

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 Has phenotypic confirmation of HeFH (e.g., pathogenic variants at the low-density lipoprotein receptor, apo B, 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 apo 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
 - 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 [apo 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 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 [apo 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; July 2023.
2. Repatha® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; September 2021.
3. Praluent® subcutaneous injection [prescribing information]. Tarrytown, NY: Regeneron; March 2024.
4. Stone NJ, Robinson J, Lichtenstein AH, 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. *J Am Coll Cardiol*. 2014;63(25 Pt B):2889-2934.
5. Grundy SM, Stone NJ, Bailey AL, et al. ACC/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*. 2019;139:e1082-e1143.
6. Haase A, Goldberg AC. Identification of people with heterozygous familial hypercholesterolemia. *Curr Opin Lipidol*. 2012;23:282-289.
7. 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.
8. 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.
9. American Diabetes Association Professional Practice Committee. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2024. *Diabetes Care*. 2024;47(Suppl 1):S179-S218.
10. 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.
11. Hect HS, Cronin P, Blaha M, et al. 2016 SCCT/STR guidelines for coronary artery calcium scoring of noncontrast noncardiac chest CT scans: A report of the Society of Cardiovascular Computed Tomography and Society of Thoracic Radiology. *J Thorac Imaging*. 2017;32(5):W54-S66.
12. Greenland P, Blaha MJ, Budoff MJ, et al. Coronary calcium score and cardiovascular risk. *J Am Coll Cardiol*. 2018;72(4):434-447.
13. Razavi AC, Agatston AS, Shaw LJ, et al. Evolving role of calcium density in coronary artery calcium scoring and atherosclerotic cardiovascular disease risk. *JACC Cardiovas Imaging*. 2022;15:1648-1662.
14. Lehker A, Mukherjee D. Coronary calcium risk score and cardiovascular risk. *Curr Vasc Pharmacol*. 2021;19(3):280-284.