

Leqvio® (inclisiran subcutaneous injection)

When requesting Leqvio® (inclisiran), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications 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 statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C).

Approved Off-Label Compendial Use

Established cardiovascular disease

Coverage Guidelines

Heterozygous Familial Hypercholesterolemia

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

- Is 18 years of age or older;
- Meets one of the following criteria:
 - o Has an untreated LDL-C level ≥ 190 mg/dL (prior to treatment with antihyperlipidemic agents); OR
 - o The diagnosis has been confirmed by genetic testing (e.g., pathogenic variants at the low-density lipoprotein receptor, APOB, proprotein convertase subtilisin kexin type 9, or low-density lipoprotein receptor adaptor protein 1 gene); OR
 - o Has been diagnosed with HeFH meeting one of the following diagnostic criteria thresholds:
 - Dutch Lipid Network criteria score was > 5 ; OR
 - Simon Broome criteria for definite, possible, or probable familial hypercholesterolemia;
- Meets ONE of the following criteria:
 - o Meets all of the following:
 - Has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily or rosuvastatin ≥ 20 mg daily [as a single entity or as a combination product]); AND
 - Has tried one high-intensity statin along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks; AND
 - LDL-C level after this treatment regimen remains ≥ 70 mg/dL;

OR

- o Has been determined to be statin intolerant by meeting one of the following:
 - Has experienced statin-related rhabdomyolysis (*Note: rhabdomyolysis is associated with 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 [a $\geq$ 0.5 mg/dL increase in serum creatinine {SCr} levels or doubling of the SCr] and/or myoglobinuria [myoglobin present in urine];* OR
 - Meets all of the following:
 - Has experienced skeletal-related muscle symptoms (i.e., myopathy or myalgia) that occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND
 - The skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin);

The individual must meet the following criteria for reauthorization:

- Has experienced a response to 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.

Primary Hyperlipidemia

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

- Is 18 years of age or older;
- Meets one of the following criteria:
 - o Has diabetes; OR
 - o Has a coronary artery calcium or calcification score $\geq$ 300 Agatston units;
- Meets ONE of the following criteria:
 - o Meets all of the following:
 - 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]); AND
 - Has tried one high-intensity statin along with ezetimibe (as a single-entity or as a combination product) for $\geq$ 8 continuous weeks; AND
 - LDL-C level after this treatment regimen remains $\geq$ 70mg/dL;

OR

- o Has been determined to be statin intolerant by meeting one of the following:
 - Has experienced statin-related rhabdomyolysis (*Note: rhabdomyolysis is associated with 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 [a $\geq$ 0.5 mg/dL increase in serum creatinine {SCr} levels or doubling of the SCr] and/or myoglobinuria [myoglobin present in urine];* OR
 - Meets all of the following:

- Has experienced skeletal-related muscle symptoms (i.e., myopathy or myalgia) that occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND
- The skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin);

The individual must meet the following criteria for reauthorization:

- Has experienced a response to 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.

Established Cardiovascular Disease

The individual must meet **all** of the following criteria for 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 criteria:
 - o Meets all of the following:
 - 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]); AND
 - Has tried one high-intensity statin along with ezetimibe (as a single-entity or as a combination product) for $\geq$ 8 continuous weeks; AND
 - LDL-C level after this treatment regimen remains $\geq$ 55 mg/dL;

OR

- o Has been determined to be statin intolerant by meeting one of the following:
 - Has experienced statin-related rhabdomyolysis (*Note: rhabdomyolysis is associated with 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 [$a \geq 0.5$ mg/dL increase in serum creatinine {SCr} levels or doubling of the SCr] and/or myoglobinuria [myoglobin present in urine];*); OR
 - Meets all of the following:

- Has experienced skeletal-related muscle symptoms (i.e., myopathy or myalgia) that occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND
- The skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin);

The individual must meet the following criteria for reauthorization:

- Has experienced a response to 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 Recommendations

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; June 2024.
2. Repatha® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; November 2024.
3. Praluent® subcutaneous injection [prescribing information]. Tarrytown, NY: Regeneron; March 2024.
4. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. *J Am Coll Cardiol*. 2022;80(14):1366-1418.
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16. 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.