Elranatamab (ELREXFIO) in Multiple Myeloma
National Drug Mini-Monograph
June 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. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Bispecific BCMA-directed, CD3 T-cell engager
Indication Under Review[1]	Accelerated approval for adults with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy (LOT) including a proteasome inhibitor, an immunomodulatory agent (IMiD) and an anti-CD38 monoclonal antibody; continued approval contingent upon clinical benefit verified in a confirmatory trial
Dosage Regimen	Day 1: Step Up 1: 12mg SQ Day 4: Step Up 2: 32mg SQ Day 8: 76mg SQ, first full dose, then weekly through week 24 After 6 cycles, responders receive doses every 2 weeks (if Partial Response or better at 6 months & maintained > 2 months) until disease progression or unacceptable toxicity
Dosage Forms Under Review	Injectable for subcutaneous administration

EFFICACY CONSIDERATIONS

Trial	**MagnetisMM-3 – Cohort A**	**MagnetisMM-3 – Cohort B**
Design	Open-label, single-arm, multicenter study	
Population	**Refractory to at ≥ 1 PI, ≥ 1 IMiD and ≥ 1 anti-CD38 MAb naïve to prior BCMA-directed therapy**; ECOG PS 0-2 (Cohort A)	**Refractory to at > 1 PI, > 1 IMiD and > 1 anti-CD38 MAb and prior BCMA-directed ADC or CAR T-cell therapy;** ECOG PS 0-2 (Cohort B)
Demographics	mAge 68 yrs (36-89 yrs); 55% male 58% white; 13% Asian; 7% Black Rec'd median 5 prior LOT (range, 2-22); 96.7% triple-class refractory; 42.3% penta-drug refractory	Rec'd median 8 LOT (range, 4-19); 73% prior BCMA-directed ADC; 32% prior BCMA-directed CAR T-cell therapy
Intervention	N=123 Day 1: Step Up 1: 12mg SQ Day 4: Step Up 2: 32mg SQ Day 8: 76mg SQ, first full dose, then weekly through week 24; After 6 cycles, if PR or better at 6 months & maintained > 2 months, then responders received doses every 2 weeks until PD or unacceptable toxicity	N=64
Comparator	N/A	
Results	Follow-up @ 14.7 months ORR (sCR+CR+VGPR+PR) by BICR: 61% (95% CI 58.1-69.6) 35% ≥ CR; 56% ≥ VGPR Est'm PFS @15 months: 51% mDOR NR (range, 12 – NE months) 48% treated ≥ 6 mos; 36% ≥ 12 mos mDOT 5.6 mos (0.03-24 mos)	Follow-up @ 10.2 months ORR 33.3% (95% CI: 22-46.3) by BICR: 6.3% ≥ CR; 25.4% ≥ VGPR mPFS 5.5 mos (95% CI 2.2-10) mOS 12.1 mos (95% CI 7.5-NE) mDOR NR (range NE, NE) DOR rate at 9 mos: 84.3% (95% CI: 58.7-94.7)

SAFETY CONSID

Boxed Warnings	CRS and Neurotoxicity including ICANS **CRS 58%** (gr 3: 0.5%); recurrent CRS 13% **Neurotoxicity 59%** (gr 3-4: 7%), **ICANS 3.5%**
Contraindications	None

Other Warnings	Infections, neutropenia, hepatotoxicity, embryo-fetal toxicity **Infections in 42%** (gr 3-4: 31%, gr 5: 7%) Most common were pneumonia, sepsis **Neutropenia in 62%** (gr 3-4: 51%, Febrile neutropenia 2.2%) **Hepatotoxicity with Incr ALT 36%** (gr 3-4: 3.8%), **Incr AST 40%** (gr 3-4: 6%) **Embryo-Fetal toxicity.** Can cause fetal harm.
Top 5 AEs	≥ **20%:** CRS (56%; no gr 3-4)), fatigue, infection site reaction, diarrhea, upper RTI ≥ **gr 3-4 laboratory abnormalities:** decreased lymphocytes, neutrophils, hemoglobin, WBC and platelets **TEAEs (gr 3-4) in 71%;** dose-reductions 28%, including neutropenia 15% **Dose-interruptions in 77%,** including infection 50%, neutropenia 41%
Drug Interactions	No DDI noted in prescribing information. Check alternative drug resources for DDIs; this list is not exhaustive. Elranatamab may incr conc of CYP substrates (risk C: monitor) Avoid denosumab as immunosuppressive effect may be enhanced (Risk D: modify therapy)

PLACE IN THERAPY

DRUG	VANF	CFU	FDA	GUIDELINES , ORR, AE Profile
Elranatamab ELREXFIO BCMA-directed, CD3 T-cell engager	TBD		RRMM s/p > 4 LOT	**VA Multiple Myeloma pathway**: n/a **NCCN:** One of the preferred BsAbs s/p > 4 LOT (cat 2A) ORR (no prior BCMA): 61%, (prior BCMA): 33% SubQ dosing; hospitalization recommended x2 Boxed warnings: CRS, Neuro tox including ICANS REMS program CRS 58% (all gr 1-2); recurrent 13% ICANS 3.4% (all gr 1-2) Neurotox 59% (gr 3-4: 7%)
Teclistamab TECVAYLI BCMA-directed, CD3 T-cell engager	PA-F	Yes	RRMM s/p > 4 LOT	**VA Multiple Myeloma pathway**: RRMM s/p ≥ 4 LOT **NCCN**: A preferred BsAbs s/p > 4 LOT (cat 2A) ORR: 63%, 39% ≥ CR; mDOR 18.4 mos SubQ dosing; hospitalization recommended x3 Boxed warnings: CRS, ICANS REMS program CRS 72% (gr 3-4: 0.6%); recurrent 33% ICANS 6% Neurotox 57% (gr 3-4: 2.4%)
Talquetamab TALVEY GPRC5D-directed, CD3 T-cell engager	TBD		RRMM s/p > 4 LOT	**VA Multiple Myeloma pathway**: n/a **NCCN**: A preferred BsAbs s/p > 4 LOT (cat 2A) ORR (no prior BCMA): 73%; 35% ≥ CR; mDOR 9-13 mos ORR (N=32, prior BCMA): 72% (95% CI, 53-86%) SubQ dosing; hospitalization recommended x2 Boxed warnings: CRS, ICANS REMS program CRS 76% (gr 3-4: 2%); recurrent 30% ICANS 9% Neurotox 46% (gr 3-4: 6%) Other: oral toxicity 80% (gr 3-4: 6%); wgt loss 62%; skin toxicity 62%

VHA PLACE IN THERAPY		

	Potential Use in VHA	• Bispecific antibody therapies provide an option to patients with limited access (due to specialized centers and/or manufacturing issues) to CAR T-cell therapy
		• Through indirect cross-trial comparisons of other BCMA-directed bispecific antibody therapies in a similar setting of RRMM:
		  • ORR of elranatamab is comparable to those reported with teclistamab
		  • Hematologic toxicity rates are similar
		  • Reported CRS rates and ICANS rates are lower with elranatamab, although neurotoxicity is higher
		• Data from Cohort B of MagnetisMM-3 demonstrates activity in those who received prior BCMA-directed therapies, therefore may be an option in patients with prior BCMA-therapy exposure, although ORR in this population is half that of those not previously exposed.

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References

1 Elranatamab ELREXFIO [prescribing information online]. New York, New York: Pfizer. August 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761345s000lbl.pdf Accessed April 8,2024.
2 Lesokhim AM, Tomasson MH, Arnulf B, et al. Elranatamab in relapse or refractory multiple myeloma: phase 2 MagnetisMM-3 trial results. Nature Medicine 2023; 29: 2259-2267
3 NCCN Guidelines Version 3.2024 Multiple Myeloma. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf
5 Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in Relapsed or Refractory Multiple Myeloma. N Engl J Med 2022; 387: 495-505.
6 Chari A, Minnema MC, Berdeja JG, et al. Talquetamab, a T-cell-redirecting GPRC5D bispecific antibody for multiple myeloma. N Engl J Med 2022; 387: 223s.
7 Talquetamab-tgvs TALVEY [prescribing information] Janssen Biotech, Inc. Horsham, PA. August 2023
8 Teclistamab-cqvv TECVAYLI [prescribing information] Janssen Biotech, Inc. Horsham, PA. February 2024
9 Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in Relapsed or Refractory Multiple Myeloma. N Engl J Med 2022; 387: 495.