

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 maximally tolerated statin therapy for the treatment of adults who are diagnosed with the following and require additional lowering of low-density lipoprotein cholesterol (LDL-C):

- Heterozygous familial hypercholesterolemia (HeFH)
- Clinical atherosclerotic cardiovascular disease (ASCVD)

Coverage Guidelines

Atherosclerotic 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 $\geq$ 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);
- This medication is prescribed by, or in consultation with, a cardiologist, an endocrinologist, or a physician who focuses in the treatment of cardiovascular risk management and/or lipid disorders.

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.

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 genetic confirmation of HeFH by mutations in 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 met the threshold for “definite” or “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);
- This medication is prescribed by, or in consultation with, a cardiologist, an endocrinologist, or a physician who focuses in the treatment of cardiovascular risk management and/or lipid disorders.

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.

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; December 2021.
2. 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.
3. 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.
4. Goldberg AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients. *J Clin Lipidol*. 2011;5:S1-S8.
5. Haase A, Goldberg AC. Identification of people with heterozygous familial hypercholesterolemia. *Curr Opin Lipidol*. 2012;23:282-289.
6. Newman CB, Blaha MJ, Boord JB, et al. Lipid management in patients with endocrine disorders: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2020;105(12):3613-3682.
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. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1-full report. *J Clin Lipidol*. 2015;9:129-169.
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.