



## Evkeeza™ (Evinacumab-Dgnb) (for Louisiana Only)

Policy Number: **CSLA2022D00104B**

Effective Date: TBD

[Instructions for Use](#)

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### 4.4.22 Review

[This is more restrictive than the state's policy for this class of medication: Heart Disease - Hyperlipidemia - Lipotropics \(Other\)](#)

[Reviewed by: Cedric Cloud, PharmD.](#)  
[LA\\_PAM](#)

## Application

This Medical Benefit Drug Policy only applies to the state of Louisiana.

## Coverage Rationale

Evkeeza (evinacumab-dgnb) is proven and medically necessary for the treatment of homozygous familial hypercholesterolemia (HoFH) patients who meet all of the following criteria:

- For initial therapy, all of the following:
  - Diagnosis of HoFH by, or in consultation with, a lipid specialist (e.g., cardiologist, endocrinologist, lipid specialist/lipidologist) experienced in the management of HoFH; **and**
  - Confirmation of the HoFH diagnosis based on one of the following:
    - Submission of medical records (e.g., chart notes, laboratory values) confirming genetic confirmation of two mutant alleles at the *LDLR*, *APOB*, *PCSK9*, or *LDLRAP1* gene locus; **or**
    - Submission of medical records (e.g., chart notes, laboratory values) confirming both of the following:
      - One of the following:
        - Pre-treatment LDL-C greater than 500 mg/dL; **or**
        - Treated LDL-C greater than 300 mg/dL or history of treatment with Juxtapid (lomitapide)
      - and**
      - One of the following:
        - Xanthoma before 10 years of age; **or**
        - Heterozygous familial hypercholesterolemia (HeFH) in both parents

- and
- o Patient has failed to achieve an LDL-C goal of <100 mg/dL despite use of both of the following:
  - One of the following:
    - Patient is currently treated with maximally tolerated statin therapy; **or**
    - Patient is unable to tolerate statin therapy as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms:
      - Myalgia (muscle symptoms without CK elevations); **or**
      - Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN]); **or**
      - Patient has a labeled contraindication to all statins as documented in medical records; **or**
      - Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN
  - and
  - One of the following:
    - Patient has been treated with PCSK9 therapy or did not respond to PCSK9 therapy; **or**
    - Physician attests that the patient is known to have two LDL-receptor negative alleles (little to no residual function) and therefore would not respond to PCSK9 therapy; **or**
    - Patient has a history of intolerance or contraindication to PCSK9 therapy; **or**
    - Patient has previously been treated with Juxtapid (lomitapide); **or**
    - Patient has previously been treated with lipoprotein apheresis
- and
- o Patient will continue other traditional low-density lipoprotein-cholesterol (LDL-C) lowering therapies (e.g., maximally tolerated statins, ezetimibe) in combination with Evkeeza; **and**
- o Evkeeza will not be used in combination with Juxtapid (lomitapide); **and**
- o Evkeeza dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- o Initial authorization will be for no more than 6 months.
- For **continuation of therapy**, all of the following:
  - o Documentation of a positive clinical response to therapy from pre-treatment baseline; **and**
  - o Patient continues treatment with other traditional low-density lipoprotein-cholesterol (LDL-C) lowering therapies (e.g., statin, ezetimibe) in combination with Evkeeza; **and**
  - o Evkeeza will not be used in combination with Juxtapid (lomitapide); **and**
  - o Evkeeza dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - o Reauthorization will be for no more than 12 months.

## Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1305	Injection, evinacumab-dgnb, 5 mg

Diagnosis Code	Description
E78.01	Familial Hypercholesterolemia

Diagnosis Code	Description
Z83.42	Family History of FH

## Background

Familial hypercholesterolemia (FH) is an autosomal hereditary disease with 3 major clinical features of 1) hyper-LDL cholesterolemia, 2) premature CAD and 3) tendon and skin xanthomas. FH is caused by pathogenic mutations in genes of the LDL receptor, apolipoprotein B-100 (Apo-B100) and proprotein convertase subtilisin/kexin type 9 (PCSK9) which play an important role in LDL receptor pathway. In homozygous familial hypercholesterolemia (HoFH), 2 pathogenic mutations are found in 2 alleles of the causative gene. Consequently, HoFH is characterized by markedly elevated levels of low-density lipoprotein cholesterol (LDL-C) and premature cardiovascular risk. The loss-of-function variants in the LDL receptor causes low or zero clearance of LDL-C from circulation. HoFH affects approximately 1 in 300,000 people. If left untreated, mortality is common before age 30.

Evinacumab-dgnb is a recombinant human monoclonal antibody that binds and inhibits ANGPTL3.<sup>1</sup> ANGPTL3 is a regulator of lipoprotein metabolism, affecting lipoprotein lipase- and endothelial lipase-mediated hydrolysis of triglycerides and phospholipids. Inactivity of ANGPTL3 has been associated with potential for correcting hyperlipidemia.<sup>2,3</sup> Evinacumab-dgnb binds and blocks ANGPTL3 activity, thereby lowering TG and HDL-C by rescuing lipoprotein lipase and endothelial lipase activities. Additionally, evinacumab-dgnb promotes very low-density lipoprotein (VLDL) processing and clearance upstream of LDL formation.

## Clinical Evidence

Evinacumab-dgnb is indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH).<sup>1</sup>

ELIPSE HoFH (NCT03399786), was a phase 3, randomized, double-blind, placebo-controlled trial, that evaluated the efficacy of evinacumab in HoFH patients. The study randomly assigned 65 patients, 12 years of age and older, with HoFH who were already stable on lipid-lowering therapy (e.g., maximally tolerated statins, ezetimibe, PCSK9 inhibitor antibodies, lomitapide, and lipoprotein apheresis), in a 2:1 ratio to receive evinacumab or placebo. Most of the trial patients (94%) were receiving a statin (a high-intensity statin in 77%). Additionally, a PCSK9 inhibitor was being administered in 77% of the patients, ezetimibe in 75%, and lomitapide in 25%; 34% of the patients were undergoing apheresis. A total of 63% of the patients were taking at least three lipid modifying drugs. 43 patients were randomized to receive evinacumab 15 mg/kg every 4 weeks and 22 patients to receive placebo. After the double-blind treatment period, 64 of 65 patients entered a 24-week open-label extension period where all patients received evinacumab 15 mg/kg IV every 4 weeks. The primary outcome was the percent change from baseline in the LDL cholesterol level at week 24. The mean baseline LDL-C was 255 mg/dL. At week 24, the relative risk reduction from baseline was 47.1% in those treated with evinacumab, compared to an increase of 1.9% in the placebo group for a between-group least-squares mean (LSM) difference of -49.0 percentage points (95% CI: -65.0, -33.1; p <0.001). The between-group LSM absolute difference in the LDL-C level was -132.1 mg/dL (95% CI: -175.3, -88.9; p <0.001).<sup>4</sup>

## Professional Societies

The American College of Cardiology/American Heart Association Task Force published their clinical practice guidelines for the management of blood cholesterol in 2018. In regards to those with severe hypercholesterolemia (LDL-C ≥190 mg/dL), the guideline recommends:<sup>5</sup>

In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher (≥4.9 mmol/L) maximally tolerated statin therapy is recommended (Level I; B-R)

- In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher ( $\geq 4.9$  mmol/L) who achieve less than a 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of 100 mg/dL or higher ( $\geq 2.6$  mmol/L) ezetimibe therapy is reasonable (Level IIa; B-R)
- In patients 20 to 75 years of age with a baseline LDL-C level 190 mg/dL or higher ( $\geq 4.9$  mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides 300 mg/dL or lower ( $\leq 3.4$  mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a bile acid sequestrant may be considered (Level IIb; B-R)
- In patients 30 to 75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL or higher ( $\geq 2.6$  mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered (Level IIb; B-R)
- In patients 40 to 75 years of age with a baseline LDL-C level of 220 mg/dL or higher ( $\geq 5.7$  mmol/L) and who achieve an on-treatment LDL-C level of 130 mg/dL or higher ( $\geq 3.4$  mmol/L) while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered (Level IIb; C-LD)

The Hyperlipidaemia Education and Atherosclerosis Research Trust United Kingdom (HEART UK) published a consensus statement on a strategy for managing HoFH in the UK and treating to lower lipid targets suggested by the European Atherosclerosis Society (EAS) in 2017. The recommended target LDL-C is  $< 2.5$  mmol/L in adults ( $< 1.8$  mmol/L if CVD) and  $< 3.5$  mmol/L in children. With regards to treatment of HoFH, the consensus statement recommends the following:<sup>6</sup>

- Aged 12 and under: Consider lipid apheresis from the age of 2 and no later than 8, combined with maximum tolerated statin, ezetimibe, and bile acid sequestrants (BAS) (if effective).
- Aged over 12: Consider lipid apheresis and evolocumab, unless known LDLR negative, together. Apheresis frequency may be discontinued, be less frequent or not started.
- All patients should be offered maximum doses of atorvastatin or rosuvastatin combined with ezetimibe. Other statins may be tried in the event of intolerance.
- All HoFH patients on apheresis and standard drug treatment with LDL-C above target, who are receptor defective, should have a trial of treatment with evolocumab.
- Homozygotes or compound heterozygotes with gain of function PCSK9 alleles or double heterozygotes with, for example, an LDLR defective allele and a gain of function PCSK9 allele (digenic) are likely to respond well to PCSK9 inhibition.
- Patients who respond with 10–15% reduction in LDL-C (or interval mean LDL-C if on lipid apheresis) should continue treatment.
- Evolocumab should be injected subcutaneously directly after apheresis.
- Lomitapide should be considered for adults with HoFH, who have failed to achieve treatment targets while on apheresis and standard drug treatment and have had a trial of evolocumab.
- The frequency of lipid apheresis may be reduced when combined with lomitapide and/or evolocumab.

The Japan Atherosclerosis Society and Asian Pacific Society of Atherosclerosis and Vascular Diseases published guidelines for diagnosis and treatment of familial hypercholesterolemia in 2017. With regards to treatment of HoFH, the guideline recommends the following:<sup>7</sup>

- Intensive lipid-lowering therapy is necessary for the treatment of FH, first-line drug should be statins (recommendation level A, evidence level 3)
- For homozygous FH, consider LDL apheresis and treatment with PCSK9 inhibitors or (microsomal triglyceride protein inhibitor) MTP inhibitors (recommendation level A)

## U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Evkeeza indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH).<sup>1</sup>

## References

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4. Raal FJ, Rosenson RS, Reeskamp LF, et al. Evinacumab for Homozygous Familial Hypercholesterolemia. *N Engl J Med*. 2020;383(8):711-720. doi:10.1056/NEJMoa2004215.
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7. Harada-Shiba M, Arai H, Ishigaki Y, et al. Guidelines for Diagnosis and Treatment of Familial Hypercholesterolemia 2017. *J Atheroscler Thromb*. 2018;25(8):751-770. doi:10.5551/jat.CR003.

## Policy History/Revision Information

Date	Summary of Changes
TBD	<ul style="list-style-type: none"><li>• Annual review. No changes to clinical criteria.</li></ul>

## Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

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