



Formulary Exception

Proprotein convertase subtilisin kexin type 9 (PCSK9) Inhibitors – Praluent® (alirocumab injection for subcutaneous use)

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Product Identifier(s)

51801

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. 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.

National Formulary Medical Necessity

Cigna covers alirocumab (Praluent®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

All approvals are provided for 1 year.

1. **Atherosclerotic Cardiovascular Disease (ASCVD) [Clinical].*** Approve for 1 year if the individual meets the following criteria (A, B, C, D and E):
 - A) Individual is ≥ 18 years of age; AND
 - B) Individual has had one of the following conditions or diagnoses (i, ii, iii, iv, or v):
 - i. Individual has had a previous myocardial infarction (MI) or has a history of an acute coronary syndrome (ACS); OR
 - ii. Individual has a diagnosis of angina (stable or unstable); OR
 - iii. Individual has a past history of stroke or transient ischemic attack (TIA); OR
 - iv. Individual has peripheral arterial disease (PAD); OR
 - v. Individual has undergone a coronary or other arterial revascularization procedure in the past; AND

- vi. Note: Examples include coronary artery bypass graft (CABG) surgery, percutaneous coronary intervention (PCI), angioplasty, and coronary stent procedures.
- C) Individual meets one of the following criteria (i or ii):
 - i. Individual meets both of the following criteria (a and b):
 - a) Individual has tried one high-intensity statin therapy (i.e., atorvastatin \geq 40 mg daily; rosuvastatin \geq 20 mg daily [as a single-entity or as a combination product]) for \geq 8 continuous weeks; AND
 - b) The low-density lipoprotein cholesterol (LDL-C) level after this treatment remains \geq 70 mg/dL; OR
 - ii. Individual has been determined to be statin intolerant by meeting one of the following criteria (a or b):
 - a) Individual experienced statin-related rhabdomyolysis; OR
Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase (CK) 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 \geq 0.5 mg/dL increase in Scr or doubling of the Scr}) and/or myoglobinuria [myoglobin present in urine]).
 - b) Individual meets all of the following [(1), (2), and (3)]:
 - 1) Individual 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).
 - 2) The skeletal-related muscle symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products); AND
 - 3) 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); AND
- D) Individual meets both of the following (i and ii):
 - i. Individual has tried Repatha (evolocumab injection for subcutaneous use); AND
 - ii. Individual has experienced inadequate efficacy or significant intolerance according to the prescriber; AND
- E) Medication is prescribed by, or in consultation with, a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders.

2. Heterozygous Familial Hypercholesterolemia [HeFH].* Approve for 1 year if the individual meets the following criteria (A, B, C, D and E):

- A) Individual is \geq 18 years of age; AND
- B) Individual meets one of the following criteria (i, ii, iii, iv, or v):
 - i. Individual has an untreated low-density lipoprotein cholesterol (LDL-C) \geq 190 mg/dL (prior to treatment with antihyperlipidemic agents); OR
 - ii. Individual has genetic confirmation of HeFH by mutations in 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; OR
 - iii. Individual has been diagnosed with HeFH meeting one of the following diagnostic criteria thresholds (a or b):
 - a) Individual meets both of the following [(1) and (2)]:
 - 1) Prescriber used the Dutch Lipid Network criteria to diagnose HeFH; AND
 - 2) Individual had a score $>$ 5; OR
 - b) Individual meets both of the following [(1) and (2)]:
 - 1) Prescriber used the Simon Broome criteria to diagnose HeFH; AND
 - 2) Individual met the threshold for “definite” or “possible” familial hypercholesterolemia; OR
 - iv. Individual has a treated low-density lipoprotein cholesterol (LDL-C) level \geq 100 mg/dL (after treatment with antihyperlipidemic agents but prior to PCSK9 inhibitor therapy such as Praluent or Repatha [evolocumab injection for subcutaneous use]); AND
 - v. Individual has clinical manifestations of HeFH; AND
Note: Examples of clinical manifestation of HeFH include cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas or xanthelasma.

- C)** Individual meets one of the following criteria (i or ii):
- i.** Individual meets both of the following criteria (a and b):
 - a)** Individual has tried one high-intensity statin therapy (i.e., atorvastatin \geq 40 mg daily; rosuvastatin \geq 20 mg daily [as a single-entity or as a combination product]) for \geq 8 continuous weeks; AND
 - b)** The low-density lipoprotein cholesterol (LDL-C) level after this treatment remains \geq 70 mg/dL; OR
 - ii.** Individual has been determined to be statin intolerant by meeting one of the following criteria (a or b):
 - a)** Individual experienced statin-related rhabdomyolysis; OR
Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase (CK) 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 \geq 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR
 - b)** Individual meets all of the following [(1), (2), and (3)]:
 - 1)** Individual 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).
 - 2)** The skeletal-related muscle symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products); AND
 - 3)** 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); AND
- D)** Individual meets both of the following (i and ii):
- i.** Individual has tried Repatha (evolocumab injection for subcutaneous use); AND
 - ii.** Individual has experienced inadequate efficacy or significant intolerance according to the prescriber; AND
- E)** Medication is prescribed by, or in consultation with, a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders.

3. Primary Hyperlipidemia.* Approve Praluent for 1 year if the individual meets the following criteria (A, B, C, D and E):

Note: This is not associated with atherosclerotic cardiovascular disease (ASCVD) 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)** Individual is \geq 18 years of age; AND
- B)** Individual has a coronary artery calcium or calcification (CAC) score \geq 300 Agatston units; AND
- C)** Individual meets one of the following criteria (i or ii):
- i.** Individual meets all of the following criteria: (a, b and c):
 - a)** Individual has tried one high-intensity statin therapy (i.e., atorvastatin \geq 40 mg daily; rosuvastatin tablets \geq 20 mg daily [as a single-entity or as a combination product]); AND
 - b)** Individual has tried the one high-intensity statin therapy above along with ezetimibe (as a single-entity or as a combination product) for \geq 8 continuous weeks; AND
 - c)** The low-density lipoprotein cholesterol (LDL-C) level after this treatment regimen remains \geq 100 mg/dL; OR
 - ii.** Individual has been determined to be statin intolerant by meeting one of the following criteria (a or b):
 - a)** Individual experienced statin-related rhabdomyolysis; OR
Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase (CK) 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 \geq 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).
 - b)** Individual meets all of the following [(1), (2), and (3)]:
 - 1)** Individual 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).

- 2) The skeletal-related muscle symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products); AND
 - 3) 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); AND
- D) Individual meets both of the following (i and ii):
- i. Individual has tried Repatha (evolocumab injection for subcutaneous use); AND
 - ii. Individual has experienced inadequate efficacy or significant intolerance according to the prescriber; AND
- E) Medication is prescribed by, or in consultation with, a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders.

Note:

* Individuals may have a diagnoses that pertain to more than one FDA-approved indication, therefore, consider review under different approval conditions, if applicable (e.g., individuals with HeFH have had a clinical ASCVD event, individuals with primary hyperlipidemia may have HeFH).

Conditions Not Covered

Alirocumab (Praluent®) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Concurrent use of Praluent with Repatha (evolocumab injection for subcutaneous use) or Juxtapid® (lomitapide capsules).**

References

1. U.S. Food and Drug Administration. Drugs@FDA. U.S. Department of Health & Human Services: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>

Revision History

Type of Revision	Summary of Changes	Approval Date
New Policy	--	10/28/2020

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