CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hyperlipidemia – PCSK9 Inhibitors – Leqvio Utilization Management Medical Policy
- Leqvio® (inclisiran subcutaneous injection – Novartis)

REVIEW DATE: 03/04/2026

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

Multiple clinical guidelines address the management of dyslipidemia, including in patients with HeFH and atherosclerotic cardiovascular disease (ASCVD).[6–10] Across guidelines, statins are consistently recommended as first-line therapy and should be used at maximally tolerated doses due to their established cardiovascular (CV) risk-reduction benefits. High-intensity statins (i.e., atorvastatin 40 to 80 mg once daily or rosuvastatin 20 to 40 mg once daily) are expected to reduce LDL-C by ≥ 50%.

- The **American College of Cardiology (ACC) Expert Consensus Decision Pathway on Non-Statin Therapies for LDL-C Lowering (2022)** recommends that adults with clinical ASCVD at very high risk (e.g., prior major ASCVD events, HeFH, diabetes) receiving statins for secondary prevention target a ≥ 50% reduction in LDL-C and an LDL-C level < 55 mg/dL.[6] If these goals are not achieved with maximally tolerated statin therapy, ezetimibe and/or a PCSK9 monoclonal antibody (Repatha or Praluent) are recommended, with Leqvio as a potential consideration. In adults without clinical ASCVD or diabetes or LDL-C ≥ 190 mg/dL who have evidence of significant subclinical atherosclerosis (e.g., coronary artery calcium score ≥ 1,000 Agatston units), PCSK9 monoclonal antibodies may be considered after high-intensity statin therapy and ezetimibe to achieve a ≥ 50% LDL-C reduction and an LDL-C < 70 mg/dL.
- **TheAmerican Heart Association (AHA)/ACC Guideline on the Management of Blood Cholesterol (2018 update)** defines ASCVD as acute coronary syndrome, prior myocardial infarction, stable or unstable angina, coronary or other revascularization, stroke, transient ischemic attack, or peripheral arterial disease.[7,8] Although specific LDL-C thresholds are not uniformly defined, an LDL-C < 70 mg/dL is generally recommended to reduce CV risk in patients with

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ASCVD. Addition of a PCSK9 inhibitor is supported when LDL-C goals are not achieved with maximally tolerated statins. Additionally, patients with elevated coronary artery calcium scores (e.g., ≥ 300 Agatston units) are recognized as being at increased risk for CV events.[13-16]

- The **ACC/AHA Guideline for the Management of Patients with Acute Coronary Syndrome (2025)** recommends adding a non-statin lipid-lowering agent in patients receiving maximally tolerated statin therapy who have an LDL-C ≥ 70 mg/dL to further reduce the risk of major adverse cardiac events (MACE).[17] Some recommendations also support lower LDL-C targets in the range of 55-69 mg/dL.
- The **American Diabetes Association Standards of Care in Diabetes (2026)** recommend high-intensity statin therapy for adults 40 years to 75 years of age with diabetes who are at higher CV risk, including those with one or more ASCVD risk factors, to achieve a ≥ 50% reduction in LDL-C and a target LDL-C < 70 mg/dL.[9] In patients with multiple ASCVD risk factors and LDL-C ≥ 70 mg/dL despite maximally tolerated statin therapy, addition of ezetimibe or a PCSK9 inhibitor may be reasonable.
- Guidelines for **Chronic Coronary Disease from the AHA and ACC** (along with other organizations) [2023] state that in patients at very high risk who are receiving maximally tolerated statin therapy and have an LDL-C ≥ 70 mg/dL, ezetimibe can further reduce the risk of MACE.[10] For patients who remain above this LDL-C threshold despite statin and ezetimibe therapy, a PCSK9 monoclonal antibody may provide additional benefit.
- **American Association of Clinical Endocrinology (AACE) Clinical Practice Guideline for Dyslipidemia (2025)** recommends Praluent or Repatha for adults with dyslipidemia who have ASCVD or are at increased ASCVD risk and are not at LDL-C goal (< 70 mg/dL) despite maximally tolerated statin therapy.[18] In adults without ASCVD, AACE suggests against the use of PCSK9 monoclonal antibodies. Due to limited trial data and few CV events, there is insufficient evidence to recommend for or against the use of Leqvio, and the balance of benefits and harms remains uncertain.
- **AHA Scientific Statement on Familial Hypercholesterolemia (2015)** and other sources provide guidance on the diagnosis of familial hypercholesterolemia, including HeFH.[11,12] Diagnostic approaches include the Dutch Lipid Clinic Network scoring system and the Simon Broome criteria.

POLICY STATEMENT

Prior Authorization is recommended for medical 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Leqvio is recommended in those who meet one of the following criteria:

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, and iii):
     - **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); 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; 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; OR
         - **(2)** Prescriber confirms that Simon Broome criteria met the threshold for "definite" or "possible (or probable)" familial hypercholesterolemia; 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 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 a 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) and 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.

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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 the Coverage Review Department, 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.

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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, and iii):
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; 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 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 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

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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 a 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) and 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.

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 the Coverage Review Department, 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.

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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, and iii):

i. Patient is ≥ 18 years of age; AND

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ii. Patient meets ONE of the following (a or b):
- **a)** Patient has a coronary artery calcium or calcification score ≥ 300 Agatston units; OR
- **b)** Patient has diabetes; AND

iii. Patient meets ONE of the following (a or b):
- **a)** Patient meets ALL of the following [(1]), (2), and (3)]:
  - **(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)** Patient has tried one high-intensity statin therapy above along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks; AND
  - **(3)** 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 a 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) and 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.

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 the Coverage Review Department, 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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3. 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, and iii):
i. Patient is ≥ 18 years of age; AND

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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 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 a 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) and 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.

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 the Coverage Review Department, 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):

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

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

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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 primary hyperlipidemia may have heterozygous familial hypercholesterolemia).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Leqvio is not recommended in the following situations:

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.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	It was removed from the Policy Statement that the agent is prescribing by or in consultation with a physician who specializes in the condition being treated. In addition, the following changes were made: **Established Cardiovascular Disease:** The name of the indication was changed to as stated (previously "Atherosclerotic Cardiovascular Disease"). For Initial Therapy, the requirement that the 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 was removed. The requirement that the low-density lipoprotein cholesterol level after treatment with one high-intensity statin therapy and ezetimibe be ≥ 70 mg/dL was changed to ≥ 55 mg/dL. For a Patient Currently Receiving the Medication, the requirement that the "prescribing physician" notes that the patient has experienced a response to therapy was changed to "prescriber". **Heterozygous Familial Hypercholesterolemia:** For Initial Therapy, the requirement that the 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 was removed. 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 adaptor protein 1 gene was changed to state that the patient has had phenotypic confirmation of heterozygous familial hypercholesterolemia with the above examples moved to a Note. Regarding the diagnosis of heterozygous familial hypercholesterolemia by meeting the Dutch Lipid Network criteria score or the Simon Broome criteria, the requirement that this be confirmed by the "prescribing physician" was changed to "prescriber". For a Patient Currently Receiving the Medication, the requirement that the "prescribing physician" notes that the patient has experienced a response to therapy was changed to "prescriber". **Primary Hyperlipidemia:** For Initial Therapy, the requirement that the 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 was removed. A patient with diabetes now qualifies for this indication (if requirements are met); previously, high risk was only defined by a patient who had a "coronary artery calcium or calcification score ≥ 300 Agatston units". 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. For a Patient Currently Receiving the Medication, the requirement that the "prescribing physician" notes that the patient has experienced a response to therapy was changed to "prescriber".	05/08/2024
Annual Revision	**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".	05/28/2025

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HISTORY (CONTINUED)

Type of Revision	Summary of Changes	Review Date
Selected Revision	**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.	08/06/2025
Update	The policy name was changed to as listed. Previously, it was Proprotein Convertase Subtilisin Kexin Type 9 Related Products – Leqvio UM Medical Policy.	N/A
Early Annual Revision	**Heterzygous Familial Hypercholesterolemia:** The age requirement was changed to approve for a patient ≥ 12 years of age; previously was ≥ 18 years of age. For a patient between 12 and 17 years of age, a requirement was added that untreated low-density lipoprotein cholesterol (LDL-C) is ≥ 160 mg/dL prior to treatment with antihyperlipidemic agents, and that, according to the prescriber, the patient has a family history of early atherosclerotic cardiovascular disease or elevated LDL-C or total cholesterol in a parent. **Homozygous Familial Hypercholesterolemia**: This was added as a new condition of approval. **Hypercholesterolemia**: The diagnosis of Primary Hyperlipidemia was changed to as listed. A Note was also updated with this reworded indication. **Conditions Not Recommended for Approval**: Lerochol was added as an agent that cannot be taken concurrently with Leqvio.	03/04/2026

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APPENDIX A

Simon Broome Register Diagnostic Criteria.[11,12]

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.

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APPENDIX B.

Dutch Lipid Network Criteria.[11,12]

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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