Medical Policy:

Leqvio® (inclisiran) subcutaneous injection

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.348	May 3, 2024	February 10, 2022

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

Leqvio®, a small interfering ribonucleic acid (RNA) directed to proprotein convertase subtilisin kexin type 9 (PCSK9) messenger RNA, is indicated as an adjunct to diet and maximally tolerated stating therapy for the treatment of adults with the following:

1. Clinical atherosclerotic cardiovascular disease (ASCVD) for those who require additional lowering of low-density lipoprotein cholesterol (LDL-C).
2. Heterozygous familial hypercholesterolemia (HeFH) for those who require additional lowering of LDL-C.
3. Primary Hyperlipidemia

The effect of Leqvio on cardiovascular (CV) morbidity and mortality have not been established. The safety and effectiveness have not been established in pediatric patients.

Length of Authorization

Coverage is provided for 12 months and may be renewed

Dosing Limits [Medical Benefit]

Approve the following dosage regimens (1 **or** 2):

1. Initial dose is 284 mg given as a single subcutaneous injection, again at 3 months, and then once every 6 months; **OR**
2. Maintenance dose is 284 mg given as a subcutaneous injection once every 6 months.

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

• 284 billable units (284 mg) at months 0, 3 and then every 6 months

Guideline

I. INITIAL APPROVAL CRITERIA

1. **Atherosclerotic Cardiovascular Disease.** Approve if the patient meets the following criteria (A, B, C **and** D):
   A. Patient is ≥ 18 years of age; **AND**
   B. Patient has had one of the following conditions or diagnoses (i, ii, iii, iv, v or vi):
      i. A previous myocardial infarction or a history of an acute coronary syndrome; **OR**
      ii. Angina (stable or unstable); **OR**
      iii. A past history of stroke or transient ischemic attack; **OR**
      iv. Coronary artery disease; **OR**
      v. Peripheral arterial disease; **OR**
      vi. Patient has undergone a coronary or other arterial revascularization procedure in the past; **AND**

      Note: Examples include coronary artery bypass graft surgery, percutaneous coronary intervention, angioplasty, and coronary stent procedures.
   C. Patient meets one of the following criteria (i **or** ii):
      i. Patient meets all of the following (a, b **and** c):
         a. 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**
         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. Low-density lipoprotein cholesterol level after this treatment regimen remains ≥ 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 ≥ 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 [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).

               Note: Examples of skeletal muscle symptoms include myopathy or myalgia.
   D. 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.

2. **Heterozygous Familial Hypercholesterolemia (HeFH).** Approve if the patient meets the following criteria (A, B, C **and** D):

A. Patient is ≥ 18 years of age; **AND**

B. Patient meets one of the following criteria (i, ii, **or** iii):
   i. Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level ≥ 190 mg/dL (prior to treatment with antihyperlipidemic agents); **OR**
   ii. Patient has genetic confirmation of heterozygous familial hypercholesterolemia by mutations in the low-density lipoprotein receptor, apolipoprotein B, proprotein convertase subtilisin kexin type 9, or low-density lipoprotein receptor adaptor protein 1 gene; **OR**
   iii. Patient has been diagnosed with heterozygous familial hypercholesterolemia meeting one of the following diagnostic criteria thresholds (a **or** b):
      a. Patient meets both of the following [1 **and** 2]:
         1. Prescriber used the Dutch Lipid Network criteria to diagnose heterozygous familial hypercholesterolemia; **AND**
         2. Patient had a score > 5; **OR**
      b. Patient meets both of the following [1 **and** 2]:
         1. Prescriber used the Simon Broome criteria to diagnose heterozygous familial hypercholesterolemia; **AND**
         2. Patient met the threshold for "definite" or "possible (or probable)" familial hypercholesterolemia; **AND**

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 ≥ 40 mg daily; rosuvastatin ≥ 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. LDL-C level after this treatment regimen remains ≥ 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 ≥ 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 [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 muscle-related 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).

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

D. 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.

3. **Primary Hyperlipidemia**

Note: This is not associated with atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH) and may be referred to as combined hyperlipidemia, hypercholesterolemia (pure, primary), dyslipidemia, or increased/elevated low-density lipoprotein cholesterol (LDL-C) levels.

Approve if the patient meets all of the following (A, B, C, and D):

A. Patient is ≥ 18 years of age; **AND**
B. Patient has a coronary artery calcium or calcification score ≥ 300 Agatston units; **AND**
C. Patient meets one of the following (i. or ii):
    i. Patient meets all of the following [a, b, and c]:
        a. 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**
        b. Patient has tried the one high-intensity statin therapy above along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks; **AND**
        c. LDL-C level after this treatment regimen remains ≥ 100 mg/dL; **OR**
    ii. Patient has been determined to be statin intolerant by meeting one of the following [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 ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).
        b. Patient meets all of the following [a), b), and c)]:
            a) 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).
            b) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); **AND**
            c) 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. 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

RENEWAL CRITERIA

1. Member has responded positively to the treatment as determined by the prescribing physician; **AND**
2. Member has not experienced unacceptable toxicity from the drug.

Limitations/Exclusions:

1. Concurrent use of Leqvio with Repatha (evolocumab subcutaneous injection) or Praluent (alirocumab subcutaneous injection).

Applicable Procedure Codes

Code	Description
J1306	Injection, inclisiran, 1 mg
96372	Therapeutic, prophylactic or diagnostic injection; subcutaneous or intramuscular

Applicable NDCs

Code	Description
00078-1000-60	Leqvio 284mg/1.5mL Solution Prefilled Syringe

ICD-10 Diagnoses

Code	Description
E78.0	Pure hypercholesterolemia
E78.00	Pure hypercholesterolemia unspecified
E78.01	Familial Hypercholesterolemia
E78.2	Mixed hyperlipidemia
E78.4	Other hyperlipidemia
E78.5	Hyperlipidemia, unspecified
I21	Acute myocardial infarction
I21.0	ST elevation (STEMI) myocardial infarction of anterior wall
I21.1	ST elevation (STEMI) myocardial infarction of inferior wall
I21.2	ST elevation (STEMI) myocardial infarction of other sites
I21.9	Acute myocardial infarction, unspecified
I21.A9	Other myocardial infarction type

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	5/3/2024	Annual Review: Updated dosing limits, Initial Criteria: Atherosclerotic Cardiovascular Disease. Added: " Coronary artery disease; OR"
EmblemHealth & ConnectiCare	10/27/2023	Update: Added Primary Hyperlipidemia indication and criteria
EmblemHealth & ConnectiCare	6/12/2023	Annual Review: removed code: E78.0 Added codes: E78.2, E78.4, E78.5, I21, I21.0, I21.1, I21.2, I21.9, I21.A9
EmblemHealth & ConnectiCare	09/06/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	2/10/2022	New Policy

References

1. Leqvio® subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis; December 2021.