Evkeeza® (Evinacumab-Dgnb)

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➲ Instructions for Use

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Related Policy

- Review at Launch for New to Market Medications

Applicable States

This Medical Benefit Drug Policy applies to Individual Exchange benefit plans in all states except for Nevada. For Nevada, refer to the UnitedHealthcare Commercial Medical Benefit Drug Policy.

Coverage Rationale

➲ See Benefit Considerations

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 bi-allelic pathogenic/likely pathogenic variants on different chromosomes at the low-density lipoprotein receptor (*LDLR*), apolipoprotein B (*APOB*), proprotein convertase subtilisin kexin type 9 (*PCSK9*), or low-density lipoprotein receptor adaptor protein 1 (*LDLRAP1*) genes or ≥ 2 such variants at different loci; **or**
    - **Both** of the following:
      - Untreated low-density lipoprotein cholesterol (LDL-C) greater than 400 mg/dL; **and**
      - **One** of the following:
        - Xanthoma before 10 years of age; **or**
        - Evidence of familial hypercholesterolemia in at least one parent

  and
  - **One** of the following:
    - Patient is less than 10 years of age; **or**
    - Patient has failed to achieve an LDL-C goal of < 55 mg/dL despite **all** 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 creatine kinase (CK) elevations]; **or**
          - Myositis [muscle symptoms with CK elevations < 10 times upper limit of normal (ULN)];

or

- Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN; **or**
- Patient has a contraindication to all statins

and

– **One** of the following:

- Patient has been receiving ezetimibe therapy as adjunct to maximally tolerated statin therapy; **or**
- Patient has a history of intolerance or contraindication to ezetimibe

and

– **One** of the following:

- Patient has been treated with PCSK9 therapy [e.g., Praluent (alirocumab), Repatha (evolocumab)] 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

- Patient will continue other traditional low-density lipoprotein-cholesterol (LDL-C) lowering therapies (e.g., maximally tolerated statins, ezetimibe) in combination with Evkeeza; **and**
- Evkeeza will not be used in combination with Juxtapid (lomitapide); **and**
- Evkeeza dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Initial authorization will be for no more than 12 months

- For **continuation of therapy**, **all** of the following:
  - Documentation of a positive clinical response to Evkeeza therapy; **and**
  - Evkeeza will not be used in combination with Juxtapid (lomitapide); **and**
  - Evkeeza dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - 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 the member specific benefit plan document 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
E78.010	Homozygous familial hypercholesterolemia [HoFH]

Background

Familial hypercholesterolemia (FH) is an autosomal hereditary disease with three 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), two pathogenic mutations are found in two 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. ANGPTL3 is a regulator of lipoprotein metabolism, affecting lipoprotein lipase- and endothelial lipase-mediated hydrolysis of triglycerides and phospholipids. Inactivity of ANGPLT3 has been associated with potential for correcting hyperlipidemia. 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.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Evinacumab-dgnb is indicated as an adjunct to diet and exercise and other low-density lipoprotein-cholesterol (LDL-C) lowering therapies to reduce LDL-C in adults and pediatric patients, aged 1 year and older, with homozygous familial hypercholesterolemia (HoFH).

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. Forty-three patients were randomized to receive evinacumab 15 mg/kg every four 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; $p < 0.001$). The approval of Evkeeza for the expanded indication in patients aged 5 years and older was based on a three-part, single-arm, open-label study (NCT04233918) in 14 pediatric patients aged 5 to 11 years with HoFH. Part B of this trial evaluated the efficacy of Evkeeza every 4 weeks as an adjunct to other lipid-lowering therapies (e.g., statins, ezetimibe, lomitapide, and lipoprotein apheresis) for 24 weeks. The primary endpoint was percent change in calculated LDL-C from baseline to week 24. At week 24, the mean percent change in calculated LDL-C from baseline was -48% (95% CI: -69% to -28%).

Professional Societies

The European Atherosclerosis Society published in 2023 an updated consensus statement on homozygous familial hypercholesterolaemia (HoFH). The 2023 statement updated criteria for the clinical diagnosis of HoFH, including that a low-density lipoprotein cholesterol (LDL-C) > 10 mmol/L (> 400 mg/dL) is suggestive of HoFH, requiring further evaluation, including a detailed medical and family history and/or genetic testing. Additional criteria for medical and family history include cutaneous or tendon xanthomas before age of 10 years and/or untreated elevated LDL-C levels consistent with heterozygous FH in both parents. Genetic criteria include genetic confirmation of bi-allelic pathogenic/likely pathogenic variants on different chromosomes at the LDLR, APOB, PCSK9, or LDLRAP1 genes or ≥ 2 such variants at different loci.

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

- 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 (≥ 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 (≥ 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 (≥ 4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides 300 mg/dL or lower (≤ 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 (≥ 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 (≥ 5.7 mmol/L) and who achieve an on-treatment LDL-C level of 130 mg/dL or higher (≥ 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)

Per a 2022 ACC Expert Consensus Decision Pathway (ECDP), specialized therapies, such as evinacumab or lomitapide, may be needed to control LDL-C in patients with HoFH who have an inadequate response to statins with or without ezetimibe and PCSK9 inhibitors. In the opinion of the writing committee for the ECDP, these therapies are best administered under the care of a lipid specialist.

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 is indicated as an adjunct to diet and exercise and other low-density lipoprotein-cholesterol (LDL-C) lowering therapies to reduce LDL-C in adults and pediatric patients, aged 1 year and older, with homozygous familial hypercholesterolemia (HoFH).

References

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Policy History/Revision Information

Date	Summary of Changes
04/01/2026	**Applicable States** ***Massachusetts*** *and* ***New York*** • Removed language indicating this Medical Benefit Drug Policy does not apply to the states of **Massachusetts** and **New York**

Date	Summary of Changes
	Nevada • Added instruction to refer to the UnitedHealthcare Commercial policy version for the state of **Nevada** **Applicable Codes** • Removed ICD-10 diagnosis codes E78.011, E78.019, and Z83.42 **Supporting Information** • Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version IEXD0104.11

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. 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.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.