Drug Coverage Policy

Effective Date.....05/15/2026
Coverage Policy Number.....IP0250
Policy Title.....Praluent

Hyperlipidemia – PCSK9 Inhibitors – Praluent

- Praluent® (alirocumab subcutaneous injection - Regeneron)

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

Praluent, a proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor antibody, is indicated for the following uses:[1]

- To reduce the **risk of major adverse cardiovascular (CV) events** (coronary heart disease death, myocardial infarction [MI], stroke, and unstable angina requiring hospitalization) in adults at increased risk for these events.
- To reduce low-density lipoprotein cholesterol (LDL-C), as an adjunct to diet and exercise, in:
  - **i. Hypercholesterolemia** in adults.
  - **ii. Heterozygous familial hypercholesterolemia** (HeFH) in adults and pediatric patients ≥ 8 years of age.
  - **iii. Homozygous familial hypercholesterolemia** (HoFH) in adults.

Lerochol™ (lerodalcibep-liga subcutaneous injection) and Repatha® (evolocumab subcutaneous injection) are other PCSK9 inhibitors.[2,3] Leqvio® (inclisiran subcutaneous injection), a small interfering ribonucleic acid (RNA) directed to PCSK9 messenger RNA, is a similar product.[4]

Guidelines

Multiple clinical guidelines address the management of dyslipidemia, including in patients with HeFH and atherosclerotic cardiovascular disease (ASCVD).[5-10] Across guidelines, statins are consistently recommended as first-line therapy and should be used at maximally tolerated doses due to their established 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.[5] 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.
- The **American 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.[6,7] 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 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.[8] 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.
- The **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.
- The **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.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Praluent. All approvals are provided for the duration noted below. A patient who has previously met initial therapy criteria for Praluent for the requested indication under the Coverage Review Department and is currently receiving the requested therapy 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 Praluent, or is restarting Praluent, initial 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.

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

FDA-Approved Indications

1. **Reduce Major Adverse Cardiovascular Events in Patients at Increased Risk.*** Approve for 1 year if the patient meets ONE of the following (A or B):
   Note: This includes only patients with established cardiovascular disease.
   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 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 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(s)

B) Patient is Currently Receiving Praluent. 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 Praluent for this specific indication through Cigna, review under criteria for Initial Therapy. If the patient is restarting therapy with Praluent, Initial Therapy criteria must be met.

2. Heterozygous Familial Hypercholesterolemia (HeFH).* Approve for 1 year if the patient meets ONE 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 ≥ 8 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 8 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 antihyperlipidemic 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

d) Patient has been diagnosed with heterozygous familial hypercholesterolemia meeting one of the following diagnostic criteria thresholds [(1) or (2)]:
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.
(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) Low-density lipoprotein cholesterol 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]).
(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); AND
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(s)

B) Patient is Currently Receiving Praluent. 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 Praluent for this specific indication through Cigna, review under criteria for Initial Therapy. If the patient is restarting therapy with Praluent, Initial Therapy criteria must be met.

3. 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 ≥ 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 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); AND
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(s)

B) Patient is Currently Receiving Praluent. 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 Praluent for this specific indication through Cigna, review under criteria for Initial Therapy. If the patient is restarting therapy with Praluent, Initial Therapy criteria must be met.

4. 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, heterozygous familial hypercholesterolemia (HeFH), or homozygous familial hypercholesterolemia (HoFH) 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) Patient has a coronary artery calcium or calcification score ≥ 300 Agatston units [may require prior authorization] **[documentation required]**; 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 the 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 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); AND
Note: Examples of skeletal-related muscle symptoms include myopathy or myalgia.

iv. Preferred product criteria is met for the product(s) as listed in the below table(s)

B) Patient is Currently Receiving Praluent. 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 Praluent for this specific indication through Cigna, review under criteria for Initial Therapy. If the patient is restarting therapy with Praluent, Initial Therapy criteria must be met.

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 or homozygous familial hypercholesterolemia may have established cardiovascular disease/or an increased risk for major adverse cardiovascular events, a patient with hypercholesterolemia may have heterozygous familial hypercholesterolemia).

Employer Plans:

Product	Criteria
Praluent (alirocumab)	**1.** Patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets ONE of the following (i or ii): **i.** Patient meets BOTH of the following (a and b): **a)** Patient has tried Repatha (evolocumab subcutaneous injection) [may require prior authorization]; AND **b)** According to the prescriber, patient has experienced inadequate efficacy or significant intolerance; OR **ii.** Patient meets BOTH of the following (a and b): **a)** Patient has heterozygous familial hypercholesterolemia; AND **b)** Patient is ≥ 8 to < 10 years of age.

Individual and Family Plans:

Product	Criteria
Praluent (alirocumab)	**1.** Patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets ONE of the following (i or ii): **i.** Patient meets BOTH of the following (a and b): **a)** Patient has tried Repatha (evolocumab subcutaneous injection) [may require prior authorization]; AND **b)** According to the prescriber, patient has experienced inadequate efficacy or significant intolerance; OR **ii.** Patient meets BOTH of the following (a and b): **a)** Patient has heterozygous familial hypercholesterolemia; AND **b)** Patient is ≥ 8 to < 10 years of age.

Conditions Not Covered

Praluent 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 Praluent with Lerochol (lerodalcibep-liga subcutaneous injection), Repatha (evolocumab subcutaneous injection) or Leqvio (inclisiran subcutaneous injection).** Lerochol and Repatha are other PCSK9 inhibitors and should not be used with Praluent.[2] Leqvio, a small interfering ribonucleic acid (RNA) directed to PCSK9 messenger RNA, is a similar product and should not be given with Praluent.[3]

References

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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.
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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 Alirocumab to Proprotein Convertase Subtilisin Kexin Type 9 Inhibitors – Praluent. **All Indications**: Clarified "Initial Therapy" versus "Currently Receiving Praluent" 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; Updated the preferred	06/20/2024	08/15/2024

product criteria to include an exception for patients between the ages of 8 and 10 years old with heterozygous familial hypercholesterolemia; 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 or homozygous familial hypercholesterolemia may have established cardiovascular disease, a patient with primary hyperlipidemia may have heterozygous familial hypercholesterolemia). **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. **Heterozygous Familial Hypercholesterolemia:** For Initial Therapy, the age of approval was changed from ≥ 18 years of age to ≥ 8 years of age. 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 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. **Homozygous Familial Hypercholesterolemia:** For Initial Therapy, the specialist physician requirement was removed. The requirement that the patient has had genetic confirmation by two mutant alleles at the low-density lipoprotein receptor, apolipoprotein B, proprotein convertase subtilisin kexin type 9, or low-density lipoprotein receptor adaptor protein 1 gene locus was changed to state that the patient has phenotypic confirmation of homozygous familial hypercholesterolemia and the above examples moved to a Note. The diagnostic criterion which stated that the patient has an untreated low-density lipoprotein cholesterol level > 500 mg/dL was changed to > 400 mg/dL. The criterion (which is in two places [those with an untreated low-density lipoprotein cholesterol level > 400 mg/dL and a treated low-density lipoprotein cholesterol		

level ≥ 300 mg/dL]) that both parents of the patient had untreated low-density lipoprotein cholesterol levels or total cholesterol levels consistent with heterozygous familial hypercholesterolemia was changed to state that at least one parent of the patient had untreated low-density lipoprotein cholesterol levels or total cholesterol levels consistent with familial hypercholesterolemia. The related Note that "An example of heterozygous familial hypercholesterolemia in both parents would be if both had an untreated low-density lipoprotein cholesterol level ≥ 190 mg/dL and/or an untreated total cholesterol level > 250 mg/dL" was changed to state "An example of familial hypercholesterolemia is an untreated low-density lipoprotein cholesterol level ≥ 190 mg/dL and/or an untreated total cholesterol level > 250 mg/dL." **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.		
Heterozygous Familial Hypercholesterolemia: 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". **Homozygous Familial Hypercholesterolemia:** For Initial Therapy, the phrase "phenotypic confirmation of homozygous familial hypercholesterolemia" was replaced with "The diagnosis has been confirmed by genetic testing". Also, "apo B" was changed to "APOB".	06/12/2025	08/15/2025
The policy name was changed to as listed. Previously, it was Proprotein Convertase Subtilisin Kexin Type 9 Inhibitors – Praluent PA policy.	3/19/2026	05/15/2026

Documentation requirements were added throughout the policy. **Reduce Major Adverse Cardiovascular Events in Patients at Increased Risk**: The diagnosis of Established Cardiovascular Disease was changed to as listed. A Note was added that this includes only patients with established cardiovascular disease. A Note was also updated with this reworded indication. **Heterozygous Familial Hypercholesterolemia:** For a patient between 8 and 17 years of age, a requirement was added that untreated 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. Previously, these patients were required to have an LDL-C ≥ 190 mg/dL. **Hypercholesterolemia**: The diagnosis of Primary Hyperlipidemia was changed to as listed. A Note was also updated with this reworded indication. **Conditions Not Recommended for Coverage**: Lerochol was added as an agent that cannot be taken concurrently with Praluent.		

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

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 child < 16 years; OR
--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in an adult (aged > 16 years);
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 child < 16 years; OR
--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in an adult (aged > 16 years);
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 child < 16 years; OR
--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in an adult (aged > 16 years);
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.[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
Children aged < 18 years 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.