PCKS9 INHIBITORS PRIOR AUTHORIZATION CRITERIA
PRALUENT (ALIROCUMAB) AND REPATHA (EVOLOCUMAB)

FDA-Approved Indications

- Alirocumab (Praluent): Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of LDL-cholesterol (LDL-C)

- Evolocumab (Repatha): Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with homozygous familial hypercholesterolemia, heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of LDL-cholesterol (LDL-C)

Mechanism of Action

The PCSK9 enzyme binds to LDL receptors present on the surface of hepatocytes and degrades the receptors. This results in fewer LDL receptors available on hepatocytes to remove excess LDL-C from the blood. Therefore, PCSK9 inhibitors hinder this process and lower LDL levels.

Background

- Clinical atherosclerotic cardiovascular disease (ASCVD) includes acute coronary syndromes, or a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin.

- The 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults makes the following statements:
  - Lower-intensity statin therapy has been shown to reduce ASCVD events. Therefore, individuals that merit guideline-recommended statin therapy should be treated with the maximum appropriate intensity of a statin that does not cause adverse effects.
  - The long-term adverse effects of statin-associated cases of diabetes over a 10-year period are unclear and are unlikely to be equivalent to a myocardial infarction, stroke, or ASCVD death.
  - No evidence was found that titration or combination drug therapy to achieve specific LDL-C or non-HDL-C levels or percent reduction improved ASCVD outcomes. Therefore, this guideline does not recommend their use as performance measures.
The panel could find no data supporting the routine use of nonstatin drugs combined with statin therapy to reduce further ASCVD events.

In individuals at higher ASCVD risk receiving the maximum tolerated intensity of statin therapy who continue to have a less-than-anticipated therapeutic response, addition of a nonstatin cholesterol-lowering drug(s) may be considered if the ASCVD risk-reduction benefits outweigh the potential for adverse effects. Preference should be given to drugs shown to reduce ASCVD events in RCTs.

- According to the National Lipid Association, statins should be the initial treatment for all adults with familial hypercholesterolemia. Ezetimibe (Zetia), niacin, and bile acid sequestrants are reasonable treatment options for intensification of therapy, or for those intolerant of statins.

<table>
<thead>
<tr>
<th>Low-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>High-Intensity Statin Therapy</th>
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</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL-C by &lt; 30% on average</td>
<td>Daily dose lowers LDL-C by 30% to 50%, on average</td>
<td>Daily dose lowers LDL-C by ≥ 50%, on average</td>
</tr>
<tr>
<td>• Simvastatin 10 mg</td>
<td>• Atorvastatin 10-20 mg</td>
<td>• Atorvastatin 40-80 mg</td>
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<tr>
<td>• Pravastatin 10-20 mg</td>
<td>• Rosuvastatin (Crestor) 5-10 mg</td>
<td>• Rosuvastatin (Crestor) 20-40 mg</td>
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<tr>
<td>• Lovastatin 20 mg</td>
<td>• Simvastatin 20-40 mg</td>
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<tr>
<td>• Fluvastatin 20-40 mg</td>
<td>• Pravastatin 40-80 mg</td>
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<tr>
<td>• Pitavastatin (Livalo) 1 mg</td>
<td>• Lovastatin 40 mg</td>
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<tr>
<td></td>
<td>• Fluvastatin XL (Lescol XL) 80 mg</td>
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<td></td>
<td>• Fluvastatin 40 mg twice daily</td>
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<td></td>
<td>• Pitavastatin (Livalo) 2-4 mg</td>
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</tbody>
</table>

**Approval Criteria**

When a benefit, alirocumab (Praluent) or evolocumab (Repatha) may be approved when the following criteria are met:

**Homozygous Familial Hypercholesterolemia [evolocumab (Repatha) only]**

1. The member is ≥ 13 years of age.

   **AND**

2. Evolocumab (Repatha) must be prescribed by or in consultation with a cardiologist, lipid specialist, or endocrinologist and there is clinical documentation of one of the following (a or b):
   
   a. Genetic confirmation of two mutant alleles at the LDLR, APOB, OCSK9, or LDLRAP1 gene locus

      **OR**

   b. An untreated LDL-C of > 500 mg/dL (or a treated LDL-C of > 300 mg/dL) with either:
      
      i. Cutaneous or tendon xanthoma before age 10 years

      **OR**

      ii. Evidence of heterozygous familial hypercholesterolemia in both parents

   **AND**
3. Evolocumab (Repatha) will be used concomitantly with a statin (which is dosed at its maximally tolerated dose), unless all statins are contraindicated or not tolerated.

AND

4. Evolocumab (Repatha) is not being used concomitantly with lomitapide (Juxtapid), mipomersen (Kynamro), or another PCSK9 inhibitor.

**Heterozygous Familial Hypercholesterolemia**

1. The member is ≥ 18 years of age.

AND

2.Alirocumab (Praluent) and evolocumab (Repatha) must be prescribed by or in consultation with a cardiologist, lipid specialist, or endocrinologist and there is clinical documentation of one of the following (a, b, or c):
   a. Presence of causal mutation for familial hypercholesterolemia by genetic testing  
   OR
   b. Physical signs of FH, such as presence of tendon xanthomas, corneal arcus in a member < 45 years of age, tuberous xanthomas, or xanthelasma  
   OR
   c. Clinical diagnosis based on the WHO criteria/Dutch Lipid Clinical Network criteria with a score > 8 points or the Simon Broome register diagnostic criteria with a criterion for definite familial hypercholesterolemia

AND

3. Documentation of LDL-C ≥ 190 mg/dL (≥ 130 mg/dL if < 20 years of age) prior to initiating lipid-lowering therapy.

AND

4. Treatment with at least two 8-week trials of different high-intensity statins has been ineffective*. Adherence to the current statin regimen must be evidenced by consistent pharmacy claims over the past 8 weeks, unless new to the plan. Note: If treatment with one high-intensity statin plus ezetimibe (Zetia) was ineffective after 8 weeks of treatment, treatment with a second high-intensity statin will not be required.

AND

5. The member will be using the PCSK9 inhibitor concomitantly with a maximally-tolerated statin.

*Treatment is considered ineffective if it results in a < 50% reduction in LDL-C or an LDL-C ≥ 130 mg/dL. In higher risk patients, treatment is considered ineffective if it results in an LDL-C ≥ 100 mg/dL.

1. Higher risk is defined as: clinically evident coronary heart disease (CHD) or other atherosclerotic cardiovascular disease, diabetes, a family history of very early CHD (men < 45 years of age and women < 55 years of age), current smoking, or high lipoprotein (a) 50 ≥ mg/dL.
Hypercholesterolemia, ASCVD

1. Alirocumab (Praluent) and evolocumab (Repatha) must be prescribed by or in consultation with a cardiologist, lipid specialist, or endocrinologist.

AND

2. The member (≥18 years of age) has a documented diagnosis of clinical atherosclerotic cardiovascular disease (ASCVD), defined as one of the following: acute coronary syndrome, or a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin.

AND

3. Treatment with at least two 8-week trials of different high-intensity statins has been ineffective (LDL-C ≥ 100 mg/dL). Adherence to the current statin regimen must be evidenced by consistent pharmacy claims over the past 8 weeks, unless new to the plan. Note: If treatment with one high-intensity statin plus ezetimibe (Zetia) was ineffective (LDL-C ≥ 100 mg/dL) after 8 weeks of treatment, treatment with a second high-intensity statin will not be required.

AND

4. The member will be using the PCSK9 inhibitor concomitantly with a maximally-tolerated statin.

AND

5. Confirmation of patient enrollment in a lipid clinic or disease management program.

Reauthorization Criteria

Reauthorization Criteria


OR

2. HeFH: Documentation of an LDL-C reduction by at least 50% from pre-treatment level or an LDL-C < 130 mg/dl (if pre-treatment LDL-C was > 130 mg/dl).

OR

3. Hypercholesterolemia, ASCVD: Documentation that LDL-C < 100 mg/dL or there has been at least a 40% LDL-C reduction from pre-treatment level.

AND (All Indications)

4. Documentation that the member has been adherent to treatment with statin and PCSK9 inhibitor as demonstrated by consistent pharmacy claims.

AND (ASCVD only)

5. Hypercholesterolemia, ASCVD: Confirmation of patient enrollment in a lipid clinic or disease management program.
Quantity Level Limitation

Members who meet the above clinical criteria will be eligible for approval of 2 syringes/autoinjectors per 28 days or 6 syringes/autoinjectors per 84 days (if benefit allows). The following additional criteria must be met for approval of 3 syringes/autoinjectors per 30 days or 9 syringes/autoinjectors per 90 days (if benefit allows):

1. The member has a diagnosis of homozygous familial hypercholesterolemia.

Duration of Authorization

- Initial: If approved, initial coverage will be granted for up to 6 months.
- Maintenance: If approved, maintenance coverage will be granted for up to 12 months.

References