Reference number(s)
4672-A

STANDARD MEDICARE PART B MANAGEMENT

EVKEEZA (evinacumab-dgnb)

POLICY

I. 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
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 will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:
A. Genetic testing or medical records confirming the diagnosis of HoFH.
B. LDL-C level dated within the six months preceding the authorization request.
C. 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.
D. 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.

III. CRITERIA FOR INITIAL APPROVAL

Homozygous familial hypercholesterolemia (HoFH)
Authorization of 6 months may be granted for members 5 years of age and older for the treatment of homozygous familial hypercholesterolemia when both of the following criteria are met:
A. Member has a documented diagnosis of homozygous familial hypercholesterolemia confirmed by any of the following criteria:
    1. Variant in two low-density lipoprotein receptor (LDLR) alleles.
    2. Presence of homozygous or compound heterozygous variants in apolipoprotein B (APOB) or proprotein convertase subtilisin-kexin type 9 (PCSK9).

3. Member has compound heterozygosity or homozygosity for variants in the gene encoding low-density lipoprotein receptor adaptor protein 1 (LDLRAP1).
4. An untreated LDL-C of greater than 400 mg/dL and either of the following:
   a. Presence of cutaneous or tendinous xanthomas before the age of 10 years.
   b. An untreated LDL-C level of greater than or equal to 190 mg/dL in both parents.

B. Prior to initiation of treatment with the requested medication, both of the following criteria are/were met:
1. Member has a treated LDL-C of greater than or equal to 100 mg/dL (or greater than or equal to 70 mg/dL with clinical atherosclerotic cardiovascular disease [ASCVD])
2. Member meets one of the following:
   a. Member is 10 years of age or older and meets both of the following:
      i. Member is receiving stable treatment with at least 2 lipid-lowering therapies (e.g., statins, ezetimibe, proprotein convertase subtilisin/kexin type 9 [PCSK9] directed therapy) at the maximally tolerated dose.
      ii. Member will continue to receive concomitant lipid-lowering therapy at the maximally tolerated dose.
   b. Member is 7 years of age to less than 10 years of age and meets either of the following:
      i. 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.
      ii. Member has an intolerance or contraindication to other lipid-lowering therapies.
   c. Member is 5 years of age to less than 7 years of age.

Commented [PLR1]: Current:
1.An untreated LDL-C of greater than 500 mg/dL or treated LDL-C greater than or equal to 300 mg/dL and either of the following:

a.Presence of cutaneous or tendinous xanthomas before the age of 10 years.

a.An untreated LDL-C level of greater than or equal to 190 mg/dL in both parents.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with Evkeeza.
B. Evkeeza is being used to treat an indication enumerated in Section III.
C. Member meets one of the following:
1. Member is 10 years of age or older and is currently receiving concomitant lipid-lowering therapy at the maximally tolerated dose.
2. Member is 7 years of age to less than 10 years of age and meets either of the following:
   a. Member is currently receiving concomitant lipid-lowering therapy at the maximally tolerated dose.
   b. Member has an intolerance or contraindication to other lipid-lowering therapies.
3. Member is 5 years of age to less than 7 years of age.
D. The member is receiving benefit from therapy. Benefit is defined as either of the following:
1. LDL-C is now at goal.
2. Member has had at least a 30% reduction of LDL-C from baseline.

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Evkeeza.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology

3. Update on European atherosclerosis society consensus statement on homozygous familial hypercholesterolaemia: new treatments and clinical guidance.
4. National Lipid Association recommendations for patient-centered management of dyslipidemia.
5. 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.
6. Diagnosis and Treatment of Heterozygous Familial Hypercholesterolemia from the American Heart Association.
7. 2022 American College of Cardiology Expert Consensus Decision Pathway on the Role of Nonstatin therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Evkeeza are included.

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the above diagnostic criteria can be found in the inclusion criteria for the ELIPSE HoFH trial. If the patient does not have the any of the above-mentioned genetic mutations, it is possible to approve the drug based on the patient's untreated LDL-C level. According to the guidelines published by the European Atherosclerosis Society, the diagnosis of HoFH can be assumed if the patient has an untreated LDL-C greater than 400 mg/dL and has a history of cutaneous or tendinous xanthomas before the age of 10. Alternatively, if both parents have an untreated LDL-C of at least 190 mg/dL, then the diagnosis of HoFH can also be assumed.

Currently, there is not a statin marketed in the United States FDA-approved for children under the age of seven, therefore for children between the ages of five and seven, there is no requirement for prior pharmacotherapy.

VII. REFERENCES

1. Evkeeza [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals Inc.; March 2023.
2. Raal FJ, Rosenson RS, Reeskamp LF, et al. Evinacumab for homozygous familial hypercholesterolemia. *N Engl J Med.* 2020;383:711-20.
3. 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.
4. 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:e1082– e1143.
5. McGowan MP, Hosseini Dehkordi SH, Moriarty PM, et al. Diagnosis and treatment of heterozygous familial hypercholesterolemia. *J Am Heart Assoc*. 2019;8(24):e013225.
6. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Evaluate the efficacy and safety of evinacumab in pediatric patients With homozygous familial hypercholesterolemia. Identifier: NCT04233918. Updated June 7, 2023. Accessed November 13, 2023. https://clinicaltrials.gov/ct2/show/record/NCT04233918.
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.