2 hours if C#1 doses are tolerated C#3+ Day 1 – 30mg IV
Comparator	Historical control using copanlisib CR rate 14% in a similar population
Results	Independent review committee (IRC)-assessed complete response (CR) Median follow-up for DoR 15 months ORR 80% (95% CI 70 – 88); CR 60% (95% CI 49 – 70); PR 20% (95% CI 12 - 30); Median DoR 22.8 months (10, NR) Results suggest improved responses as compared to historical control with copanlisib.
Notes	**NCCN guidelines FL v3.2024:** 3L and subsequent therapy Preferred regimens: • CAR T-cell therapy (CD19-directed) • BiTE (epcoritamab, **mosunetuzumab**) **VA Oncology Clinical Pathway**: Multiply relapsed FL, in patients with unfavorable characteristics (i.e. relapse after antiCD20 antibody, cytotoxic chemotherapy and lenalidomide or progression < 24 months from all prior treatments and not a candidate for cellular therapy) **Alternative options:** Refer to **Appendix A**.

SAFETY CONSIDERATIONS		
	Boxed Warnings	CRS 39%; (Gr 1-28%; Gr 2-15%, Gr 3-2%, Gr 4-0.5%); recurrent CRS 11%
	Contraindications	None
	Other Warnings	Neurologic toxicity 39%; HA 21%, PN 13%, dizziness 11%, MS changes 6%, ICANS 1% (Gr 1-0.5%, Gr 2-0.5%) Infections 17%; Upper RTI 14% (Gr 3–2.2%), UTI 10% (Gr 3-1.1%) Cytopenias Neutropenia 38% (Gr 4-19%), FN 2%, anemia 19%, tcp 12% (Gr 4-5%) Tumor flare 4% Embryo-fetal toxicity
	Top 5 AEs	CRS, fatigue, rash, pyrexia, headache
	Drug Interactions	

VHA PLACE IN THERAPY		
	Potential Use in VHA	1. Follicular lymphoma is the most common indolent non-Hodgkin lymphoma with no therapy defined as the standard of care in patients with multiple relapses or refractory disease. 2. CAR T-cell therapy is preferred due to high response rates, yet limitations exist, such as patient comorbid conditions, baseline organ function, access to treatment sites and the manufacturing process, to name a few. 3. The bispecific T-cell engagers are a more convenient (i.e. off-the-shelf product) alternative to CAR T-cell therapy, yet they are not without limitations. As VA facilities share expertise with establishing BiTE therapy protocols and the patient experience, anticipate utilization will increase. 4. Epcoritamab and mosunetuzumab are BiTE therapies that have been investigated, resulting in FDA-approval in the R/R FL setting. They have not been compared to each other or to other therapies. Indirectly, both are effective with response rates in the 80-82% range with 60-63% achieving CR. These products vary by dosing route (SubQ vs. IV), schedule (q21 vs. q28-day cycle), duration of therapy (indefinite vs. fixed-duration), toxicity profile and drug cost.

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References

1 LUNSUMIO (mosunetuzumab-axgb) injection [prescribing information online]. South San Francisco, CA: Genentech. December 2022. Available at: label (fda.gov). Accessed October 2024.
2 Budde LE, Sehn LH, Marasar M, et al. Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicenter, phase 2 study. Lancet Oncol 2022; 23: 1055-1065.
3 National Comprehensive Cancer Network Guidelines Version 3.2024 Classic Follicular Lymphoma (nccn.org) Accessed October, 2024.
4 Budde LE, Assouline S, Sehn LH, et al. Durable responses with mosunetuzumab in relapsed/refractory indolent and aggressive B-cell non-hodgkin lymphomas: extended follow-up of a phase I/II study. J Clin Oncol 2024; 42: 2250-2256

Appendix A. BiTE alternatives for R/R FL

	Mosunetuzumab LUNSUMIO CD20-directed CD3 T-cell engager Genentech, Inc.	Epcoritamab EPKINLY CD20-directed CD3 T-cell engager Genmab, Inc.
FDA approval	• 12/2022 Accelerated approval based on response rate.	• 5/2023 R/R DLBCL • 6/2024 FL Accelerated approval based on RR and durability of response
Indication	R/R follicular lymphoma (FL) after ≥ 2 prior LOT	r/r DLBCL and high-grade B-cell lymphoma, not otherwise specified, including DLBCL s/p ≥ 2 prior LOT r/r FL after ≥ 2 prior LOT
Recommended hospitalization?	None	DLBCL: for 24 hrs after C#1, day 15 dose None for FL
Dosing	Time-limited dosing (8 or 17 cycles)	Continuous dosing
Dosing route	IV infusion	Subcutaneous
Cycle length	21-day cycle	28-day cycle
Boxed warning(s)	CRS	CRS ICANS
REMS	No	No
Warnings/pre-cautions	**CRS 39%** (Gr 1-28%; Gr 2-15%, Gr 3-2%, Gr 4-0.5%); recurrent CRS 11% **Neurologic toxicity 39%** HA 21%, PN 13%, dizziness 11%, MS changes 6%, ICANS 1% (Gr 1-0.5%, Gr 2-0.5%) **Infections 17%** Upper RTI 14% (Gr 3–2.2%), UTI 10% (Gr 3-1.1%) **Cytopenias** Neutropenia 38% (Gr 4-19%), FN 2%, anemia 19%, tcp 12% (Gr 4-5%) **Tumor Flare 4%** **Embryo-fetal toxicity**	**CRS 51%** (Gr 1-37%; Gr 2-17%; Gr 3-2.5%); CRS in C1- 92%; recurrent CRS 16% **ICANS 6%** (Gr 1-4.5%; Gr 2-1.3%; Gr 5-0.6%) **Infections 15%** (Gr 3/4-14%; Gr 5-1.3%) **Cytopenias** neutropenia (Gr 3/4-32%); FN 2.5% anemia 12%; tcp 12%, **Embryo-fetal toxicity**
VA Oncology Clinical Pathway	Follicular Lymphoma V1.2024 Multiply relapsed in patients who are not candidates for SCT or CAR T-cell therapy	n/a, either DLBCL or FL
NCCN Guidelines	NCCN guidelines FL v3.2024 3L and subsequent therapy Preferred regimens: • BiTE (epcoritamab, **mosunetuzumab**) • CAR T-cell therapy	NCCN guidelines DLBCL v3.2024: 3L and subsequent therapy Preferred regimens: • CAR T-cell therapy • BiTE (**epcoritamab**, glofitamab) NCCN guidelines FL v3.2024 3L and subsequent therapy Preferred regimens: • BiTE (**epcoritamab**, mosunetuzumab) • CAR T-cell therapy