

Leqvio® (inclisiran) (Subcutaneous)

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I. Length of Authorization

Coverage is provided for 6 months for initial approval and may be renewed every 12 months.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Leqvio 284 mg/1.5 mL single-dose pre-filled syringe: 1 syringe at month 0 and 3 initially then every 6 months thereafter

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

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

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

Patient must try and have an inadequate response, contraindication, or intolerance to at least a three (3) month trial of Repatha (evolocumab); **OR**

Patient is continuing treatment

- Patient is at least 18 years of age; **AND**
- Baseline low-density lipoprotein cholesterol (LDL-C) labs have been obtained prior to initiating treatment (required for renewal); **AND**

Universal Criteria ¹

- Patient is not on concomitant treatment with PCSK9- or ANGPTL3- inhibitors (i.e., alirocumab, evolocumab, evinacumab, etc.); **AND**
- Must be prescribed by, or in consultation with, a specialist in cardiology, lipidology, or endocrinology; **AND**
- Therapy will be used in conjunction with diet and/or other lipid-lowering therapies, unless the patient is unable to tolerate (e.g., statins, ezetimibe); **AND**

Primary Hyperlipidemia † 1,3,9,12-22

- Patient has prior treatment history with the highest available age-appropriate dose or maximally-tolerated dose* of high intensity HMG-CoA reductase inhibitors (i.e., ‘statin’ therapy: atorvastatin 40 mg or 80 mg daily, rosuvastatin 20 mg or 40 mg daily, or simvastatin 80 mg daily), unless contraindicated; **AND**
- Patient has failed to reach a target LDL-C despite physician attestation that the patient is adherent to maximally-tolerated doses* of statins prior to the lipid panel demonstrating suboptimal reduction; **AND**
 - Patient has a diagnosis of atherosclerotic cardiovascular disease (ASCVD) (i.e., coronary heart disease [myocardial infarction, angina pectoris], cerebrovascular disease [non-hemorrhagic stroke, transient ischemic attack], peripheral arterial disease, aortic atherosclerosis); **OR**
 - Patient is at increased risk for ASCVD as classified by ONE of the following risk groups:
 - Extremely high risk ASCVD (defined as extensive burden of or active ASCVD, or ASCVD with extremely high burden of adverse poorly controlled cardiometabolic risk factors including HeFH or severe hypercholesterolemia (SH) with untreated LDL-C ≥ 220 mg/dL) with LDL-C ≥ 70 mg/dL
 - Very high risk ASCVD (defined as less extensive ASCVD and poorly controlled cardiometabolic risk factors) with LDL-C ≥ 100 mg/dL
 - High risk ASCVD with LDL-C ≥ 130 mg/dL; **AND**
 - Less extensive ASCVD and well-controlled cardiometabolic risk factors; **OR**
 - SH with untreated LDL-C ≥ 220 mg/dL with poorly controlled cardiometabolic risk factors; **OR**
 - Patient has a diagnosis of Heterozygous Familial Hypercholesterolemia (HeFH) and ONE of the following:
 - Positive genetic testing to confirm mutation in the *LDLR*, *apoB*, or *PCSK9* gene(s)
 - History of LDL-C greater than 190 mg/dL (greater than 4.9 mmol/L)
 - Patient has clinical manifestations of HeFH (e.g., cutaneous xanthomas, tendon xanthomas, arcus cornea)
 - Probable or definite diagnosis of HeFH according to Simon Broome diagnostic criteria§
 - Probable or definite diagnosis of HeFH according to the Dutch Lipid Clinic diagnostic criteria¥

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓞ Orphan Drug

*If the patient is not able to use a maximum dose of atorvastatin or rosuvastatin due to muscle symptoms, a causal relationship must be established between statin use and muscle symptoms.

- Patient has evidence of pain, tenderness, stiffness, cramping, weakness, and/or fatigue and all of the following:
 - Muscle symptoms resolve after discontinuation of statin; **AND**
 - Muscle symptoms occurred when re-challenged at a lower dose of the same statin; **AND**
 - Muscle symptoms occurred after switching to an alternative statin; **AND**
 - Non-statin causes of muscle symptoms (e.g., hypothyroidism, reduced renal function, reduced hepatic function, rheumatologic disorders, such as polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, or primary muscle disease) have been ruled-out; **OR**
- The patient has been diagnosed with rhabdomyolysis associated with statin use; **AND**
 - The diagnosis should be supported by acute neuromuscular illness or dark urine **AND** an acute elevation in creatine kinase (usually > 5,000 IU/L or 5 times the upper limit of normal [ULN])

§ Simon Broome diagnostic criteria for HeFH ^{3,15,21}

Criteria	Description
<i>a</i>	Total cholesterol concentration above 7.5 mmol/liter (290 mg/dL) in adults; OR Low-density lipoprotein cholesterol concentration above 4.9 mmol/liter (189 mg/dL) in adults
<i>b</i>	Tendinous xanthomata in the patient or a first-degree relative
<i>c</i>	DNA-based evidence of mutation in the LDLR, PCSK9, or APOB gene
<i>d</i>	Family history of myocardial infarction before age 50 years in a second-degree relative or before age 60 years in a first-degree relative
<i>e</i>	Family history of raised total cholesterol concentration above 7.5 mmol/liter (290 mg/dL) in a first- or second-degree relative

NOTE: A "definite" FH diagnosis requires either criteria a and b, or criterion c. A "probable" FH diagnosis requires either criteria a and d, or criteria a and e.

¥ Dutch Lipid Clinic network diagnostic criteria for HeFH ^{3,22}

Criteria	Points
<u>Family history:</u>	
– First-degree relative with known premature (men: <55 years; women: <60 years) coronary or vascular disease	1
– First-degree relative with known LDL-C above the 95th percentile	1
– First-degree relative with tendinous xanthomata and/or arcus cornealis	2
<u>Clinical history:</u>	
– Patient with premature (men: <55 years; women: <60 years) coronary artery disease	2
– Patient with premature (men: <55 years; women: <60 years) cerebral or peripheral vascular disease	1
<u>Physical examination:</u>	
– Tendinous xanthomata	6
– Arcus cornealis before age 45 years	4
<u>LCL-C levels:</u>	
– LDL-C ≥8.5 mmol/L (325 mg/dL)	8
– LDL-C 6.5 to 8.4 mmol/L (251-325 mg/dL)	5

– LCL-C 5 to 6.4 mmol/L (191-250 mg/dL)	3
– LCL-C 4 to 4.9 mmol/L (155-190 mg/dL)	1
DNA analysis:	
– Functional mutation in the LDLR, apoB, or PCSK9 gene	8
<p>NOTE: Choose only one score per group, the highest applicable diagnosis (diagnosis is based on the total number of points obtained)</p> <ul style="list-style-type: none"> • A "definite" FH diagnosis requires >8 points • A "probable" FH diagnosis requires 6 to 8 points • A "possible" FH diagnosis requires 3 to 5 points 	

IV. Renewal Criteria ^{1,9,13,19}

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from therapy. Examples of unacceptable toxicity include: severe injection site reactions, etc.; **AND**
- Patient has had a reduction in LDL-C when compared to the baseline labs (prior to initiating inclisiran)

V. Dosage/Administration ¹

Indication	Dose
Primary Hyperlipidemia	Administer 284 mg as a subcutaneous injection (in combination with maximally tolerated statin therapy) initially, again at 3 months, and then every 6 months.
<p>– Assess LDL-C when clinically indicated. The LDL-lowering effect of Leqvio may be measured as early as 30 days after initiation and anytime thereafter without regard to timing of the dose.</p> <p>– Leqvio should be administered by a healthcare professional.</p> <p>– Inject Leqvio subcutaneously into the abdomen, upper arm, or thigh. Do not inject in areas of active skin disease or injury, such as sunburns, skin rashes, inflammation, or skin infections.</p>	

VI. Billing Code/Availability Information

HCPCS Code:

- J1306 – Injection, inclisiran, 1 mg; 1 billable unit = 1 mg

NDC(s):

- Leqvio 284 mg/1.5 mL single-dose prefilled syringe: 00078-1000-xx

VII. References

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC