POLICY Document for EVKEEZA (evinacumab-dgnb)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

Site of Care Criteria
Evkeeza

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated.

Brand Name	Generic Name	Dosage Form
Evkeeza	evinacumab-dgnb	intravenous

Criteria for Approval for Administration in Outpatient Hospital Setting

This policy provides coverage for administration of Evkeeza in an outpatient hospital setting for up to 45 days when a member is new to therapy or is reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Evkeeza in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

- The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
- The member is medically unstable (e.g., respiratory, cardiovascular, or renal conditions).
- The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
- The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
- Alternative infusion sites (pharmacy, physician office, ambulatory care, etc.) are greater than 30 miles from the member's home.
- The member is less than 14 years of age.

For situations where administration of Evkeeza does not meet the criteria for outpatient hospital infusion, coverage for Evkeeza is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

Required Documentation

The following information is necessary to initiate the site of care prior authorization review (where applicable):

- Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
- Medical records supporting the member is medically unstable
- Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
- Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
- Records supporting alternative infusion sites are greater than 30 miles from the member's home.
- Medical records supporting the member is new to therapy

Section 2: Clinical Criteria

Specialty Guideline Management
Evkeeza

CVS/caremark™

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Evkeeza	evinacumab-dgnb

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indication[1]

Evkeeza is indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 5 years and older, with homozygous familial hypercholesterolemia (HoFH).

Limitations of Use

- The safety and effectiveness of Evkeeza have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH).
- The effects of Evkeeza on cardiovascular morbidity and mortality have not been determined.

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Both initial and continuation requests:

- Genetic testing or medical records confirming the diagnosis of HoFH.
- LDL-C level dated within the six months preceding the authorization request.
- With clinical atherosclerotic cardiovascular disease (ASCVD): Chart notes confirming clinical ASCVD (if applicable) (see Appendix).
- For members 10 years of age and older: chart notes, medical record documentation, or claims history confirming the member is currently on maximally tolerated lipid-lowering therapy.

- For members 7 years of age to less than 10 years of age: chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

Coverage Criteria

Homozygous familial hypercholesterolemia (HoFH)[1-6]

Authorization of 6 months may be granted for members 5 years of age or older for the treatment of homozygous familial hypercholesterolemia when all of the following criteria are met:

- Member has a documented diagnosis of homozygous familial hypercholesterolemia confirmed by any of the following criteria:
  - Variant in two low-density lipoprotein receptor (LDLR) alleles.
  - Presence of homozygous or compound heterozygous variants in apolipoprotein B (APOB) or proprotein convertase subtilisin-kexin type 9 (PCSK9) gene.
  - Member has compound heterozygosity or homozygosity for variants in the gene encoding low-density lipoprotein receptor adaptor protein 1 (LDLRAP1).
  - Member has an untreated LDL-C of > 400 mg/dL and has either of the following:
    - Presence of cutaneous or tendinous xanthomas before the age of 10 years.
    - An untreated LDL-C level of ≥ 190 mg/dL in both parents.
- Prior to initiation of treatment with the requested medication, member meets/has met either of the following criteria:
  - Member has a treated LDL-C level ≥ 70 mg/dL.
  - Member has a treated LDL-C level ≥ 55 mg/dL and meets either of the following criteria:
    - Member has a history of a clinical ASCVD event (see Appendix).
    - Member has major ASCVD risk factors (e.g., 65 years of age or older, familial hypercholesterolemia, diabetes, chronic kidney disease, history of congestive heart failure).
- Prior to initiation of treatment with the requested medication, member meets/has met one of the following criteria:
  - Member is 10 years of age or older and meets both of the following criteria:
    - Member is receiving stable treatment with at least 3 lipid-lowering therapies (e.g., statins, ezetimibe, PCSK9 directed therapy) at the maximally tolerated dose.
    - Member will continue to receive concomitant lipid-lowering therapy at the maximally tolerated dose.

- Member is 7 years of age to less than 10 years of age and meets either of the following criteria:
  - Member is receiving stable treatment with at least one lipid-lowering therapy (e.g., statins, LDL apheresis) at the maximally tolerated dose and will continue to receive concomitant lipid-lowering therapy at the maximally tolerated dose.
  - Member has an intolerance or contraindication to other lipid-lowering therapies.
- Member is 5 years of age to less than 7 years of age.

Continuation of Therapy[1,2,5]

Authorization of 12 months may be granted for continued treatment in members (including new members) who meet all of the following criteria:

- Member meets all requirements in the coverage criteria.
- Member meets one of the following criteria:
  - Member is 10 years of age or older and is currently receiving concomitant lipid-lowering therapy at the maximally tolerated dose.
  - Member is 7 years of age to less than 10 years of age and meets either of the following criteria:
    - Member is currently receiving concomitant lipid-lowering therapy at the maximally tolerated dose.
    - Member has an intolerance or contraindication to other lipid-lowering therapies.
  - Member is 5 years of age to less than 7 years of age.
- The member is receiving benefit from therapy. Benefit is defined as either of the following:
  - LDL-C is now at goal.
  - Member has had at least 30% reduction of LDL-C from baseline.

Appendix

Clinical ASCVD[4,6-9]

- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)

- Non-cardiac peripheral arterial disease (PAD) of presumed atherosclerotic origin (e.g., carotid artery stenosis, lower extremity PAD)
- Obstructive coronary artery disease (defined as ≥ 50% stenosis on cardiac computed tomography angiogram or catheterization)
- Coronary artery calcium (CAC) Score ≥ 300

REFERENCES

SECTION 1

1. Evkeeza [package insert]. Tarrytown, NY: Regeneron Pharmaceutical Inc; March 2023.

SECTION 2

2. Evkeeza [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals Inc.; March 2023.
3. Raal FJ, Rosenson RS, Reeskamp LF, et al. Evinacumab for homozygous familial hypercholesterolemia. N Engl J Med. 2020;383:711-720.
4. Cuchel M, Raal FJ, Hegele RA, et al. Update on European atherosclerosis society consensus statement on homozygous familial hypercholesterolaemia: new treatments and clinical guidance. Eur Heart J. 2023;44(25):2277-2291.
5. Grundy SM, Stone NJ, Bailey, AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139(25):e1082– e1143.
6. A Wiegman, Greber-Platzer S, Ali S, et al. Evinacumab in pediatric patients With homozygous familial hypercholesterolemia. Circulation. 2024;149(5):343-353.
7. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 ACC Expert consensus decision pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: A report of the American college of cardiologic solution set oversight committee. J Am Coll Cardiol. 2022;80(14):1366–1418.
8. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 — full report. J Clin Lipidol. 2015;9:129–169.
9. Min JK, Labounty TM, Gomez MJ, et al. Incremental prognostic value of coronary computed tomographic angiography over coronary artery calcium score for risk prediction of major adverse cardiac events in asymptomatic diabetic individuals. Atherosclerosis. 2014;232(2):298-304.
10. Budoff MJ, Kinninger A, Gransar H, et al. When does a calcium score equate to secondary prevention?: Insights from the multinational CONFIRM registry. JACC Cardiovasc Imaging. 2023;16(9):1181-1189.