VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Homozygous Familial Hypercholesterolemia – Evkeeza Utilization Management Medical Policy
- Evkeeza® (evinacumab-dgnb intravenous infusion – Regeneron)

REVIEW DATE: 03/11/2026

OVERVIEW

Evkeeza, an angiopoietin-like 3 inhibitor, is indicated as an adjunct to diet and exercise, as well as to other low-density lipoprotein cholesterol (LDL-C) lowering therapies, for the treatment of **homozygous familial hypercholesterolemia** (HoFH) in patients ≥ 1 years of age.[1]

In the pivotal trial that led to approval of Evkeeza, patients (most of whom were adults) were receiving additional medications to lower LDL-C levels such as statins (94% [77% of patients at high-intensity statin doses]), a proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor (77%), ezetimibe (75%), and Juxtapid® (lomitapide capsules).[2] Although some Phase II data are available,[3] the safety and effectiveness of Evkeeza have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH).[1] The effects of Evkeeza on cardiovascular (CV) morbidity and mortality have not been determined.

Disease Overview

Familial hypercholesterolemias (FH), including heterozygous (HeFH) and homozygous (HoFH) forms, is a group of inherited disorders that cause markedly elevated LDL-C levels.[4,5] HoFH is rare, affecting approximately 1 in 300,000 to 1,000,000 individuals, and is most commonly caused by impaired LDL receptor function, resulting in little to no LDL-C clearance. FH is associated with variations in the LDL receptor, apolipoprotein B, or PCSK9 genes and may present with tendon or cutaneous xanthomas, sometimes beginning in childhood. Patients with FH are at very high risk for premature atherosclerotic cardiovascular disease (ASCVD). Treatment targets generally aim for LDL-C < 100 mg/dL or < 70 mg/dL in adults with ASCVD or additional risk factors. High-intensity statin therapy is a first-line recommendation, with ezetimibe and PCSK9 inhibitors (e.g., Repatha® [evolocumab subcutaneous injection] and Praluent® [alirocumab subcutaneous injection]) added as needed; patients with HoFH often require combination therapy, including agents such as Juxtapid, Evkeeza, or LDL apheresis.

HoFH can be diagnosed using genetic or clinical criteria, with untreated LDL-C > 400 mg/dL and early xanthomas or elevated LDL-C in parents being strongly suggestive.[4] In the digenic form, one parent may have normal LDL-C levels and the other may have LDL-C levels consistent with HoFH.

Guidelines

Guidelines provide strategies for managing familial hypercholesterolemia, including HoFH, and mention the role of Evkeeza.[5,6]

- **American College of Cardiology (2022):** Specialized therapies, one of which includes Evkeeza, may be needed to control LDL-C in certain patients (e.g., those with HoFH) who have had an inadequate response to statins, with or without ezetimibe, and PCSK9 inhibitors.[6]
- **European Atherosclerosis Society (2023):** Clinical guidance by this organization recommends lipid-lowering therapy be initiated with high-intensity statin therapy and ezetimibe.[5] A PCSK9 inhibitor can be added as well. If patients are not at LDL-C goals, other agents can be alternatives as well (e.g., Juxtapid, Evkeeza). Lipoprotein apheresis may also be considered. The goal is to

reduce LDL-C to < 115 mg/dL in children and adolescents, < 70 mg/dL in adults if no major ASCVD risk factors are present, and < 55 mg/dL if patients have ASCVD or major ASCVD risk factors.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Evkeeza. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. A patient who has previously met Initial Therapy criteria for Evkeeza for the requested indication under the Coverage Review Department and is currently receiving Evkeeza is only required to meet continuation of therapy criteria (i.e., currently receiving therapy). If past criteria has not been met under the Coverage Review Department and the patient is currently receiving Evkeeza, or is restarting Evkeeza, Initial Therapy criteria must be met.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Evkeeza is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Homozygous Familial Hypercholesterolemia.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i and ii):
     - **i.** Patient meets ONE of the following (a, b, or c):
       - **a)** The diagnosis has been confirmed by genetic testing; OR
         Note: Examples include pathogenic variants 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) gene.
       - **b)** Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level > 400 mg/dL AND meets ONE of the following [(1) or (2)]; OR
         Note: Untreated refers to prior to therapy with any antihyperlipidemic agent.
         - **(1)** Patient had clinical manifestations of homozygous familial hypercholesterolemia before the age of 10 years; OR
           Note: Clinical manifestations of homozygous familial hypercholesterolemia are cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas, or xanthelasma.
         - **(2)** At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with familial hypercholesterolemia; OR
           Note: An example of familial hypercholesterolemia is an untreated LDL-C level ≥ 190 mg/dL and/or an untreated total cholesterol level > 250 mg/dL.
       - **c)** Patient has a treated LDL-C level ≥ 300 mg/dL AND meets ONE of the following [(1) or (2)]; AND
         Note: Treated refers to after therapy with at least one antihyperlipidemic agent. Some examples of antihyperlipidemic agents include statins (e.g., atorvastatin, rosuvastatin, lovastatin, simvastatin, pravastatin), ezetimibe, a PCSK9 inhibitor (i.e., Repatha

[evolocumab subcutaneous injection, Praluent [alirocumab subcutaneous injection]), or Juxtapid (lomitapide capsules).

(1) Patient had clinical manifestations of homozygous familial hypercholesterolemia before the age of 10 years; OR

Note: Examples of clinical manifestations of homozygous familial hypercholesterolemia are cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas, or xanthelasma.

(2) At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with familial hypercholesterolemia; AND

Note: An example of familial hypercholesterolemia is an untreated LDL-C ≥ 190 mg/dL and/or an untreated total cholesterol > 250 mg/dL.

ii. Patient meets ONE of the following (a or b):

a) Patient is 1 year to < 10 years of age; OR

b) Patient ≥ 10 years of age meets BOTH of the following [(1) and (2)]:

(1) Patient meets ONE of the following [(a) or (b)]:

(a) Patient meets BOTH of the following ([1] and [2]):

[1] Patient has tried one proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor for ≥ 8 continuous weeks; AND

Note: Examples of PCSK9 inhibitors include Repatha (evolocumab subcutaneous injection) and Praluent (alirocumab subcutaneous injection).

[2] The LDL-C after this PCSK9 inhibitor therapy remains ≥ 70 mg/dL; OR

(b) Patient is known to have two LDL-receptor negative alleles; AND

(2) Patient meets ONE of the following [(a) or (b)]:

a) Patient meets ALL of the following ([1], [2], and [3]):

[1] Patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single entity or as a combination product]); AND

[2] Patient has tried one high-intensity statin along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks; AND

[3] Low-density lipoprotein cholesterol level after this treatment regimen remains ≥ 70 mg/dL; OR

b) Patient has been determined to be statin intolerant by meeting ONE of the following ([1] or [2]):

[1] Patient experienced statin-related rhabdomyolysis; OR

Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).

[2] Patient meets ALL of the following [aa, bb, and cc]:

aa) Patient experienced skeletal-related muscle symptoms; AND

Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) and myalgia (muscle aches, soreness, stiffness, or tenderness).

bb) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND

cc) When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle

symptoms resolved upon discontinuatioin of each respective statin therapy (atorvastatin and rosuvastatin); OR
Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

B) Patient Currently Receiving Evkeeza. Approve if according to the prescriber, the patient has experienced a response to therapy.
Note: Examples of a response to therapy include decreasing LDL-C, total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Evkeeza for this specific indication through the Coverage Review Department, review under criteria for Initial Therapy. If the patient is restarting therapy with Evkeeza, Initial Therapy criteria must be met.

Dosing. Approve 15 mg/kg administered by intravenous infusion no more frequently than once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Evkeeza is not recommended in the following situations:

1. **Heterozygous Familial Hypercholesterolemia.** The safety and effectiveness of Evkeeza have not been established in patients with hypercholesterolemia who do not have HoFH, including those with HeFH.[1]

2. **Hyperlipidemia.** Although data are available, the prescribing information for Evkeeza states that the safety and efficacy of Evkeeza have not been established in patients with other forms of hypercholesterolemia.[1,3]
Note: This is not associated with HoFH and is referred to as combined hyperlipidemia, hypercholesterolemia (pure, primary), dyslipidemia, or increased/elevated LDL-C levels.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Evkeeza® intravenous infusion [prescribing information]. Tarrytown, NY: Regeneron; September 2025.
2. Raal FJ, Rosenson RS, Reeskamp LF, et al, for the ELIPSE HoFH investigators. Evkeeza for homozygous familial hypercholesterolemia. *N Engl J Med*. 2020;383(8):711-720.
3. Rosenson RS, Burgess LJ, Ebenbichler CF, et al. Evkeeza in patients with refractory hypercholesterolemia. *N Engl J Med*. 2020;383(24):2307-2319.
4. Raal FJ, Hovingh GK Catapano AL. Familial hypercholesterolemia treatments: guidelines and new therapies. *Atherosclerosis*. 2018;277:483-492.
5. Cuchel M, Raal FJ, Hegele RA, et al. 2023 update on European Atherosclerosis Society Consensus Statement on Homozygous Familial Hypercholesterolaemia: new treatments and clinical guidance. *Eur Heart J*. 2023;44:2277-2291.
6. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. *J Am Coll*. 2022;80(14):1366-1418.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	It was added to the Policy Statement that a patient who has previously met initial therapy criteria for Evkeeza for the requested indication under the Coverage Review Department and is currently receiving Evkeeza is only required to meet continuation of therapy criteria (i.e., currently receiving therapy). If past criteria has not been met under the Coverage Review Department and the patient is currently receiving Evkeeza, or is restarting Evkeeza, initial criteria must be met. In addition, the following changes were made: **Homozygous Familial Hypercholesterolemia:** Requirements were divided to distinguish between initial therapy and patient currently receiving Evkeeza (previously there was only one criteria set). For a patient who is currently receiving Evkeeza and has previously met initial therapy criteria for the requested indication under the Coverage Review Department, only the continuation of therapy criteria has to be met. The continuation of therapy criteria states that according to the prescribing physician, the patient has experienced a response to therapy with examples provided in a Note.	04/26/2023
Annual Revision	It was removed from the Policy Statement that the agent is prescribing by or in consultation with a physician who specializes in the condition being treated. In addition, the following changes were made: **Homozygous Familial Hypercholesterolemia:** For Initial Therapy, the requirement that the medication is prescribed by or in consultation with a cardiologist, an endocrinologist, or a physician who focuses in the treatment of cardiovascular risk management and/or lipid disorders was removed. The requirement that the patient has had genetic confirmation by two mutant alleles at the low-density lipoprotein receptor, apolipoprotein B, proprotein convertase subtilisin kexin type 9, or low-density lipoprotein receptor adaptor protein 1 gene locus was changed to state that the patient has phenotypic confirmation of homozygous familial hypercholesterolemia with the above examples moved to a Note. The diagnostic criterion which stated that the patient has an untreated low-density lipoprotein cholesterol level > 500 mg/dL was changed to > 400 mg/dL. The criterion (which is in two places [those with an untreated low-density lipoprotein cholesterol level > 400 mg/dL and a treated low-density lipoprotein cholesterol level ≥ 300 mg/dL]) that both parents of the patient had untreated low-density lipoprotein cholesterol levels or total cholesterol levels consistent with heterozygous familial hypercholesterolemia was changed to state that at least one parent of the patient had untreated low-density lipoprotein cholesterol levels or total cholesterol levels consistent with familial hypercholesterolemia. The related Note that "An example of heterozygous familial hypercholesterolemia in both parents would be if both had an untreated low-density lipoprotein cholesterol level ≥ 190 mg/dL and/or an untreated total cholesterol level > 250 mg/dL" was changed to state "An example of familial hypercholesterolemia is an untreated low-density lipoprotein cholesterol level ≥ 190 mg/dL and/or an untreated total cholesterol level > 250 mg/dL." For a Patient Currently Receiving the Medication, the requirement that the "prescribing physician" notes that the patient has experienced a response to therapy was changed to "prescriber".	05/08/2024

HISTORY (CONTINUED)

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Homozygous Familial Hypercholesterolemia:** For Initial Therapy, the phrase "phenotypic confirmation of homozygous familial hypercholesterolemia" was replaced with "The diagnosis has been confirmed by genetic testing". Also, "apo B" was changed to "APOB".	05/28/2025
Selected Revision	**Homozygous Familial Hypercholesterolemia:** For Initial Criteria, the criteria were divided based on age as follows: ≥ 10 years of age and 1 year to < 10 years of age. Previously, all patients ≥ 5 years of age were required to try one high-intensity statin along with ezetimibe for 8 continuous weeks (and have an LDL-C ≥ 70 mg/dL) or be statin intolerant; these requirements were removed for the new group of patients who are 1 year to < 10 years of age. Also, the criterion that allowed an exception for the requirement to try one proprotein convertase subtilisin kexin type 9 inhibitor for a patient 5 years or 9 years of age was removed as it is no longer needed. A patient 1 year to < 10 years of age are no longer required to try previous therapies, but must meet the previously defined diagnostic criteria for homozygous familial hypercholesterolemia.	10/08/2025
Selected Revision	**Homozygous Familial Hypercholesterolemia:** For initial therapy, a change was made in the Note that addresses a patient with a treated low-density lipoprotein cholesterol (LDL-C) level ≥ 300 mg/dL. For the requirement cited that at least one parent of the patient has untreated LDL-C levels or total cholesterol levels consistent with familial hypercholesterolemia, the Note was revised to remove the phrase that starts with "in both parents", as it only is required in one parent.	11/12/2025
Early Annual Revision	No criteria changes.	03/11/2026