Tafasitamab-cxix (MONJUVI)
National Drug Monograph
September 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	Tafasitamab is a humanized CD19-directed monoclonal antibody that binds to CD19 antigen expressed on B-cells and mediates cell lysis through apoptosis and immune-mediated mechanisms (i.e. ADCC, ADCP)
Indication Under Review[1]	In combination with lenalidomide for treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant (ASCT) Indication expedited through accelerated approval processes; continued approval contingent on verification and description of clinical benefit in a confirmatory trial
Dosage Regimen	Tafasitamab 12 mg/kg IV given on a 28-day cycle: Cycle 1: days 1, 4, 8, 15, 22 Cycles 2, 3: days 1, 8, 15, 22 Cycles 4 +: days 1, 15 Administer in combination with lenalidomide 25 mg PO daily for maximum 12 cycles; Tafasitamab monotherapy can be continued until disease progression or unacceptable toxicity
Dosage Forms Under Review	200 mg tafasitamab lyophilized powder in a SDV for reconstitution

EFFICACY CONSIDERATIONS

Trial	**L-MIND (NCT02399085)**
Design	Open-label, multicenter, single-arm trial
Population	Relapsed or refractory DLBCL s/p 1-3 prior systemic therapies, including anti-CD20 MAb (i.e. rituximab); not eligible for ASCT Excluded: primary refractory DLBCL (i.e. fail to achieve a CR or relapse within 6 mos), double or triple hit genetics (i.e. *MYC*, *BCL2*, and/or *BCL6* translocations)
Demographics	N=71; mAge 71 years (41-86); 55% male, 100% prior anti-CD20 MAb; 95% white; 3% Asian; 45% refractory to last therapy; 42% refractory to rituximab Median LOT 2; 49% 1 LOT; 51% 2-4 LOT
Intervention	Tafasitamab 12 mg/kg IV given on a 28-day cycle: Cycle 1: days 1, 4, 8, 15, 22 Cycles 2, 3: days 1, 8, 15, 22 Cycles 4 +: days 1, 15 Lenalidomide 25 mg PO daily days 1 to 21 to max 12 cycles Repeat cycles every 28-days
Comparator	none
Results	Approval based on Overall Response Rate (ORR) and Duration of Response (DoR) ORR 55% (95% CI, 43-67); CR 37%; PR 18% DoR 21.7 months (0-24)[2] Final 5-year analysis reveals[3]: ORR 57.5%; CR 41.3% mDoR not reached; median follow-up 44 mos mPFS 11.6 months (95% CI 5.7-45.7); median follow-up 45.6 mos mOS 33.5 months (95% CI: 18.3 – not reached); median follow-up 65.6 mos ORR s/p 1 LOT 67.5% (CR 52.5%); ORR s/p $\geq$ 2 LOT 47.5% (CR 30%)

Notes	**NCCN guidelines DLBCL v2.2024 includes:** Tafasitamab + lenalidomide (preferred 2L option, category 2A) With note that it is unclear is antiCD 19-directed therapy could have a negative impact on efficacy of subsequent CAR T-cell therapy **VA Oncology Clinical Pathway: DLBCL, Relapsed, 2L:** Tafasitamab + lenalidomide in relapsed in the following 2L setting: Patient is not eligible for ASCT and not a candidate for CAR T-cell therapy **Alternative options:** Refer to **Appendix A. *Antibody-Based Therapies for R/R DLBCL***

SAFETY CONSIDERATIONS

Boxed Warnings	None
Contraindications	None
Other Warnings	Infusion-related reactions Myelosuppression Infections Embryo-fetal toxicity
Top 5 AEs	(≥ 20%) neutropenia, fatigue, anemia, diarrhea, thrombocytopenia
Drug Interactions	

VHA PLACE IN THERAPY

Potential Use in VHA	1. DLBCL is the most common subtype of non-Hodgkin lymphoma. Advanced stage disease includes stages III or IV disease. Initial chemoimmunotherapy with an antiCD-20 MAb regimen (i.e. R-CHOP or Pola-R-CHP) results in response in ~60% of patients. For those who do not respond initially (i.e. primary refractory) or have a relapse in disease, prognosis is poor. 2. In a select population of patients who are not candidates for ASCT or CAR T-cell, the combination of tafasitamab and lenalidomide resulted in ORR 55% that remained consistent with ORR 57.5% at the final 5-year analysis; median duration of response had not been reached at a median follow-up of 44 months; median OS at 65 months was reported as 33.5 months. 3. Patients with primary refractory DLBCL (i.e. fail to achieve a CR or relapse within 6 mos), double or triple hit genetics (i.e. *MYC*, *BCL2*, and/or *BCL6* translocations) were excluded from L-MIND, so efficacy of tafasitamab + lenalidomide in these populations is unknown.

Prepared August 2024
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References

1 Tafasitamab-cxix (MONJUVI) solution for injection [prescribing information online]. Boston, MA: MorphoSYS, Inc. June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761163s001lbl.pdf. Accessed Date: Aug. 26, 2024

2 Salles G, Duell J, Gonzalez Barca E, et al. Tafasitamab plus lenalidomide in relapsed or refractory diffuse large B-cell lymphoma (L-MIND): a multicenter, prospective, single-arm, phase 2 study. Lancet Oncol 2020; 21: 978-988

3 Duell J, Abrisqueta P, Andre M, et al. Tafasitamab for patients with relapsed or refractory diffuse large B-cell lymphoma: final 5-year efficacy and safety findings in the phase II L-MIND study. Haematological 2024; 109: 553-566.

4 National Comprehensive Cancer Network Guidelines Version 2.2024 Diffuse Large B-Cell Lymphoma. b-cell.pdf (nccn.org) Accessed Aug 26, 2024.

5 Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicenter seamless design study. Lancet 2020; 396: 839-852.

Appendix A. Antibody-Based Therapies for Relapsed/Refractory Diffuse Large B-cell Lymphoma (Sept 2024) page 1

	Tafasitamab-cxix MONJUVI CD19-directed Monoclonal antibody	Polatuzumab-vedotin antiCD79b antibody and microtubule inhibitor conjugate	Loncastuximab CD19-directed antibody drug conjugate
FDA approval	7/31/2020 Accelerated approval based on ORR	6/10/2019	4/23/2021 Accelerated approval based on ORR
Indication	In combination with lenalidomide for treatment of R/R DLBCL who are not eligible for autologous stem cell transplant (ASCT)*	In combination with bendamustine and rituximab for the treatment of R/R DLBCL after at least 2 prior lines of therapy (LOT)	R/R DLBCL after > 2 LOT; including DLBLC from low-grade lymphoma and high-grade B-cell lymphoma
Dosing	Tafasitamab 12 mg/kg IV given on a 28-day cycle: Cycle 1: days 1, 4, 8, 15, 22 Cycles 2, 3: days 1, 8, 15, 22 Cycles 4 +: days 1, 15 Lenalidomide 25 mg PO daily days 1 to 21 to max 12 cycles Repeat cycles every 28-days	Pola-Bendamustine + Rituximab (BR) R 375 mg/m2 IV on Day 1, Cycles 1-6; Pola 1.8 mg/kg IV on Day 2, Cycle 1; Bendamustine 90mg/m2 IV, Days 2, 3; Cycle 1 Days 1, 2; Cycles 2-6; Repeat every 21 days for 6 cycles	Loncastuximab IV on day 1 of 21-d cycle: Cycles 1, 2: 0.15mg/kg Cycles 3+: 0.075mg/kg
Recommended hospitalization?	n/a	n/a	n/a
Boxed warning(s)	none	None	none
REMS	none	None	none
Warnings/precautions	**Infusion-related reactions 6%** 80% during cycles 1 or 2 **Myelosuppression** Neutropenia Gr 3-25%; Gr 4-25% Thrombocytopenia Gr 3-12%; Gr 4-6% Anemia Gr 3-7% **Infections** 73% developed an infection; RTI 24%, UTI 17%, bronchitis 16% PNA Gr 3-7% **Embryo-fetal toxicity**	**Peripheral neuropathy (PN)** **Infusion-related reactions** **Myelosuppression** **Serious and opportunistic infections** **Progressive multifocal leukoencephalopathy (PML)** **Tumor lysis syndrome** **Hepatotoxicity** **Embryo-fetal toxicity**	**Effusion and edema** Gr 3-3% edema; Gr 3-3% Pleural effusion **Myelosuppression** Gr 3/4-32% neutropenia; 20% tcp; 12% anemia; FN 3% **Infections** ≥ Gr 3 – 10% sepsis, pna **Cutaneous Reactions** Gr 3 – 4%, incl photosensitivity **Embryo-Fetal Toxicity**

Appendix A. Antibody-Based Therapies for Relapsed/Refractory Diffuse Large B-cell Lymphoma (Sept 2024) page 2

	Tafasitamab-cxix MONJUVI CD19-directed Monoclonal antibody	Polatuzumab-vedotin antiCD79b antibody and microtubule inhibitor conjugate	Loncastuximab CD19-directed antibody drug conjugate
Studies	**L-MIND (NCT02399085)** Open-label, multicenter, single-arm; N=71; R/R DLBCL s/p 1-3 LOT, including anti-CD20 MAb; Not ASCT candidate **Excluded: primary refractory DLBCL (i.e. fail to achieve a CR or relapse within 6 mos), double or triple hit genetics (i.e. MYC, BCL2, and/or BCL6 translocations)** ORR 55% (95% CI, 43-67); CR 37%; PR 18%; DoR 21.7 months (0-24) Final 5-year analysis: ORR 57.5%; CR 41.3% mDoR NR; median F/U 44 mos mPFS 11.6 months (95% CI 5.7-45.7); median F/U 45.6 mos mOS 33.5 months (95% CI: 18.3 – NR); median F/U 65.6 mos	**Study GO29365 (NCT02257567)** Open-label, single-arm, phase 1b/2 N=80; R/R DLBCL s/p > 1 LOT; Not ASCT candidate mAge 69 yrs (30-86); 66% male; 71% white; 98% DLBCL; Ineligible for ASCT due to: age 40%, insufficient response to salvage therapy 26%; prior ASCT failure 20% Median # prior therapies: 2 (1-7) In transplant ineligible patients Pola-BR vs. BR; CR 40 vs. 18% mPFS 10 vs. 4 mos mOS 12 vs. 5 mos	**LOTIS-2 (NCT03589469)** Open-label, single-arm, phase 2 N=145; R/R DLBCL s/p ≥ 2 LOT; **Including *MYC* and *BCL2* and/or *BCL6* rearrangements** **Excluded: bulky disease ≥ 10cm; and active CNS lymphoma** mAge 66 yrs (56-71); 59% male; 88% DLBCL; 8% HGBCL; 20% transformed DLBCL; stage III-IV 77%; median 3 LOT (2-4); prior AutoSCT 14%; prior CAR T 9% ORR 48.3% (95% CI 39.9-56.7), CR 24% (95% CI 17.4-31.9) PR 24%; SD 15%; PD 21% mDOR 10.3 mos; PFS 4.9 mos; OS 9.9 mos
VA Oncology Clinical Pathway Recs	VA Oncology Clinical Pathway: DLBCL, Relapsed, 2L: Tafasitamab + lenalidomide in relapsed in the following 2L setting: Patient is not eligible for ASCT and not a candidate for CAR T-cell therapy	VA Oncology Clinical Pathways: DLBCL, Multiply Relapsed: Pola-BR in patients who are not candidates for ASCT or CAR T-cell therapy	Not on Pathway
NCCN Guidelines Recs	NCCN guidelines DLBCL v3.2024: 2L therapy Preferred regimens (cat 2A) • CAR T-cell therapy (Liso-cel) • Pola ± benda ± rituximab • **Tafasitamab + lenalidomide** •	NCCN guidelines DLBCL 3.2024: 2L therapy Preferred regimens (cat 2A) • CAR T-cell therapy (Liso-cel) • **Pola ± benda ± rituximab** • Tafasitamab + lenalidomide Bridging Therapy to CAR T-cell includes 6 options, all category 2A: Pola ± rituximab ± bendamustine (only after leukapheresis, as it may impact cell collection)	NCCN guidelines DLBCL 3.2024: 3L and subsequent therapy Preferred regimens: • CAR T-cell therapy • BITE (epcoritamab, glofitamab) Other recommended regimens (cat 2A): • **Loncastuximab tesirine** • Selinexor

Key: SU step up, D day, C cycle, CRS Cytokine Release Syndrome, ICANS Immune Cell-Associated Neurotoxicity Syndrome