

Leqvio® (inclisiran subcutaneous injection)

When requesting Leqvio® (inclisiran), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-Approved Indications

Leqvio is indicated as an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in:

- adults with hypercholesterolemia.
- adults and pediatric patients aged 12 years and older with heterozygous familial hypercholesterolemia (HeFH).
- pediatric patients aged 12 years and older with homozygous familial hypercholesterolemia (HoFH).

Approved Off-Label Compendial Use

Established cardiovascular disease

Coverage Guidelines

Heterozygous Familial Hypercholesterolemia (HeFH)

The individual must meet all of the following criteria for initial authorization:

- Is 12 years of age or older;
- Meets one of the following:
 - o Has an untreated low-density lipoprotein cholesterol (LDL-C) $\geq$ 190 mg/dL (i.e., prior to treatment with any antihyperlipidemic agents); OR
 - o If the patient is between 12 and 17 years of age with an untreated LDL-C $\geq$ 160 mg/dL but $<$ 190 mg/dL, must have a family history of early atherosclerotic cardiovascular disease (ASCVD) or elevated LDL-C or total cholesterol in a parent; OR
 - o The diagnosis has been confirmed by genetic testing (e.g., pathogenic variants at the low-density lipoprotein receptor [LDLR], apolipoprotein B [APOB], proprotein convertase subtilisin kexin type 9 [PCSK9], or low-density lipoprotein receptor adaptor protein 1 [LDLRAP1] gene); OR
 - o Has been diagnosed with HeFH by meeting one of the following diagnostic criteria thresholds:
 - Dutch Lipid Network criteria score greater than 5; OR

- Simon Broome criteria met the threshold for 'definite' or 'possible (or probable)' familial hypercholesterolemia;
- Meets one of the following:
 - o Has tried one high-intensity statin therapy (i.e., atorvastatin $\geq$ 40 mg daily; rosuvastatin $\geq$ 20 mg daily [as a single-entity or as a combination product]) for $\geq$ 8 continuous weeks AND LDL-C level still remains $\geq$ 70 mg/dL; OR
 - o Has experienced statin-related rhabdomyolysis (*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 $\geq$ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]);* OR
 - o Has experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) while receiving separate trials of both atorvastatin and rosuvastatin (as single entity or combination products) and skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin).

Homozygous Familial Hypercholesterolemia (HoFH)

The individual must meet all of the following criteria for initial authorization:

- Is $\geq$ 12 years of age and $<$ 18 years of age;
- Meets one of the following:
 - o The diagnosis has been confirmed by genetic testing (e.g., pathogenic variants at the low-density lipoprotein receptor [LDLR], apolipoprotein B [APOB], proprotein convertase subtilisin kexin type 9 [PCSK9], or low-density lipoprotein receptor adaptor protein 1 [LDLRAP1] gene); OR
 - o Has an untreated low-density lipoprotein cholesterol (LDL-C) $>$ 400 mg/dL (i.e., prior to treatment with any antihyperlipidemic agent) OR has a treated LDL-C level $\geq$ 300 mg/dL (i.e., after therapy with at least one antihyperlipidemic agent) AND meets one of the following:
 - Had clinical manifestation of HoFH before 10 years of age (e.g., cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas, or xanthelasma); OR
 - At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with familial hypercholesterolemia (*Note: an example of familial hypercholesterolemia is an untreated LDL-C $\geq$ 190 mg/dL and/or an untreated total cholesterol $>$ 250 mg/dL;*
- Meets one of the following:
 - o Has tried one high-intensity statin therapy (i.e., atorvastatin $\geq$ 40 mg daily; rosuvastatin $\geq$ 20 mg daily [as a single-entity or as a combination product]) for $\geq$ 8 continuous weeks AND LDL-C level still remains $\geq$ 70 mg/dL; OR

- o Has experienced statin-related rhabdomyolysis (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 [≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR
- o Has experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) while receiving separate trials of both atorvastatin and rosuvastatin (as single entity or combination products) and skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin).

Hypercholesterolemia

The individual must meet all of the following criteria for initial authorization:

- Is 18 years of age or older;
- Meets one of the following:
 - o Is at elevated risk for atherosclerotic cardiovascular disease (ASCVD), an ASCVD event, or a major adverse cardiovascular event; OR
 - o Has diabetes;
- Meets one of the following:
 - o 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 LDL-C level still remains ≥ 70 mg/dL; OR
 - o Has experienced statin-related rhabdomyolysis (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 [≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR
 - o Has experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) while receiving separate trials of both atorvastatin and rosuvastatin (as single entity or combination products) and skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin).

Established Cardiovascular Disease

The individual must meet all of the following criteria for initial approval:

- Is 18 years of age or older;
- Has had one of the following conditions or diagnoses:

- o A previous myocardial infarction or a history of an acute coronary syndrome; OR
- o Angina (stable or unstable); OR
- o A past history of stroke or transient ischemic attack; OR
- o Coronary artery disease; OR
- o Peripheral arterial disease; OR
- o Has undergone a coronary or other arterial revascularization procedure in the past (e.g., coronary artery bypass graft surgery, percutaneous coronary intervention, angioplasty, and coronary stent procedure);
- Meets ONE of the following:
 - o Has tried one high-intensity statin therapy (i.e., atorvastatin $\geq$ 40 mg daily or rosuvastatin $\geq$ 20 mg daily [as a single entity or as a combination product]) for $\geq$ 8 continuous weeks AND LDL-C level still remains $\geq$ 55 mg/dL;
 - o Has experienced statin-related rhabdomyolysis (*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 [$a \geq 0.5$ mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR
 - o Has experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) while receiving separate trials of both atorvastatin and rosuvastatin (as single entity or combination products) and skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin).

The individual must meet the following criteria for reauthorization (for all indications):

- Has experienced a response to Leqvio therapy (e.g., decreasing LDL-C, total cholesterol, non-high-density lipoprotein cholesterol, or apolipoprotein B levels).
Note: An individual who is currently on therapy but has not been previously approved via EviCore coverage determination or is restarting therapy is reviewed under criteria for initial therapy.

Approval duration (initial and renewal): 12 months

Dosing Recommendation

The recommended dose is 284 mg administered as a single subcutaneous injection initially, again at 3 months, and then every 6 months.

References

1. Leqvio® subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis; February 2026.
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3. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Non-Statins Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. *J Am Coll Cardiol*. 2022;80(14):1366-1418.
4. Blumenthal RS, Morris PB, Gaudino M, et al. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of dyslipidemia: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *JACC*. 2026 March 13. [Online ahead of print].
5. American Diabetes Association Professional Practice Committee. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2026. *Diabetes Care*. 2026;49(Suppl 1):S216-S245.
6. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2023;82(9):833-955.
7. Rao SV, O'Donoghue ML, Ruel M, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes. *J Am Coll Cardiol*. 2025 Feb 27. [Online ahead of print].
8. Patel SB, Wyne KL, Afreen S, et al. American Association of Clinical Endocrinology clinical practice guideline on pharmacologic management of adults with dyslipidemia. *Endocrine Pract*. 2025;31:236-262.
9. Gidding SS, Champagne MA, de Ferranti SD, et al. The agenda for familial hypercholesterolemia. A scientific statement from the American Heart Association. *Circulation*. 2015;132(22):2167-2192.
10. Haase A, Goldberg AC. Identification of people with heterozygous familial hypercholesterolemia. *Curr Opin Lipidol*. 2012;23:282-289