Original Effective Date: 04/28/2021
Current Effective Date: 11/02/2022
Last P&T Approval/Version: 07/27/2022
Next Review Due By: 07/2023
Policy Number: C21101-A

Evkeeza (evinacumab-dgnb)

PRODUCTS AFFECTED

Evkeeza (evinacumab-dgnb)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Homozygous familial hypercholesterolemia (HoFH)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review.

A. HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA (HoFH):
1. Documented diagnosis of homozygous familial hypercholesterolemia (HoFH) confirmed by clinical diagnosis based on ONE the following [DOCUMENATION REQUIRED]:
   a) Genetic evidence of functional mutation or mutation in both low-density lipoprotein receptor (LDLR) alleles OR presence of homozygous or compound heterozygous mutations in apolipoprotein B or proprotein convertase subtilisin/kexin type 9 (PCSK9) mutation

OR

b) Untreated LDL-C greater than 500mg/dL, with triglycerides less than 300 mg/dL, or treated LDL-C greater than or equal to 300 mg/dL AND documented xanthomata at less than 10 years of age

OR

c) Untreated LDL-C greater than 500mg/dL, with triglycerides less than 300 mg/dL, or treated LDL-C greater than or equal to 300 mg/dL AND both parents with documented total cholesterol greater than 250 mg/dL

AND

2. Laboratory documentation of member's current LDL-C while on background maximized treatment for HoHF [DOCUMENATION REQUIRED].
   AND
3. Documentation that member has been adherently treated (adherence defined as 85% of the time as confirmed by claims history or provider attestation) with ALL of the following used together for the previous 90 days and continues to have LDL-C greater than target goal (adults: <70 mg/dL; children < 135 mg/dL):
   a) High intensity (daily dose of atorvastatin 40 to 80 mg or rosuvastatin 20 to 40mg) or maximally tolerated statin dose, unless contraindicated*.
      *Contraindications to statins defined as one or more of the following: Hypersensitivity to statins or any component of the product, Active liver disease or CK levels (defined as >10 times the Upper Limit of Normal [ULN]), Unexplained persistent elevation of hepatic transaminases [greater than 3 times the upper limit of normal (ULN) occurring on 2 or more occasions], Women who are pregnant or may become pregnant or Breastfeeding
      NOTE: Laboratory tests showing evidence of muscle inflammation, alterations of liver function tests from baseline and/or liver damage required.
      AND
   b) Ezetimibe 10 mg daily, unless contraindicated or member has a history of intolerance
      AND
   c) For Members at least 13 years of age: PCSK9 inhibitor or LDL apheresis, unless contraindicated or member has a history of intolerance

   AND
4. Documentation that member will continue adherent treatment with maximally tolerated statin therapy and ezetimibe 10 mg daily (unless contraindicated) while treated with Evkeeza.
   AND
5. For female members of childbearing potential, provider attests that member has had a negative pregnancy screening and has been counseled to use effective contraception during treatment with Evkeeva, and for 5 months following final dose. Note: Based on animal studies, Evkeeza may cause fetal harm when administered to a pregnant member.
   AND
6. Provider attestation that member has not used or that member is on stable (i.e. dosing stable for at least 6 weeks) treatment with any of the following therapies which may affect LDL-C: systemic corticosteroids, estrogen, or testosterone.
   AND
7. Documentation that Evkeeza will not be used concomitantly with lomitapide
   AND
8. Documentation of member's current weight (within last 30 days)

CONTINUATION OF THERAPY:

A. Homozygous familial hypercholesterolemia (HoHF)

1. Laboratory documentation that member has had a positive response to therapy defined as achieving treatment goal (adults: <70 mg/dL; children < 135 mg/dL) OR at least a 50 percent reduction from baseline since treatment initiation. Note: Baseline defined as LDL-measured prior to initiation of Evkeeza while on lipid lowering therapies. [DOCUMENTATION

REQUIRED]
AND

2. Documentation that member has continued to use and will continue Evkeeza in combination with maximally tolerated statin (unless contraindicated) and ezetimibe.
AND
3. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance.
AND
4. Prescriber attest to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
5. Documentation of member's current weight (within the last 30 days)

DURATION OF APPROVAL:
Initial authorization: 6 months
Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Must be prescribed by a cardiologist, lipid specialist, or endocrinologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
12 years of age and older

QUANTITY:
15 mg/kg every 4 weeks

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Evkeeza (evinacumab-dgnb). For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Angiopoietin-like 3 (ANGPTL3) inhibitor

FDA-APPROVED USES:
Indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric members, aged 12 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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Evkeeza (evinacumab-dgnb) is a recombinant human monoclonal antibody produced from Chinese hamster ovary cell suspension culture which binds and inhibits the angiopoietin-like protein 3 (ANGPTL3). ANGPTL3 is a protein that is primarily expressed in the liver and regulated lipid metabolism through the inhibition of lipoprotein lipase and endothelial lipase. This inhibition results in a reduction in LDL-C, HDL-C and triglycerides.

Homozygous familial hypercholesteremia (HoFH) is a rare disease, with a genetic defect inherited from both parents, resulting in very high cholesterol levels. HoFH affects 1 in 300,000 people. If not treated, the very high LDL-C levels that result from this condition can result in the development of atherosclerosis before age 20.

Evkeeza was studied in the ELIPSE-HoFH (NCT03399786), which was a multicenter randomized control, placebo-controlled trial of patients (n=65) with HoFH. Patients were required to be receiving stable lipid lowering therapy. Patients were randomized 2:1 for treatment with Evkeeza or placebo, respectively. In the trial, patients were receiving background therapy with statins (94%), PCSK9 inhibitors (77%), ezetimibe (75%), lomitapide (25%) or apheresis (34%). 63 percent of the patients were taking at least 3 lipid modifying therapies. The primary trial endpoint was met, with the treated patients experiencing an average of 49% reduction in LDL-C from baseline compared to placebo. No patient discontinued treatment during the study due to an adverse event and drug antibodies did not develop during the study period.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Evkeeka (evinacumab-dgnb) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Evkeeka (evinacumab-dgnb) include a history of serious hypersensitivity reaction to evinacumab-dgnb or to any of the excipients in Evkeeza. Additionally, Evkeeza will not be authorized for the treatment of other causes of hypercholesteremia, including heterozygous familial hypercholesteremia, as the safety and efficacy have not been established in these populations.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J1305	Injection, evinacumab-dgnb, 5 mg

AVAILABLE DOSAGE FORMS:
Evkeeza 345 mg/2.3 mL (150 mg/mL) single dose vial
Evkeeza 1,200 mg/8 mL (150 mg/mL) single-dose vial

REFERENCES

1. Raal, F. J., Rosenson, R. S., Reeskamp, L. F., Hovingh, G. K., Kastelein, J., Rubba, P., Ali, S., Banerjee, P., Chan, K. C., Gipe, D. A., Khilla, N., Pordy, R., Weinreich, D. M., Yancopoulos, G. D., Zhang, Y., Gaudet, D., & ELIPSE HoFH Investigators (2020). Evinacumab for Homozygous Familial Hypercholesterolemia. *The New England journal of medicine*, *383*(8), 711–720. https://doi.org/10.1056/NEJMoa2004215
2. EVKEEZA Prescribing Information. Tarrytown, NY: Regeneron Pharmaceuticals; February 2021.
3. Cuchel, M., Bruckert, E., Ginsberg, H. N., Raal, F. J., Santos, R. D., Hegele, R. A., Kuivenhoven, J. A., Nordestgaard, B. G., Descamps, O. S., Steinhagen-Thiessen, E., Tybjærg-Hansen, A., Watts, G. F., Averna, M., Boileau, C., Borén, J., Catapano, A. L., Defesche, J. C., Hovingh, G. K., Humphries, S. E., Kovanen, P. T., … European Atherosclerosis Society Consensus Panel on Familial Hypercholesterolaemia (2014). Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. *European heart journal*, *35*(32), 2146–2157. https://doi.org/10.1093/eurheartj/ehu274
4. David T W Lui, Alan C H Lee, Kathryn C B Tan, Management of Familial Hypercholesterolemia: Current Status and Future Perspectives, Journal of the Endocrine Society, Volume 5, Issue 1, January 2021, bvaa122, https://doi.org/10.1210/jendso/bvaa122

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file