Telisotuzumab vedotin-tllv (EMRELIS)
National Drug Monograph
November 2025

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	A c-Met-directed antibody and microtubule inhibitor (monomethyl auristatin E; MMAE) conjugate.
	Indication Under Review	For the treatment of previously treated patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with high c-Met protein overexpression [≥50% of tumor cells with strong (3+) staining]. *Currently approved under accelerated approval
	Dosage Regimen	Telisotuzumab vedotin (Teliso-V) 1.9mg/kg every 2 weeks until disease progression or unacceptable toxicity.
	Dosage Forms Under Review	20 mg or 100 mg telisotuzumab vedotin as lyophilized powder in a single-dose vial.

EFFICACY CONSIDERATIONS		
	Trial	**LUMINOSITY (NCT03539536)**
	Design	Phase II, multicenter, nonrandomized, two-stage study with multiple cohorts
	Population	N= 161; ≥18 years of age; c-Met protein overexpressing, locally advanced or metastatic NSCLC (non-squamous, *EGFR*-wildtype); ECOG performance status 0-1; 1-2 lines or prior systemic therapy (including 1 line of cytotoxic chemotherapy) Excluded: Radiation therapy to the lungs within 6 months; history of interstitial lung disease (ILD) or pneumonitis requiring steroids, or prior ILD or pneumonitis within 3 months; unresolved grade ≥2 adverse events; major surgery within 3 weeks
	Demographics	Median age 64 years (33-83); 68.9% male; 68.3% White, 29.8% Asian, 1.9% Black; 98.1% stage IV at randomization; 82.0% prior immune checkpoint inhibitor, c-Met high expression (n=78), c-Met intermediate expression (n=83) (≥25%-<50% tumor cells with 3+ staining intensity)
	Intervention	Teliso V Teliso-V 1.9mg/kg IV every 2 weeks
	Groups	Stage I: Group 1: non-squamous *EGFR* wild-type; c-Met high, c-Met intermediate Group 2: non-squamous *EGFR* mutant; c-Met high, c-Met intermediate (stopped early due to futility) Group 3: squamous cell (stopped early due to futility) **Stage II:** **Single-arm expansion of group 1 (non-squamous *EGFR* wild-type; c-Met high, c-Met intermediate)**; see efficacy analysis below
	Results	**Stage II: c-Met high vs. intermediate vs. all overexpression with EGFR WT total** @ 19.3 months **Primary endpoint- ORR (%)**: 34.6 vs. 22.9 vs. 28.6 Duration of response (months): 9.0 vs. 7.2 vs. 8.3 Duration of response ≥6 months (%): 63.0 vs. 47.4 vs. 56.5 mPFS (months): 5.5 vs. 6.0 vs. 5.7 mOS (months): 14.6 vs. 14.2 vs. 14.5 OS @ 12 months (%): 57.0 vs. 55.0 vs. 56.0
	Notes	**NCCN NSCLC 8.2025** Teliso V: Other recommended regimens (category 2A): Advanced or metastatic adenocarcinoma (subsequent): c-Met/Met ≥50% IHC 3+ and *EGFR*-wildtype Advanced or metastatic adenocarcinoma (progression): PS 0-2, c-Met/Met ≥50% IHC 3+ and *EGFR*-wildtype Alternative options: Available targetable biomarker: Biomarker-directed therapy as indicated No prior immunotherapy: Immune checkpoint inhibitors (category 1; preferred): nivolumab, pembrolizumab, atezolizumab Other recommended, with or without of prior immunotherapy (category 2A): Docetaxel, pemetrexed, gemcitabine, ramucirumab/docetaxel, albumin-bound paclitaxel

[redacted]	**VA Oncology Clinical Pathway:** Currently not listed in pathways; c-Met overexpression currently not mentioned in pathways Alternative options (subsequent therapy without identified actionable mutations): Prior chemotherapy + immunotherapy combination: docetaxel (ORR ~15%) Prior immunotherapy alone: carboplatin/pemetrexed (ORR 29-32%)

SAFETY CONSIDERATIONS

Boxed Warnings	None
Contraindications	None
Other Warnings	Peripheral neuropathy: Occurred in 51% of patients (11% grade 3); onset 105 days; led to discontinuation of Teliso-V in 13% of patients. Interstitial lung disease (ILD)/pneumonitis: Occurred in 10% of patients (3% grade 3, 0.6% grade 4); 3 fatal adverse events; onset 48 days; led to discontinuation of Teliso-V in 7% of patients. Ocular surface disorders: Occurred in 25% of patients (1.2% grade 3); onset 47 days.. Monitor for vision changes, dry eye, and other ocular symptoms; hold and consider discontinuation of Teliso-V according to severity. Infusion-related reaction: Occurred in 3% of patients (1.2% grade 3, 0.6% grade 4); onset 28 days; led to discontinuation of Teliso-V in 0.6% of patients. Provide pre-medications for subsequent doses of Teliso-V. Ensure adequate venous access or administer via central line to reduce discomfort that has been seen with various vedotin-containing therapies. Embryo-fetal toxicity: Can cause fetal harm in a pregnant woman. Advise effective contraception.
Pre-medications	Pre-medications recommended for patients who experience an infusion-related reaction, to be given 30-60 minutes prior to subsequent infusions: Diphenhydramine 25-50mg PO/IV or equivalent Famotidine 20mg PO/IV or equivalent Acetaminophen 650-1,000mg PO/IV or equivalent Methylprednisolone 125mg IV or equivalent
Adverse Events	≥20% (all grades): decreased albumin, increased glucose, peripheral neuropathy, decreased calcium, increased ALT, decreased lymphocytes, increased GGT, decreased hemoglobin, increased AST, decreased phosphorous/sodium, increased alkaline phosphatase, fatigue, peripheral edema, decreased appetite Fatal events (5%): ILD/pneumonitis, pneumonia, sudden death, noninfectious endocarditis, myocardial infarction; possibly related to Teliso-V (1.2%)
Drug Interactions	Concomitant use with strong CYP3A4 inhibitors may increase AUC and toxicity of MMAE. Monitor for increased risk of adverse reactions.

VHA PLACE IN THERAPY		
	Potential Use in VHA	1. Although c-Met protein expression is not currently routinely evaluated for in VHA, there are no available therapies targeted to c-Met protein overexpression. 2. *MET* alternations are known oncogenic drivers in NSCLC. Aside from c-Met protein overexpression, *MET* exon 14 skipping mutations, MET fusions and amplifications, including acquired amplification) are other common alterations with de novo occurrence in 4% to 5% of NSCLC cases. Numerous *MET*-targeted therapies have been approved (including VA preferred capmatinib); however, there are still no targeted agents for c-Met protein overexpression. Additionally, heterogeneity in *MET* expression has been documented in NSCLC that can further complicate defining biomarkers as therapeutic targets. 3. Telisotuzumab vedotin was studied in locally advanced or metastatic NSCLC with c-Met protein overexpression and known *EGFR* status. ORR in the nonsquamous, c-Met high *EGFR*-wildtype group at 19.3 months was 34.6% with a DOR of 9.0 months. Fatal adverse reactions occurred in 5% of patients due to ILD /pneumonitis (1.8%), pneumonia (1.2%), sudden death (1.2%), noninfectious endocarditis (0.6%), and myocardial infarction (0.6%). 4. TeliMET NSCLC-01 is a phase III global study, currently in the recruiting phase, aiming to compare efficacy and safety of telisotuzumab vedotin and docetaxel in patients with previously treated NSCLC and c-Met protein overexpression and known EGFR mutation status. 5. Due to the ORR and DOR benefit in LUMINOSITY, telisotuzumab vedotin may serve as an effective option for patients with advanced/metastatic NSCLC with high c-Met protein overexpression. However, risk vs. benefit analysis should be considered due to the notable incidence of fatal adverse events in the phase II trial and pending phase III data.

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