Medical Policy:

Evkeeza® (evinacumab-dgnb) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.336	April 9, 2025	June 9, 2021

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines 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. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Evinacumab-dgnb is a recombinant human IgG4 isotype monoclonal antibody that binds to and inhibits angiopoietin-like protein 3 (ANGPTL3), a regulatory protein that plays a role in lipid metabolism through inhibition of lipoprotein lipase (LPL) and endothelial lipase (EL). Inhibition of ANGPTL3 leads to reductions in LDL-C, HDL-C, and triglycerides (TG). Evinacumab-dgnb reduces LDL-C independent of the presence of LDL receptor (LDLR) by promoting very low-density lipoprotein (VLDL) processing and clearance upstream of LDL formation. Evinacumab-dgnb blockade of ANGPTL3 lowers TG and HDL-C by rescuing LPL and EL activities, respectively.

Length of Authorization

Coverage is provided for 12 months and may be renewed.

Dosing Limits [Medical Benefit]

The recommended dosage is 15 mg/kg every 4 weeks

Max Units (per dose and over time) [HCPCS Unit]:

345 billable units (1725 mg) every 28 days

Guideline

I. **INITIAL APPROVAL CRITERIA**

1. **Homozygous Familial Hypercholesterolemia.** Coverage is provided if the patient meets the following criteria (A, B, C and D):
   A. Patient is ≥ 5 years of age; **AND**
   B. Patient meets one of the following (i, ii or iii):
      i. Patient has phenotypic confirmation of homozygous familial hypercholesterolemia; **OR**
      Note: Examples include pathogenic variants at the low-density lipoprotein receptor (LDLR), apolipoprotein B (apo B), proprotein convertase subtilisin kexin type 9 (PCSK9), or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene.
      ii. Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level greater than 400 mg/dL **AND** meets one of the following (a or b):
      Note: Untreated refers to prior to therapy with any antihyperlipidemic agent.
         a. Patient had clinical manifestations of homozygous familial hypercholesterolemia (HoFH) before the age of 10 years **OR**
         Note: Clinical manifestations of HoFH are cutaneous xanthomas, tendon xanthomas, acrus cornea, tuberous xanthomas, or xanthelasma.
         b. 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 untreated LDL-C level greater than or equal to 190 mg/dL and/or an untreated total cholesterol level greater than 250 mg/dL.
      iii. Patient has a treated low-density lipoprotein cholesterol (LDL-C) level greater than or equal to 300 mg/dL AND meets one of the following (a or b):
      Note: Treated refers to after therapy with at least one antihyperlipidemic agent.
         a. Patient had clinical manifestations of homozygous familial hypercholesterolemia (HoFH) before the age of 10 years **OR**
         Note: Examples of clinical manifestations of HoFH are cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas or xanthelasma.
         b. 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 would be if both had an untreated LDL-C greater than or equal to 190 mg/dL and/or an untreated total cholesterol greater than 250 mg/dL.
   C. Patient meets one of the following criteria (i or ii):
      i. Patient meets all of the following criteria (a, b and c):
         a. Patient has tried one high-intensity statin therapy (i.e., atorvastatin greater than or equal to 40 mg daily, rosuvastatin tablets greater than or equal to 20 mg daily [as a single-entity or as a combination product]) **AND**
         b. Patient has tried one high-intensity statin along with ezetimibe (as a single entity or as a combination product) for ≥ 8 continuous weeks; **AND**
         c. The low-density lipoprotein cholesterol (LDL-C) level after this treatment regimen remains greater than or equal to 70 mg/dL **OR**
      ii. Patient has been determined to be statin intolerant by meeting one of the following criteria (a or b):
         a. 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 greater than or equal to 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine])
         OR
         b. Patient meets all of the following criteria [1, 2, and 3]:
            1. Patient experienced skeletal-related muscle symptoms **AND**

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

2. The skeletal-related muscle symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) **AND**
3. When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin) **AND**

Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

D. Patient meets one of the following (i, ii, or iii):
   i. Patient meets both of the following (a and b):
      a. Patient has tried a proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor for greater than or equal to 8 continuous weeks **AND**
      b. The low-density lipoprotein cholesterol (LDL-C) level after this PCSK9 inhibitor therapy remains greater than or equal to 70 mg/dL **OR**
   ii. Patient is known to have two LDL-receptor negative alleles; **OR**
   iii. Patient is 5 to 9 years of age

II. RENEWAL CRITERIA

Coverage can be renewed based on the following criteria:

1. Absence of unacceptable toxicity from the drug.
2. Clinically significant LDL-C reduction has been shown with the treatment

Applicable Procedure Codes

Code	Description
J1305	Injection, evinacumab-dgnb, 5 mg

Applicable NDCs

Code	Description
61755-0013-01	Evkeeza Single-Dose Vial for Intravenous Infusion 345 mg/2.3 mL (150 mg/mL)
61755-0010-01	Evkeeza Single-Dose Vial for Intravenous Infusion 1200 mg/8 mL (150 mg/mL)

ICD-10 Diagnoses

Code	Description
E78.01	Familial/hereditary hypercholesterolemia

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	04/09/2025	Annual Review: Updated ICD-10 and dosing limits. Initial Criteria: Reworded the following: " Patient has had genetic confirmation of two mutant alleles at the low-density lipoprotein receptor (LDLR), apolipoprotein B (apo B), proprotein convertase subtilisin kexin type 9 (PCSK9) or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene locus OR" as: " Patient has phenotypic confirmation of homozygous familial hypercholesterolemia; OR *Note: Examples include pathogenic variants at the low-density lipoprotein receptor (LDLR),*

		apolipoprotein B (apo B), proprotein convertase subtilisin kexin type 9 (PCSK9), or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene." Updated the following from 500 to 400: "Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level greater than 400 mg/dL" Updated the following from "both parents" to "at least one parent" and removed "heterozygous" in both instances: "AND meets one of the following At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with" familial hypercholesterolemia"
EmblemHealth & ConnectiCare	3/12/2024	Annual Review: Added Max Units, no criteria changes
EmblemHealth & ConnectiCare	7/03/2023	Annual Review: Homozygous Familial Hypercholesterolemia. Initial Criteria: added "A. Patient is > 5 years of age; AND" and "C. i. b. Patient has tried one high-intensity statin along with ezetimibe (as a single entity or as a combination product) for ≥ 8 continuous weeks; **AND"** Added "D. Patient is 5 to 9 years of age; **AND"** Added ICD-10 Code: E78.00
EmblemHealth & ConnectiCare	6/14/2022	Transferred policy to new template, updated procedure code from C9079 to J1305
EmblemHealth & ConnectiCare	6/9/2021	New Policy

References

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3. Lloyd-Jones DM, Morris PB, Ballantyne CM, Birtcher KK, Daly DD Jr, DePalma SM, Minissian MB, Orringer CE, Smith SC Jr. 2017 Focused Update of the 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. J Am Coll Cardiol. 2017 Oct 3;70(14):1785-1822. doi: 10.1016/j.jacc.2017.07.745. Epub 2017 Sep 5. PMID: 28886926.
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5. Rosenson RS, Baker SK, Jacobson TA, et al. An assessment by the statin muscle safety task force: 2014 update. J Clin Lipidol. 2014;8:S58-S71. 6. Guyton JR, Bays HE, Grundy SM, Jacobson TA. An assessment by the Statin Intolerance Panel: 2014 update. J Clin Lipidol. 2014;8:S72-S81.