Leqvio® (inclisiran)
(Subcutaneous)

Document Number: OHSU HEALTHSERVICES-0652

Last Review Date: 08/05/2025
Date of Origin: 02/01/2022
Dates Reviewed: 02/2022, 07/2022, 04/2023, 08/2023, 04/2024, 08/2025

I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months.
- Renewal: Prior authorization validity may be renewed every 12 months thereafter.

II. Dosing Limits

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 exercise; **AND**

Primary Hypercholesterolemia † [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 OR rosuvastatin 20 mg or 40 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 $\geq$220 mg/dL) with LDL-C $\geq$70 mg/dL
    - Very high risk ASCVD (defined as less extensive ASCVD and poorly controlled cardiometabolic risk factors) with LDL-C $\geq$100 mg/dL
    - High risk ASCVD with LDL-C $\geq$130 mg/dL; **AND**
      - Less extensive ASCVD and well-controlled cardiometabolic risk factors; **OR**
      - SH with untreated LDL-C $\geq$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); **Φ** 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
a	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
b	Tendinous xanthomata in the patient or a first-degree relative
c	DNA-based evidence of mutation in the LDLR, PCSK9, or APOB gene
d	Family history of myocardial infarction before age 50 years in a second-degree relative or before age 60 years in a first-degree relative
e	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
Family history:	
– 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
Clinical history:	
– 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
Physical examination:	
– Tendinous xanthomata	6
– Arcus cornealis before age 45 years	4
LCL-C levels:	
– 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) – LCL-C 4 to 4.9 mmol/L (155-190 mg/dL)	3 1
DNA analysis: – Functional mutation in the LDLR, apoB, or PCSK9 gene	8
NOTE: Choose only one score per group, the highest applicable diagnosis (diagnosis is based on the total number of points obtained) • 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, severe hypersensitivity 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 Hypercholesterolemia	Administer 284 mg as a subcutaneous injection initially, again at 3 months, and then every 6 months.
– *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.* – *Leqvio should be administered by a healthcare professional.* – *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.*	

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

1. Leqvio [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; July 2025. Accessed August 2025.
2. Mozaffarian D, et al. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. Circulation. 2015 Jan 27;131(4):e29-322. doi: 10.1161/CIR.0000000000000152. Epub 2014 Dec 17.
3. Rosenson RS, Durrington P. (2025) Familial hypercholesterolemia in adults: Overview. In: Freeman MW, Botkin NF(Eds). *UpToDate.* Last updated: Apr 14, 2025. Accessed June 26, 2025. Available from: https://www.uptodate.com/contents/familial-hypercholesterolemia-in-adults-overview.
4. Ferranti et al. What is the prevalence of familial hypercholesterolemia in the US? AHA 2014; 130(A19656).
5. Stone NJ, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation, 2014; 129(25 Suppl 2): S1–45.
6. Jacobson et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1 – executive summary. Journal of Clinical Lipidology. 2014. Available at: http://www.sciencedirect.com/science/article/pii/S1933287414002748. Accessed July 29, 2015.
7. Cannon CP. Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. N Engl J Med 2015; 372:2387–2397. doi: 10.1056/NEJMoa1410489.
8. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 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.
9. Grundy SM, Stone NJ, Bailey AL, et al. 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. 2018;000:e1–e120. DOI: 10.1161/CIR.0000000000000625.
10. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1 – executive summary. Journal of Clinical Lipidology. 2014:8(5):473–488. DOI: 10.1016/j.jacl.2014.07.007.
11. Jacobson TA, Maki KC, Orringer C, et al. National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia: Part 2. J Clin Lipidol. 2015 Nov-Dec;9(6 Suppl):S1-122.e1. doi: 10.1016/j.jacl.2015.09.002.

12. Robinson JG, Jayanna MB, Brown AS, et al. Enhancing the Value of PCSK9 Monoclonal Antibodies by Identifying Patients Most Likely to Benefit, Journal of Clinical Lipidology (2019), doi: https://doi.org/10.1016/j.jacl.2019.05.005
13. Rosenson RS, Baker SK, Jacobson TA, et al, The National Lipid Association's Muscle Safety Expert Panel. An assessment by the Statin Muscle Safety Task Force: 2014 update. J Clin Lipidol. 2014 May-Jun;8(3 Suppl):S58-71. doi: 10.1016/j.jacl.2014.03.004.
14. Orringer, CE, Jacobson TA, Saseen JJ, et al. Update on the use of PCSK9 inhibitors in adults: Recommendations from an Expert Panel of the National Lipid Association. Journal of Clinical Lipidology. 2017, Vol: 11, Issue: 4, Page: 880-890.
15. Al-Rasadi K, Al-Waili K, Al-Sabti HA, et al. Criteria for Diagnosis of Familial Hypercholesterolemia: A Comprehensive Analysis of the Different Guidelines, Appraising their Suitability in the Omani Arab Population. Oman Med J. 2014;29(2):85-91. doi:10.5001/omj.2014.22.
16. Raal FJ, Kallend D, Ray KK, et al; ORION-9 Investigators. Inclisiran for the Treatment of Heterozygous Familial Hypercholesterolemia. N Engl J Med. 2020 Apr 16;382(16):1520-1530. doi: 10.1056/NEJMoa1913805. Epub 2020 Mar 18.
17. Ray KK, Wright RS, Kallend D, et al; ORION-10 and ORION-11 Investigators. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol. N Engl J Med. 2020 Apr 16;382(16):1507-1519. doi: 10.1056/NEJMoa1912387. Epub 2020 Mar 18.
18. 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 Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2022 Oct 4;80(14):1366-1418. doi: 10.1016/j.jacc.2022.07.006.
19. Mach, F, Baigent C, Catapano A et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS), *European Heart Journal*, Volume 41, Issue 1, 1 January 2020, Pages 111–188, https://doi.org/10.1093/eurheartj/ehz455
20. Orringer CE, Jacobson TA, Saseen JJ, et al. Update on the use of PCSK9 inhibitors in adults: Recommendations from an Expert Panel of the National Lipid Association. J Clin Lipidol. 2017 Jul-Aug;11(4):880-890. doi: 10.1016/j.jacl.2017.05.001. Epub 2017 May 19. PMID: 28532784.
21. National Collaborating Centre for Primary Care (UK). Identification and Management of Familial Hypercholesterolaemia (FH) [Internet]. London: Royal College of General Practitioners (UK); 2008 Aug. (NICE Clinical Guidelines, No. 71.) Appendix F, Simon Broome Diagnostic criteria for index individuals and relatives. Available from: https://www.ncbi.nlm.nih.gov/books/NBK53810/
22. WHO Human Genetics Programme. (1999). Familial hypercholesterolaemia (FH) : report of a second WHO consultation, Geneva, 4 September 1998. World Health Organization.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E75.5	Other lipid storage disorders
E78.00	Pure Hypercholesterolemia, unspecified
E78.01	Familial hypercholesterolemia
E78.2	Mixed hyperlipidemia
E78.4	Other hyperlipidemia
E78.49	Other hyperlipidemia, familial combined hyperlipidemia
E78.5	Hyperlipidemia, unspecified

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
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)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
15	KY, OH	CGS Administrators, LLC