Leqvio® (inclisiran)
(Subcutaneous)

Document Number: IC-0652

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I. Length of Authorization

Coverage is provided for six 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-use 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 mg at months 0, 3 and then every 6 months

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient is not on concomitant 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**

Heterozygous Familial Hypercholesterolemia (HeFH)/Atherosclerotic Cardiovascular Disease (ASCVD) † [1,12-14,16,21-24,26,27]

- Therapy will be used in conjunction with diet alone or in conjunction with other lipid-lowering therapies unless the patient is unable to tolerate (e.g., statins, ezetimibe); **AND**
    - Patient has a diagnosis of atherosclerotic cardiovascular disease (ASCVD) (i.e., myocardial infarction, non-hemorrhagic stroke, or peripheral arterial disease) or ASCVD risk; **AND**
        - Patient can be classified into ONE of the following risk factor groups:

- Extremely high risk ASCVD (defined as extensive burden of or active ASCVD, or ASCVD with extremely high burden of adverse poorly controlled risk 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 risk factors; **OR**
  - SH with untreated LDL-C ≥220 mg/dL with poorly controlled risk factors; **AND**

- Patient has a prior treatment history with the highest available 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; **OR**

- Patient has a diagnosis of Heterozygous Familial Hypercholesterolemia (HeFH) as confirmed by genotyping OR by patient having a first-degree relative similarly affected or with premature coronary vascular disease (CVD) or with positive genetic testing for a LDL-C raising gene defect (LDL receptor, apoB, or PCSK9); **AND**
  - 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**
  - Used as one of the following:
    - For primary prevention (i.e., patients without ASCVD) and LDL-C ≥100 mg/dL; **OR**
    - For secondary prevention (i.e., patients with ASCVD) and LDL-C ≥70 mg/dL

† 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
  - 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])

IV. Renewal Criteria[1,12-16,21-27]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet 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 including severe injection site reactions, etc.; **AND**
- Patient has had a reduction in LDL-C when compared to the baseline labs (prior to initiating inclisiran); **AND**
- Patient continues to adhere to diet and/or lipid lowering therapy established prior to the original inclisiran approval

V. Dosage/Administration [1]

Indication	Dose
Established cardiovascular disease or primary hyperlipidemia (including heterozygous familial hypercholesterolemia [HeFH])	Administer subcutaneously, in combination with maximally tolerated statin therapy, 284 mg as a single 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:

- J3490 – Unclassified drugs
- C9399 – Unclassified drugs or biologics, *(Hospital Outpatient Use Only)*

NDC(s):

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

VII. References

1. Leqvio [package insert]. East Hanover, NJ; Novartis, Inc.; December 2021. Accessed December 2021.

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the National Lipid Association. J Clin Lipidol, 13 (4), 525-537; Jul-Aug 2019. PMID: 31281070. DOI: 10.1016/j.jacl.2019.05.005

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15. 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.
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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)

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

Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered 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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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