### Praluent

#### Description

**Praluent (alirocumab)**

#### Background

Praluent is used in addition to diet and maximally tolerated statin therapy in adult patients with heterozygous familial hypercholesterolemia (HeFH) or patients with clinical atherosclerotic cardiovascular disease such as heart attacks or strokes, who require additional lowering of LDL cholesterol. HeFH is an inherited condition that causes high levels of low-density lipoprotein (LDL) cholesterol. Praluent provides another treatment option for patients with known cardiovascular disease who have not been able to lower their LDL cholesterol enough on statins. (1).

Praluent is an antibody that targets a specific protein, called PCSK9, which works by reducing the number of receptors on the liver that remove LDL cholesterol from the blood. By blocking PCSK9’s ability to work, more receptors are available to rid LDL cholesterol from the blood and, as a result, lower LDL cholesterol levels (1).

#### Regulatory Status

FDA Indicated for: Praluent is a PCSK9 (Proprotein Convertase Subtilisin Kexin Type 9) inhibitor antibody indicated as adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-cholesterol (LDL-C) (1).

#### Limitations of Use:

The effect of Praluent on cardiovascular morbidity and mortality has not been determined (1).
Praluent exposure increased in a dose-dependent manner in patients and LDL-C reduction reached apparent nadir after 150 mg administered once every two weeks (Q2W). Although there are differences in treatment effect among the individual trials, pools of the placebo-controlled and ezetimibe-controlled trials demonstrate point estimates in the range of 30 to 60 percentage point lowering with overlapping 95% confidence intervals. Based on the preferred FDA analysis, the estimated mean reduction for Praluent across trials was between 36% and 58% (2-4).

Physicians often measure CK in patients about to begin statins or already on statins. Many physicians will not start or continue statins to lower LDL-C in asymptomatic patients with high CK because of concern about possible statin-induced myositis-rhabdomyolysis. High pretreatment CK, predominantly 1 to 5 times the UNL, as in the current report, should not be an impediment to start or continue statins to lower LDLC (5).

Spectrum of statin-associated muscle adverse events: (6)

1. Myalgia—unexplained muscle discomfort often described as “flu-like” symptoms with normal CK level. The spectrum of myalgia complaints includes:
   - Muscle aches
   - Muscle soreness
   - Muscle stiffness
   - Muscle tenderness
   - Muscle cramps with or shortly after exercise (not nocturnal cramping).

2. Myopathy—muscle weakness (not attributed to pain and not necessarily associated with elevated CK)

3. Myositis—muscle inflammation

4. Myonecrosis—muscle enzyme elevations or hyperCKemia
   - Mild > 3-fold greater than baseline untreated CK levels or normative upper limit that are adjusted for age, race, and sex
   - Moderate ≥ 10-fold greater than untreated baseline CK levels or normative upper limit that are adjusted for age, race, and sex
   - Severe ≥ 50-fold above baseline CK levels or normative upper limit that are adjusted for age, race, and sex

5. Myonecrosis with myoglobinuria or acute renal failure (increase in serum creatinine ≥ 0.5 mg/dL) (clinical rhabdomyolysis)

Statin intolerance is widely defined as not being able to tolerate a registered statin dose, due to side effects such as myalgia-myopathy, myositis, or elevation of serum liver enzyme activities. Statin intolerance has been also described as a clinical syndrome with the following characteristics: (7)
1. The inability to tolerate at least 2 different statins – one statin at the lowest starting average daily dose and the other statin at any dose
2. Intolerance associated with confirmed, intolerable statin-related adverse effect(s) or significant biomarker abnormalities
3. Symptom or biomarker changes resolution or significant improvement upon dose decrease or discontinuation
4. Symptoms or biomarker changes not attributable to established predispositions such as drug-drug interactions and recognized conditions increasing the risk of statin intolerance

The ACC Statin Intolerance App guides clinicians through the process of managing and treating patients who report muscle symptoms while on statin therapy. The App is available for free online at Tools.ACC.org/StatinIntolerance or for download in the App stores. Search “ACC Statin Intolerance.”

The safety and efficacy of Praluent in pediatric patients 18 years or less have not been established (1).

**Related policies**

Juxtapid, Repatha

**Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Praluent may be considered **medically necessary** in patients 18 years of age or older for the treatment of heterozygous familial hypercholesterolemia (HeFH) or for patients that have atherosclerotic cardiovascular disease (ASCVD) that require additional lowering of LDL-C and if the conditions indicated below are met.

Praluent is considered **investigational** in patients who are less than 18 years of age and for all other indications.

**Prior-Approval Requirements**

**Age**

18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:
1. Heterozygous familial hypercholesterolemia (HeFH)
   a. Provided documentation (medical records, laboratory reports) of baseline and/or current LDL-C level ≥ 100 mg/dL in the past 90 days

   AND ONE of the following:
   a. Provided documentation (medical records, patient's chart) of confirmed diagnosis by LDL-R DNA Sequencing Test or APOB (hypercholesterolemia) Mutation Analysis
   b. Dutch Lipid Clinic Network Criteria score > 5
   c. Simon-Broome Diagnostic Criteria for definite familial hypercholesterolemia

2. Atherosclerotic cardiovascular disease (ASCVD)
   a. Laboratory report or medical records of LDL-C 70 mg/dL or greater in the past 90 days

   AND ONE of the following for ASCVD:
   a. Documented history of ONE of the following atherosclerotic cardiovascular disease (ASCVD) or cardiovascular events:
      i. Acute coronary syndrome
      ii. Myocardial infarction
      iii. Stable or unstable angina
      iv. Coronary or other arterial revascularization procedure (such as PTCA, CABG)
      v. Transient ischemic attack (TIA)
      vi. Peripheral arterial disease presumed to be of atherosclerotic origin
      vii. Findings from CT angiogram or catheterization consistent with clinical ASCVD

   b. At high risk for atherosclerotic cardiovascular disease (ASCVD) or cardiovascular event based on 10-year risk score used by ONE of the following tools:
      i. ASCVD Pooled Cohort Risk Assessment—score greater than or equal to 7.5%
      ii. Framingham Risk Score—score greater than or equal to 20%

   AND ALL of the following for ALL diagnoses:
   1. Patient will be assessed for response (ie., LDL-C reduction) and adherence to the prescribed lipid lowering regimen after 3 months
2. **NO** dual therapy with another proprotein convertase subtilisin/kexin type 9 inhibitor or Juxtapid

3. Patient **MUST** have tried the preferred product (Repatha) unless the patient has a valid medical exception (e.g. inadequate treatment response, intolerance, contraindication)

**AND ONE** of the following for **ALL** diagnoses:

1. Inadequate response to 3 months of prior therapy with at least **ONE** trial of a high intensity statin in combination with Zetia (ezetimibe)

2. Intolerance to a statin
   a. Provide medical records of documentation of the following intolerable adverse reactions with **ONE** of the following:
      i. Intolerable and persistent (ie: more than 2 weeks) muscle symptoms (eg., muscle pain, weakness, cramps) with **ONE** of the following:
         1) Myalgia (muscle symptoms without CK elevations) –Patient has undergone prior therapy with at least **TWO** trials of different statins with or without Zetia (ezetimibe) with a documented reappearance of the muscle symptoms
         2) Myositis (muscle symptoms with CK elevations) –Documentation provided indicated creatinine kinase (CK) levels greater than 3 times upper normal limit and/or rhabdomyolysis with CK levels greater than 2,500 IU/L
   b. Intolerable and persistent hepatotoxicity after **TWO** trials of different statins with or without Zetia (ezetimibe) with **ALL** of the following:
      i. Documentation indicating persistent elevations (>3 times the upper limit of normal occurring on 2 more occasions) of serum transaminases or the presence of jaundice
      ii. Secondary causes of elevations in hepatic transaminase levels have been ruled out (eg., infection, medications, herbal supplements)

3. Contraindication to a statin must have **ONE** of the following:
   a. Currently pregnant or may become pregnant
   b. Nursing mother

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.
Prior – Approval Renewal Requirements

Age
18 years of age or older

Diagnoses
Patient must have ONE of the following:

1. Heterozygous familial hypercholesterolemia (HeFH)
2. Atherosclerotic cardiovascular disease (ASCVD)

AND ALL of the following:

a. Documentation has been provided indicating the reduction in LDL-C (i.e., chart notes, medical record, and/or laboratory reports) of ONE of the following:
   i. Percentage reduction of LDL-C level is greater than or equal to (≥) 40%, compared to the level immediately prior to starting a PCSK9 inhibitor
   ii. Absolute LDL-C is less than (<) 100mg/dL
b. Patient will be assessed for adherence to the prescribed lipid lowering regimen
c. NO dual therapy with another proprotein convertase subtilisin/kexin type 9 inhibitor or Juxtapid
d. Patient MUST have tried the preferred product (Repatha) unless the patient has a valid medical exception (e.g. inadequate treatment response, intolerance, contraindication)

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

<table>
<thead>
<tr>
<th>High-intensity statin therapy</th>
<th>Moderate-intensity statin therapy</th>
<th>Low-intensity statin therapy</th>
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<tbody>
<tr>
<td>Atorvastatin (Lipitor) 40 - 80mg a day</td>
<td>Atorvastatin (Lipitor ) 10 - 20mg a day Rosuvastatin (Crestor ) 5 - 10mg a day Simvastatin (Zocor ) 20 - 40mg a day Pravastatin (Pravachol ) 40 - 80mg a day Lovastatin (Mevacor ) 40mg a day Fluvastatin XL (Lescol XL ) 80mg a day</td>
<td>Simvastatin (Zocor) 10mg a day Pravastatin (Pravachol) 10 - 20mg a day Lovastatin (Mevacor) 20mg a day Fluvastatin (Lescol) 20 -</td>
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Praluent is used in addition to diet and maximally tolerated statin therapy in adult patients with heterozygous familial hypercholesterolemia (HeFH) or patients with clinical atherosclerotic cardiovascular disease such as heart attacks or strokes, who require additional lowering of LDL cholesterol. Praluent is an antibody that targets a specific protein, called PCSK9, which works by reducing the number of receptors on the liver that remove LDL cholesterol from the blood. By blocking PCSK9’s ability to work, more receptors are available to get rid of LDL cholesterol from the blood and, as a result, lower LDL cholesterol levels. The safety and efficacy of Praluent in pediatric patients 18 years or less have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Praluent while maintaining optimal therapeutic outcomes.
References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>July 2015</td>
<td>Addition to PA</td>
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<tr>
<td>August 2015</td>
<td>Removal of non-familial hypercholesterolemia and change to Atherosclerotic cardiovascular disease and removal of documented that the patient has primary severe elevations of baseline and/or current LDL-C of ≥ 190 mg/dL and/or history or presence of xanthomas and removal of laboratory report or medical records of triglyceride level greater than 400 mg/dL in the past 30 days. Change the quantity limits to 90 days. Addition of lipidologist and no dual therapy with Juxtapid and Kynamro. Change in the ASVCD score from 7.5% to 15%.</td>
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September 2015  Annual Review
Addition of Dutch Lipid Clinic Network Criteria score \( \geq 8 \) and Simon-Broome Diagnostic Criteria for definite familial hypercholesterolemia to heterozygous familial hypercholesterolemia. Addition of med chart. Removal of baseline HDL-C level is less than 60 mg/dL, the patient must have at least two of the following or if greater than 60 mg/dL, the patient must have at least three of the following risk factors for coronary artery disease (CAD): Advancing age, Female: 55 years of age or older, Male: 45 years of age or older, Baseline or current LDL-C \( \geq 160 \) mg/dL, family history of premature CAD with onset \(< 55\) years in a first degree male relative, family history of premature CAD with onset \(< 65\) years in a first degree female relative, HDL-C less than 40 mg/dL, hypertension (BP equal to or greater than 140/90 mmHg or on hypertensive medication), polycystic ovary syndrome and change of active liver disease from the contraindications to intolerance section
Addition of “Current utilization, including samples, does not guarantee approval of coverage,” to the criteria

December 2015  Annual review

August 2016  Addition of inadequate response to initial therapy and an increase strength is needed and percentage reduction of LDL-C level is greater than or equal to \( \geq 20\% \), compared to the level immediately prior to starting a PCSK9 inhibitor to the renewal section and documentation in the past 60 days for LDL levels
Policy number change from 5.16.06 to 5.40.06

September 2016  Annual editorial review and reference update
Change in intolerable and persistent (ie: more than 2 weeks) muscle symptoms (eg., muscle pain, weakness, cramps) with ALL of the following to ONE of the following and addition of those terms
Change from documentation provided indicated creatinine kinase (CK) levels greater than 10 times upper normal limit and/or rhabdomyolysis with CK levels greater than 10,000 IU/L – to 5 times and 2,500 IU/L

December 2016  Annual review
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<th>Event Description</th>
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| September 2017  | Annual editorial review and reference update  
Removal of the following requirements: prescribed or recommended by cardiologist, endocrinologist, or lipidologist.  
Change to the requirement for intolerable and persistent muscle symptoms and hepatotoxicity from “one high intensity statin and one low or moderate intensity statin with Zetia” to “two trials of different statins with or without Zetia”.  
Change of ASCVD LDL level from 100 to 70.  
Change of ASCVD Pooled Cohort Risk Assessment from 15% to 7.5%, change in intolerance to a statin caused by muscle symptoms the requirement of combination of Zetia and change in CK levels from 5 times ULN to 3 times ULN per SME |
| December 2017   | Annual editorial review  
Change of HeFH Dutch Lipid clinical network score from ≥8 to >5, change of initiation LDL levels from past 60 days to past 90 days, change in initiation approval length from 3 months to 12 months, addition of inadequate response, intolerance, contraindication to statins to all diagnoses for initiation |
| July 2018       | Change of initiation LDL levels from past 60 days to past 90 days, change in initiation approval length from 3 months to 12 months, addition of inadequate response, intolerance, contraindication to statins to all diagnoses for initiation |
| August 2018     | Addition of 150mg to initiation approval, redefined inadequate response to statins  
Annual review  
Annual editorial review and reference update. Removal of Kynamro from dual therapy questions  
Addition of ACC Statin Intolerance App to regulatory status  
Annual review and reference update  
Annual review. Addition of requirement to trial preferred product |

**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective on January 1, 2020.