Drug Coverage Policy

Effective Date.....7/1/2026
Coverage Policy Number.....IP0380
Policy Title.....Leqvio

Hyperlipidemia – PCSK9 Inhibitors – Leqvio

- Leqvio® (inclisiran subcutaneous injection – Novartis)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Leqvio, a small interfering ribonucleic acid (RNA) directed to proprotein convertase subtilisin kexin type 9 (PCSK9) messenger RNA, is indicated as an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in:[1]

- **Hypercholesterolemia** in adults.
- **Heterozygous familial hypercholesterolemia (HeFH)** in adults and pediatric patients ≥ 12 years of age.
- **Homozygous familial hypercholesterolemia (HoFH)** in pediatric patients ≥ 12 years of age

Lerochol™ (lerodalcibep-liga subcutaneous injection), Repatha® (evolocumab subcutaneous injection) and Praluent® (alirocumab subcutaneous injection) are PCSK9 inhibitor products.[2-4]

Of note, studies of Leqvio in adults with HoFH did not show reduction in LDL-C levels.[5]

Dosing Information
Leqvio is given as a subcutaneous injection and should be administered by a healthcare professional.[1] The dose is 284 mg given as a single subcutaneous injection initially, again at 3 months, and then once every 6 months.

Guidelines
Several major guidelines address the management of dyslipidemia, including the 2026 American College of Cardiology (ACC)/American Heart Association (AHA) Guideline on the Management of Dyslipidemia, the 2023 ACC/AHA Guideline for the Management of Chronic Coronary Disease (CCD), the 2022 ACC Expert Consensus Decision Pathway (ECDP) on the Role of Non-Statin Therapies, the 2025 ACC/AHA Guideline for the Management of Patients With Acute Coronary Syndrome, the 2026 American Diabetes Association Standards of Care, and the 2025 American Association of Clinical Endocrinology Clinical Practice Guideline for Dyslipidemia.[6-11] Across these guidelines, maximally tolerated statin therapy is consistently identified as the foundation of lipid management, with ezetimibe and/or PCSK9 inhibitors added when additional LDL-C lowering is required. Among PCSK9-targeting therapies, Praluent and Repatha are generally preferred over Leqvio because they have demonstrated cardiovascular (CV) outcomes benefit in large randomized trials, whereas outcomes data for Leqvio are still pending. The guidelines converge in recommending PCSK9 inhibitors for patients with clinical atherosclerotic cardiovascular disease (ASCVD) or severe hypercholesterolemia (LDL-C ≥ 190 mg/dL) who remain above LDL-C goals despite optimized background therapy; however, they differ in how treatment targets are expressed. The 2026 ACC/AHA dyslipidemia guideline and the 2026 ADA Standards of Care define explicit LDL-C goals, including a target of < 55 mg/dL for patients with very high-risk ASCVD, whereas other guidance, such as the 2022 ACC Expert Consensus Decision Pathway and the 2023 Chronic Coronary Disease guideline, relies primarily on LDL-C thresholds to trigger treatment intensification rather than strict numeric goals.

The AHA Scientific Statement on Familial Hypercholesterolemia (2015) and other sources provide guidance on the diagnosis of familial hypercholesterolemia, including HeFH.[12,13] Diagnostic approaches include the Dutch Lipid Clinic Network scoring system and the Simon Broome criteria.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Leqvio. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a

clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. A patient who has previously met Initial Therapy criteria for Leqvio for the requested indication under the Coverage Review Department and is currently receiving Leqvio is only required to meet continuation of therapy criteria (i.e., currently receiving therapy). If past criteria have not been met under the Coverage Review Department and the patient is currently receiving Leqvio, or is restarting Leqvio, Initial Therapy criteria must be met.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Leqvio is considered medically necessary when ONE of the following is met (1, 2, 3 or 4):

FDA-Approved Indications

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1. **Heterozygous Familial Hypercholesterolemia (HeFH).*** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient meets ONE of the following (a, b, c or d):
       - **a)** Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level ≥ 190 mg/dL (prior to treatment with antihyperlipidemic agents) **[documentation required];** OR
       - **b)** If the patient is between 12 and 17 years of age, meets BOTH of the following ([1] and [2]):
         - **(1)** Patient has an untreated low-density lipoprotein cholesterol (LDL-C) ≥ 160 mg/dL (prior to treatment with antihyperlipidemia agents); AND
         - **(2)** According to the prescriber, patient has a family history of early atherosclerotic cardiovascular disease (ASCVD) or elevated low-density lipoprotein cholesterol (LDL-C) or total cholesterol (TC) in a parent; OR
       - **c)** The diagnosis has been confirmed by genetic testing **[documentation required]**; OR
         Note: Examples include 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.
       - **d)** Patient has been diagnosed with heterozygous familial hypercholesterolemia meeting ONE of the following diagnostic criteria thresholds [(1) or (2)]:
         - **(1)** Prescriber confirms that the Dutch Lipid Network criteria score was > 5 **[documentation required]**; OR
         - **(2)** Prescriber confirms that Simon Broome criteria met the threshold for "definite" or "possible (or probable)" familial hypercholesterolemia **[documentation required]**; AND
     - **iii.** Patient meets ONE of the following (a or b):
       - **a)** Patient meets BOTH of the following [(1), and (2)]:
         - **(1)** Patient 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]) for ≥ 8 continuous weeks; AND
         - **(2)** LDL-C level after this treatment regimen remains ≥ 70 mg/dL; OR
       - **b)** Patient has been determined to be statin intolerant by meeting ONE of the following [(1) or (2)]:
         - **(1)** Patient experienced statin-related rhabdomyolysis; OR

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 ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).

(2) Patient meets ALL of the following [(a), (b), and (c)]:

(a) Patient experienced skeletal-related muscle symptoms; AND
Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).

(b) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination product); AND

(c) When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as a combination product) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR
Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

iv. Preferred product criteria is met for the product(s) as listed in the below table. Note: applies for Individual and Family Plans only.

B) Patient is Currently Receiving Leqvio. Approve if according to the prescriber, the patient has experienced a response to therapy.
Note: Examples of a response to therapy include decreasing LDL-C, total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Leqvio for this specific indication through Cigna, review under criteria for Initial Therapy. If the patient is restarting therapy with Leqvio, Initial Therapy criteria must be met.

Dosing. Approve ONE of the following dosage regimens (A or B):

A) Initial dose is 284 mg given as a single subcutaneous injection, again at 3 months, and then once every 6 months; OR

B) Maintenance dose is 284 mg given as a subcutaneous injection once every 6 months.

2. Homozygous Familial Hypercholesterolemia (HoFH).* Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is ≥ 12 years of age and < 18 years of age; AND

ii. Patient meets ONE of the following (a, b, or c):

a) The diagnosis has been confirmed by genetic testing **[documentation required]**; OR
Note: Examples include 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 (LDLRAP1) gene.

b) Patient has an untreated low-density lipoprotein (LDL-C) level > 400 mg/dL **[documentation required]** AND meets ONE of the following [(1) or (2)]:
Note: Untreated refers to prior therapy with any antihyperlipidemic agent.

(1) Patient had clinical manifestations of homozygous familial hypercholesterolemia before 10 years of age; OR
Note: Clinical manifestations of homozygous familial hypercholesterolemia are cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas, or xanthelasma.

(2) At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with familial hypercholesterolemia; OR
Note: An example of familial hypercholesterolemia is an untreated LDL-C level ≥ 190 mg/dL and/or an untreated total cholesterol level > 250 mg/dL.

c) Patient has a treated LDL-C level ≥ 300 mg/dL **[documentation required]** AND meets ONE of the following [(1) or (2)]:
Note: Treated refers to after therapy with at least one antihyperlipidemic agent. Some examples of antihyperlipidemic agents include statins (e.g., atorvastatin, rosuvastatin, lovastatin, simvastatin, pravastatin), ezetimibe, a PCSK9 inhibitor (e.g., Repatha [evolocumab subcutaneous injection]), Evkeeza (evinacumab-dgnb intravenous infusion), and Juxtapid (lomitapide capsules).

(1) Patient had clinical manifestations of homozygous familial hypercholesterolemia before 10 years of age; OR
Note: Examples of clinical manifestations of homozygous familial hypercholesterolemia are cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas or xanthelasma.

(2) At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with familial hypercholesterolemia; AND
Note: An example of familial hypercholesterolemia is an untreated LDL-C ≥ 190 mg/dL and/or an untreated total cholesterol > 250 mg/dL.

iii. Patient meets ONE of the following (a or b):

a) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient 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]) for ≥ 8 continuous weeks; AND

(2) LDL-C level after this treatment remains ≥ 70 mg/dL; OR

b) Patient has been determined to be statin intolerant by meeting ONE of the following [(1) or (2)]:

(1) Patient experienced statin-related rhabdomyolysis; OR
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 ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR

(2) Patient meets ALL of the following [(a), (b), and (c)]:

(a) Patient experienced skeletal-related muscle symptoms; AND
Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).

(b) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND

(c) When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR
Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

v. Preferred product criteria is met for the product(s) as listed in the below table. Note: applies for Individual and Family Plans only.

B) Patient is Currently Receiving Leqvio. Approve if according to the prescriber, the patient has experienced a response to therapy.

Note: Examples of a response to therapy include decreasing low-density lipoprotein cholesterol (LDL-C), total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Leqvio for this specific indication through Cigna, review under criteria for Initial Therapy. If the patient is restarting therapy with Leqvio, Initial Therapy criteria must be met.

Dosing. Approve ONE of the following dosage regimens (A or B):

A) Initial dose is 284 mg given as a single subcutaneous injection, again at 3 months, and then once every 6 months; OR

B) Maintenance dose is 284 mg given as a subcutaneous injection once every 6 months.

3. Hypercholesterolemia.* Approve for 1 year if the patient meets ONE of the following (A or B): Note: This is not associated with established cardiovascular disease or heterozygous familial hypercholesterolemia (HeFH) and may be referred to as combined hyperlipidemia, hypercholesterolemia (pure, primary), dyslipidemia, or increased/elevated low-density lipoprotein cholesterol (LDL-C) levels.

A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is ≥ 18 years of age; AND

ii. Patient meets ONE of the following (a or b):

a) According to the prescriber, the patient is at elevated risk of atherosclerotic cardiovascular disease (ASCVD), ASCVD event, or major adverse cardiovascular event (MACE) ; OR

b) Patient has diabetes; AND

iii. Patient meets ONE of the following (a or b):

a) Patient meets ALL of the following [(1]) and (2)]:

(1) Patient 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

(2) LDL-C level after this treatment regimen remains ≥ 70 mg/dL; OR

b) Patient has been determined to be statin intolerant by meeting ONE of the following [(1) or (2)]:

(1) Patient experienced statin-related rhabdomyolysis; OR

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 ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).

(2) Patient meets ALL of the following [(a), (b), and (c)]:

(a) Patient experienced skeletal-related muscle symptoms; AND

Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).

(b) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination product); AND

(c) When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as a combination product) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR

Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

iv. Preferred product criteria is met for the product(s) as listed in the below table. Note: applies for Individual and Family Plans only.

B) Patient Currently Receiving Leqvio. Approve if according to the prescriber, the patient has experienced a response to therapy.
Note: Examples of a response to therapy include decreasing LDL-C, total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Leqvio for this specific indication through Cigna, review under criteria for Initial Therapy. If the patient is restarting therapy with Leqvio, Initial Therapy criteria must be met.

Dosing. Approve ONE of the following dosage regimens (A or B):

A) Initial dose is 284 mg given as a single subcutaneous injection, again at 3 months, and then once every 6 months; OR

B) Maintenance dose is 284 mg given as a subcutaneous injection once every 6 months.

Other Uses with Supportive Evidence

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4. Established Cardiovascular Disease.* Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is ≥ 18 years of age; AND

ii. Patient has had one of the following conditions or diagnoses (a, b, c, d, e, or f):

a) A previous myocardial infarction or a history of an acute coronary syndrome; OR

b) Angina (stable or unstable); OR

c) A past history of stroke or transient ischemic attack; OR

d) Coronary artery disease; OR

e) Peripheral arterial disease; OR

f) Patient has undergone a coronary or other arterial revascularization procedure in the past; AND
Note: Examples include coronary artery bypass graft surgery, percutaneous coronary intervention, angioplasty, and coronary stent procedures.

iii. Patient meets ONE of the following (a or b):

a) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient 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]) for ≥ 8 continuous weeks; AND

(2) Low-density lipoprotein cholesterol (LDL-C) level after this treatment regimen remains ≥ 55 mg/dL; OR

b) Patient has been determined to be statin intolerant by meeting ONE of the following [(1) or (2)]:

(1) Patient experienced statin-related rhabdomyolysis; OR
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 ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).

(2) Patient meets ALL of the following [(a), (b), and (c)]:

(a) Patient experienced skeletal-related muscle symptoms; AND

Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).

(b) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination product); AND

(c) When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as a combination product) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR
Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

iv. Preferred product criteria is met for the product(s) as listed in the below table.
Note: applies for Individual and Family Plans only.

B) Patient is Currently Receiving Leqvio. Approve if according to the prescriber, the patient has experienced a response to therapy.
Note: Examples of a response to therapy include decreasing LDL-C, total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Leqvio for this specific indication through Cigna, review under criteria for Initial Therapy. If the patient is restarting therapy with Leqvio, Initial Therapy criteria must be met.

Dosing. Approve ONE of the following dosage regimens (A or B):

A) Initial dose is 284 mg given as a single subcutaneous injection, again at 3 months, and then once every 6 months; OR

B) Maintenance dose is 284 mg given as a subcutaneous injection once every 6 months.

Note:
* A patient may have a diagnosis that pertains to more than one indication, therefore, consider review under different approval conditions, if applicable (e.g., a patient with heterozygous familial hypercholesterolemia may have established cardiovascular disease, a patient with hypercholesterolemia may have heterozygous familial hypercholesterolemia).

Individual and Family Plans:

Product	Criteria
Leqvio (inclisiran)	**1.** Patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii): **i.** Patient has tried Repatha (evolocumab subcutaneous injection); AND **ii.** According to the prescriber, the patient has experienced inadequate efficacy or significant intolerance to Repatha,.

Conditions Not Covered

Leqvio for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent use of Leqvio with Lerochol (lerodalcibep-liga subcutaneous injection), Repatha (evolocumab subcutaneous injection) or Praluent (alirocumab subcutaneous injection).** Lerochol, Repatha and Praluent are PCSK9 inhibitors and should

not be used with Leqvio due to a similar mechanism of action.[1] Patients receiving PCSK9 inhibitors were excluded from the pivotal trials with Leqvio.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J1306	Injection, inclisiran, 1 mg

References

1. Leqvio® subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis; July 2025.
2. Lerochol™ subcutaneous injection [prescribing information]. Cincinnati, OH: LIB; December 2025.
3. Repatha® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; August 2025.
4. Praluent® subcutaneous injection [prescribing information]. Tarrytown, NY: Regeneron; October 2025.
5. Raal F, Durst R, Bi R, et al. Efficacy, safety, and tolerability of inclisiran in patients with homozygous familial hypercholesterolemia: results from the ORION-5. *Circulation*. 2024;149:354-362.
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7. 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. *Circulation*. 2014;129(25 Suppl 2):S1-S45.
8. Grundy SM, Stone NJ, Bailey AL, et al. AHA/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.
9. American Diabetes Association Professional Practice Committee. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2026. *Diabetes Care*. 2025;49(Suppl 1):S216-S245.
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13. 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.
14. Greenland P, Blaha MJ, Budoff MJ, et al. Coronary calcium score and cardiovascular risk. *J Am Coll Cardiol*. 2018;72(4):434-447.
15. 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.
16. Lehker A, Mukherjee D. Coronary calcium risk score and cardiovascular risk. *Curr Vasc Pharmacol*. 2021;19(3):280-284.
17. 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].
18. 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.

Revision Details

Summary of Changes	Review Date	Effective Date
Updated policy title from Inclisiran to Proprotein Convertase Subtilisin Kexin Type 9 Related Products – Leqvio. **All Indications**: Clarified "Initial Therapy" versus "Currently Receiving Leqvio" criteria and added additional examples of what is considered a response to therapy; Removed "Use is adjunctive to diet and maximally tolerated statin therapy [unless contraindicated or intolerant"; Updated the statin intolerance criteria, to clearly define what is considered statin intolerant, with notes and examples also included; Added dosing to the policy; Added a Note: * A patient may have a diagnosis that pertains to more than one FDA-approved indication, therefore, consider review under different approval conditions, if applicable (e.g., a patient with heterozygous familial hypercholesterolemia may have established cardiovascular disease, a patient with primary hyperlipidemia may have heterozygous familial hypercholesterolemia). **Heterozygous Familial Hypercholesterolemia:** For Initial Therapy, The specialist physician requirement was removed. For the requirement that the patient has had genetic confirmation of heterozygous familial hypercholesterolemia by mutations in the low-density lipoprotein receptor, apolipoprotein B, proprotein convertase subtilisin kexin type 9, or low-density lipoprotein receptor	06/20/2024	08/15/2024

adaptor protein 1 gene was changed to state that the patient has had phenotypic confirmation of heterozygous familial hypercholesterolemia and the above examples moved to a Note. **Primary Hyperlipidemia:** For Initial Therapy, the specialist physician requirement was removed. Removed "Individual has a coronary artery calcium or calcification score of 100 or greater Agatston units or 75th percentile or greater for the individual's age, gender and ethnicity [coronary calcium scan may require prior authorization] OR Calculated 10 year ASCVD risk score of 7.5% or higher and replaced with "Patient has a coronary artery calcium or calcification score ≥ 300 Agatston units OR Patient has diabetes". Added a requirement that "Patient has tried the one high-intensity statin therapy (atorvastatin or rosuvastatin) along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks". The requirement that the low-density lipoprotein cholesterol level after treatment with one high-intensity statin therapy, along with ezetimibe, be ≥ 100 mg/dL was changed to ≥ 70 mg/dL. **Established Cardiovascular Disease:** The name of the indication was changed to as stated (previously "Atherosclerotic Cardiovascular Disease"). For Initial Therapy, the specialist physician requirement was removed. The requirement that the low-density lipoprotein cholesterol level after treatment with one high-intensity statin therapy be ≥ 70 mg/dL was changed to ≥ 55 mg/dL.		
Added "Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information." **Heterozygous Familial Hypercholesterolemia (HeFH):** For Initial Therapy, the phrase "phenotypic confirmation of heterozygous familial hypercholesterolemia" was replaced with "The diagnosis has been confirmed by genetic testing". Also, "apo B" was changed to "APOB". **Added "[documentation required]"** to the following criteria: Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level ≥ 190 mg/dL (prior to treatment with antihyperlipidemic agents) **[documentation required];** The	06/12/2025	08/15/2025

diagnosis has been confirmed by genetic testing **[documentation required]**; Prescriber confirms that the Dutch Lipid Network criteria score was > 5 **[documentation required]**; Prescriber confirms that Simon Broome criteria met the threshold for "definite" or "possible (or probable)" familial hypercholesterolemia **[documentation required]**;		
Heterozygous Familial Hypercholesterolemia: For initial therapy the requirement that the patient has tried one high-intensity statin along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks was removed. The requirement remains that the patient 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 the qualifier of "for ≥ 8 continuous weeks" was added for clarification. **Established Cardiovascular Disease:** For initial therapy the requirement that the patient has tried one high-intensity statin along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks was removed. The requirement remains that the patient 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 the qualifier of "for ≥ 8 continuous weeks" was added for clarification. **Primary Hyperlipidemia:** Added "**[documentation required]**" to the following criteria: Patient has a coronary artery calcium or calcification score ≥ 300 Agatston units [may require prior authorization].	09/04/2025	10/15/2025
Updated the policy statement. **Removed** Employer Plans preferred product requirements.	12/04/2025	02/01/2026
The policy name was changed to as listed. Previously, it was Proprotein Convertase Subtilisin Kexin Type 9 Related Products – Leqvio. **Heterzygous Familial Hypercholesterolemia:** The age of approval was changed to ≥ 12 years of age; previously, it was ≥ 18 years of age. The diagnostic requirement was updated to include a requirement that if the patient is between 12 and 17 years of age, they have to meet both of the following: have an untreated low-density lipoprotein cholesterol (LDL-C) ≥ 160 mg/dL (prior	3/19/2026	5/15/2026

to treatment with antihyperlipidemic agents) and according to the prescriber, have a family history of early atherosclerotic cardiovascular disease (ASCVD) or elevated low-density lipoprotein cholesterol (LDL-C) or total cholesterol (TC) in a parent. **Homozygous Familial Hypercholesterolemia**: This condition of approval was added to the policy. **Hypercholesterolemia**: The name of this indication was changed to as listed (Previously "Primary Hyperlipidemia."). The Note in the asterisk at the end of the criteria was updated to reflect this modification. **Conditions Not Recommended for Approval**: Lerochol was added as an agent that cannot be taken concurrently with Leqvio.		
Hypercholesterolemia: The requirement for a patient to have a coronary artery calcium or calcification score ≥300 was replaced with a requirement that, according to the prescriber, the patient to be at risk for atherosclerotic cardiovascular disease (ASCVD), ASCVD event, or major adverse cardiovascular event (MACE). The requirement for a patient to have tried one high-intensity statin therapy along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks was removed.	5/21/2026	7/1/2026

The policy effective date is in force until updated or retired.

APPENDIX A

Simon Broome Register Diagnostic Criteria.[9,10]

Definite Familial Hypercholesterolemia
Raised cholesterol
--Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a patient < 16 years of age; OR
--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in a patient > 16 years of age;
AND
--Tendon xanthomas in the patient or in a first (parent, sibling, or child) or second-degree relative (grandparent, aunt, or uncle);
OR
DNA-based evidence of LDL-receptor, familial defective APOB, or PCSK9 mutation.
Possible (or Probable) Familial Hypercholesterolemia
Raised cholesterol
--Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a patient < 16 years of age; OR

--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in a patient > 16 years of age;
AND
Family history of premature myocardial infarction younger than 50 years of age in second-degree relative or younger than 60 years of age in first-degree relative;
OR
Raised cholesterol
--Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a patient < 16 years of age; OR
--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in a patient > 16 years of age;
AND
Family history of raised cholesterol > 7.5 mmol (290 mg/dL) in adult first-degree or second-degree relative or > 6.7 mmol/L (260 mg/dL) in child or sibling aged < 16 years.

LDL-C – Low-density lipoprotein cholesterol; LDL – Low-density lipoprotein; APOB – Apolipoprotein B; PCSK9 – Proprotein convertase subtilisin kexin type 9.

APPENDIX B.

Dutch Lipid Network Criteria.[9,10]

Criteria	Score
Family History	
First-degree relative with known premature coronary and/or vascular disease (men < 55 years, women < 60 years)	1
First degree relative with known LDL-C > 95th percentile for age and sex	1
First-degree relative with tendon xanthomata and/or arcus cornealis, OR	2
Patient is < 18 years of age with LDL-C > 95th percentile for age and sex	2
Clinical History	
Patient with premature CAD (age as above)	2
Patient with premature cerebral or peripheral vascular disease (age as above)	1
Physical Examination	
Tendon xanthomas	6
Arcus cornealis at age < 45 years	4
LDL-C	
LDL-C ≥ 8.5 mmol/L (330 mg/dL)	8
LDL-C 6.5 to 8.4 mmol/L (250 to 329 mg/dL)	5
LDL-C 5.0 to 6.4 mmol/L (190 to 249 mg/dL)	3
LDL-C 4.0 to 4.9 mg/dL (155 to 189 mg/dL)	1
DNA Analysis	
Functional mutation LDLR, APOB or PCSK9 gene	8
Stratification	**Total score**
Definite familial hypercholesterolemia	> 8
Probable familial hypercholesterolemia	6 to 8
Possible familial hypercholesterolemia	3 to 5
Unlikely familial hypercholesterolemia	< 3

LDL-C – Low-density lipoprotein cholesterol; CAD – Coronary artery disease; LDLR – Low-density lipoprotein receptor; APOB – Apolipoprotein B; PCSK9 – Proprotein convertase subtilisin kexin type 9.

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