Lerodalcibep-liga (LEROCHOL)
National Drug Monograph
May 2026
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.

Abbreviation: ADE=adverse drug events, AE=adverse events, ApoB=apolipoprotein B, ASCVD=atherosclerotic cardiovascular disease, BMI=body mass index, CVD=cardiovascular disease, CV=cardiovascular, DB-double-blind, ESC=European Society of Cardiology Guideline, HDL-C=high density lipoprotein cholesterol, HeFH=heterozygous familial hypercholesterolemia, HoFH=homozygous familial hypercholesterolemia, Hx=history, ISR=injection site reactions, LDL-C=low-density lipoprotein cholesterol, Lip(a)=lipoprotein (a), mAb=monoclonal antibodies, MACE=major adverse cardiovascular events, MC=multicenter, PBO=placebo, PC=placebo-controlled, R=randomized, SC=subcutaneous, TC=total cholesterol, TG=triglycerides

FDA PRESCRIBING INFORMATION[1]	
Description / MOA	Lerodalcibep-liga is a recombinant fusion protein combining a proprotein convertase subtilisin Kexin type 9 (PCSK9)-binding domain (adnectin) with human serum albumin resulting in high affinity binding (picomolar affinity) to PCSK9. PCSK9 is responsible for degrading and recycling hepatic low-density lipoprotein (LDL) receptors. By inhibiting PCSK9, availability of LDL receptors is increased resulting in greater clearance of LDL-cholesterol.
Indication Under Review	Adjunct to diet and exercise to reduce LDL-cholesterol (LDL-C) in adults with hypercholesterolemia, including heterozygous familial hypercholesterolemia (HeFH). *Effect on CV events has not been established. No clinical outcome trial design or details have been published to date.*
Dosage Regimen	300 mg by subcutaneous administration once a month
Dosage Forms Under Review	300 mg single-dose prefilled syringe

EFFICACY CONSIDERATIONS

Trial[2]	**LIBERATE-HR (n=922) x 52 weeks (PHASE 3)**
Design	MC, R, DB, PC study lasting 52 weeks (intervention through 48 weeks, follow up at 50 and 52 weeks)
Population	Patients with CVD or at high risk for CVD on maximally tolerated statins + other lipid therapies Inclusion: Patients with CVD were eligible if LDL-C was ≥70 mg/dL or patients at high risk but without CVD if LDL-C ≥100 mg/dL and with TG ≤ 400 mg/dL Exclusion: Hx. of HoFH, unstable systemic disease, moderate to severe renal impairment, active liver disease, uncontrolled diabetes, etc.
Intervention	Lerodalcibep 300 mg SC once a month x 48 weeks
Comparator	Placebo once a month x 48 weeks
Key Baseline Characteristics	Mean age: 64 years % Male: 54-56% BMI: 30 ASCVD: 47.7% High to very high-risk primary prevention: 19% (high); 32.3% (very high risk) Diabetes: 43.2% HeFH: 9.6% Statin (any dose): 82-84% High intensity statin: 39.4% Ezetimibe: 16.6% Mean LDL-C: 116 mg/dL Mean HDL-C: 50 mg/dL Mean TG: 150 mg/dL Mean ApoB: 103 mg/dL Mean Lip(a): 102.6-105.6 nmol/L
Results	**LIBERATE-HR (PHASE 3)**

Outcome	Lerodalcibep (n=615)	Placebo (n=307)	Comments
Mean % LDL-C reduction from baseline to 52 weeks (co-primary)	-49.36 PBO-adjusted change (% mean): -49.67 (-54.37 to -44.97), p<0.001	0.31	
% LDL-C reduction from baseline, mean of weeks 50 and 52 (co-primary)	-55.46 PBO adjusted change (% mean): -55.33 (-59.54 to -51.12), p<0.001	-0.14	
Non-HDL, ApoB, Lip(a), HDL-C, TG, TC	----	----	All statistically improved from baseline in the lerodalcibep group vs. PBO, p<0.001 for all
% achieving ESC targets (≥ 50% reduction, <70 and <55 mg/dL)			>90% of participants in the lerodalcibep group achieved all 3 targets vs. <30% PBO. P<0.001 for all

Sources: [2]

Authors report modified intent to treat (mITT) and per-protocol (PP) analyses but only the intent to treat (ITT) analysis is reported in the table.

Author's Conclusions	LIBERATE-HR supports use in patients with or at high or very high risk for ASCVD who do not reach their LDL-C goals while receiving maximally tolerated statins plus other oral LDL-C lower agents.

Trial[3]	**LIBERATE-HeFH (n=478) x 24 weeks (PHASE 3)**
Design	MC, R, DB, PC study lasting 24 weeks
Population	Patients with a diagnosis of HeFH on maximally tolerated statins + other lipid therapies Inclusion: Patients with CVD were eligible if LDL-C was ≥70 mg/dL or patients at high risk but without CVD if LDL-C ≥100 mg/dL and with TG ≤ 400 mg/dL Exclusion: Hx of HoFH, unstable systemic disease, moderate to severe renal impairment, active liver disease, uncontrolled diabetes, etc.
Intervention	Lerodalcibep 300 mg SC x 24 weeks
Comparator	Placebo
Key Baseline Characteristics	Mean age: 53 years % male: 48.3% BMI: 28.8 ASCVD: 47.6% High to very high risk for ASCVD: 31% (high); 69% (very high risk) Diabetes: 10.5% HeFH: 100% Statin (any dose): 88.4% High intensity statin: 65.9% Ezetimibe: 48.7% Mean LDL-C: 150 mg/dL Mean HDL-C: 51.4 mg/dL Mean TG: 106 mg/dL Mean ApoB: 122 mg/dL Mean Lip(a): 51.5 nmol/L
Results	**LIBERATE-HeFH (PHASE 3)**

Outcome	Lerodalcibep (n=319)	Placebo (n=159)	Comments
Mean % LDL-C reduction from baseline to 24 weeks (co-primary)	-50.5 vs PBO: -58.6 (p<0.0001)	8.1	
% LDL-C reduction from baseline, mean of weeks 22 and 24 (co-primary)	-65 vs. PBO: (p<0.0001)	Reported as curve on graph, no specific number for LDL	
Non-HDL, ApoB, Lip(a), HDL-C, TG, TC	----	----	All statistically improved from baseline in the lerodalcibep group vs. PBO (p<0.0001 for all except HDL-C which was <0.01)
% achieving ESC targets (≥ 50% reduction, <70 and <55 mg/dL)	----	----	>85% of patients at high risk achieved ≥50% reduction in LDL and achieved LDL target vs. <4% PBO ≥68% of patients at very high risk achieved ≥50% reduction in LDL and achieved LDL target vs. <6% PBO

Sources: [3]

Authors' Conclusions	Lerodalcibep-liga can be considered as an alternative to monoclonal antibody inhibitors of PCSK9. It is administered as a SC injection once a month and significantly reduced LDL-C in patients with HeFH with a safety profile similar to placebo.

ADDITIONAL STUDIES-SUMMARY	
Trial[4]	**LIBERATE-HoFH (n=66)-**R, phase 3, open-label, crossover, noninferiority study in patients with HoFH. Of the 66 patients, 20 (30%) were pediatric patients. Patients were randomized to lerodalcibep 300 mg or evolocumab 420 mg once monthly for 24 weeks, followed by an 8-week wash-out period and then crossed over to alternative agent for 24 weeks. Mean baseline LDL-C 409 mg/dL; 88-97% were on high intensity statin and 94-97% on ezetimibe. Mean % change in LDL-C at 24 weeks: Lero: -4.9% vs. Evo: -10.3%; LS mean difference 5.4% (-0.2 to 11.1%) Although LDL-C response was noted to be highly variable, it was similar in the same patients with both agents. The mean difference of 5.4% did not show noninferiority at the prespecified 6% margin.
Trial[5]	**Pooled Analysis of Three Phase 3 studies of lerodalcibep-Adjudicated composite CV events** Week 24 total events: PBO: n=13 (1.7%) vs. Lero: n=11 (0.7%); OR 0.418 (0.185-0.936); HR 0.422 (0.189-0.943) Week 52 total events: PBO: n=25 (4.1%) vs. Lero: n=27 (2.2%); OR 0.527 (0.303-0.917); HR 0.540 (0.313-0.930) Authors note the prespecified analysis suggests potential benefit of Lero in reducing MACE, but the findings require confirmation in a large, planned CV outcomes trial.

SAFETY CONSIDERATIONS	
Boxed Warnings	None
Contraindications	None
Other Warnings	Risk for ISR and other adverse events listed in top 5 AEs row (below)
Top 5 AEs	ISR (LIBERATE-HeFH: Lero-10.1% vs. PBO-1.3%; total ISR: Lero-3.1% vs. PBO-1.3%), nasopharyngitis, diarrhea, nausea and peripheral edema. (LIBERATE-HR: Lero: 6.9% vs. PBO-0.3%; total ISR: Lero-2.7% vs. PBO: 0.5%)
Drug Interactions	None
Pregnancy	Evidence for use in pregnant women is insufficient and in general, treatment of hypercholesterolemia is generally not necessary during pregnancy. Product labeling recommends stopping lerodalcibep when pregnancy is recognized.
Lactation	Lack of evidence. Developmental and health benefits of breastfeeding should be considered along with the mother's clinical need and any potential effects of lerodalcibep on the breastfed infant or from the underlying mother's condition.
Trial Safety Results	Overall number of ADEs reported was similar between lerodalcibep and PBO in both trials. Injection site reactions were reported at a higher incidence in lerodalcibep vs. PBO and were mostly mild to moderate in severity and none led to a higher rate of study discontinuation vs. PBO.

OTHER CONSIDERATIONS	
FDA Review	Evidence of effectiveness was established with $\geq$2 adequate and well-controlled trials, including patients with HeFH.[6]
ICER Review	Not available
NICE Review	Not available

THERAPEUTIC ALTERNATIVES AND THEIR PLACE IN THERAPY

DRUG	VANF	CFU	FDA	GUIDELINES
Alirocumab	PA-F (preferred)	Yes	• To reduce the risk of major adverse cardiovascular (CV) events (coronary heart disease death, myocardial infarction, stroke, or unstable angina requiring hospitalization) in adults at increased risk for these events. • As an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in: o adults with hypercholesterolemia o adults and pediatric patients aged 8 years and older with heterozygous familial hypercholesterolemia (HeFH). o adults with homozygous familial hypercholesterolemia (HoFH).	VA/DoD 2025[7] -Secondary prevention as an option combined with moderate dose statin in high-risk patients -Secondary prevention as an option combined with maximally tolerated statin in very high-risk patients -Secondary prevention in very high-risk patients and added to maximally tolerated statin + ezetimbe ACC/AHA Joint 2026[8] -High-risk primary prevention added to statins + ezetimibe, PCSK9i and/or bempedoic acid. -Secondary prevention, at or not at very high risk, added to statins + ezetimibe, PCSK9i and/or bempedoic acid.
Evolocumab	PA-F	Yes	• To reduce the risk of major adverse cardiovascular (CV) events (CV death, myocardial infarction, stroke, unstable angina requiring hospitalization, or coronary revascularization) in adults at increased risk for these events. • As an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in: o adults with hypercholesterolemia. o adults and pediatric patients aged 10 years and older with heterozygous familial hypercholesterolemia (HeFH). o adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH).	VA/DoD 2025-same as alirocumab (above)[7] ACC/AHA Joint 2026-same as alirocumab (above)[8]
Inclisiran	NF	Yes	• As an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in: o adults with hypercholesterolemia. o adults and pediatric patients aged 12 years and older with heterozygous familial hypercholesterolemia (HeFH). o pediatric patients aged 12 years and older with homozygous familial hypercholesterolemia (HoFH).	VA/DoD 2025-Lacking evidence for improving CV outcomes. (*Clinical outcomes trials underway)*[7] ACC/AHA Joint 2026-can be added to statins +/- ezetimibe in patients unable to tolerate PCSK9i mAb in secondary prevention[8]

POTENTIAL PLACE IN THERAPY

1. In secondary prevention for patients at very high risk, including patients with HeFH and receiving maximally tolerated statins plus ezetimibe and require additional LDL-C reduction to achieve LDL-C goals and unable to tolerate alirocumab, evolocumab and inclisiran.

Revisions: N/A
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References

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