Pharmacy Policy Bulletin

Title: PCSK9 inhibitors
Policy #: Rx.01.170

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, gender or quantity restrictions. Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

_intent:
The intent of this policy is to communicate the medical necessity criteria for evolocumab (Repatha) and alirocumab (Praluent) as provided under the member's pharmacy benefit.

_description:
Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a serine protease synthesized primarily by the liver and intestines. PCSK9 promotes the degradation of low density lipoprotein (LDL) receptors, thus preventing them from being recycled back to the plasma membrane where they can bind more LDL. Inhibitors of PCSK9 increase recycling of LDL receptors which in turn increases the capacity to remove LDL cholesterol (LDL-C) from the blood. These agents are monoclonal antibodies administered subcutaneously.

Alirocumab (Praluent) and evolocumab (Repatha) are 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-C. Evolocumab (Repatha) is also indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia who require additional lowering of LDL-C.

According to current guidelines, HMG-CoA reductase inhibitors (statins) are the mainstay of pharmacologic therapy for treating elevated LDL-C for both primary and secondary prevention of atherosclerotic cardiovascular disease. Lifestyle modifications are a critical component of treating elevated LDL-C and should be used in conjunction with pharmacologic therapy.

Clinical trials of PCSK9 inhibitors demonstrated reductions in LDL-C approximately 50-60%. Reauthorization criteria will include a reduction from baseline of 25% or greater, which will assess adherence with the medication.
**Policy:**

I. Homozygous Familial Hypercholesterolemia – Evolocumab (Repatha) is approved when documentation is provided of ALL of the following:

   A. Diagnosis of Homozygous Familial Hypercholesterolemia

   B. Used as an adjunct to lipid lowering treatments and a low fat diet with ONE of the following:
      1. Genetic confirmation of 2 mutant alleles at the LDL receptor, Apo B, PCSK9, or ARH adaptor protein gene locus
      2. Untreated LDL-C > 500 mg/dL or treated LDL cholesterol ≥ 300mg/dL or treated non-HDL cholesterol ≥ 330 mg/dL together with either of the following:
         a. Cutaneous or tendinous xanthoma prior to 10 years of age
         b. Elevated LDL cholesterol prior to lipid-lowering therapy consistent with HeFH in both parents as listed below:

         | Age (years) | Total cholesterol (LDL cholesterol) (mg/dL) |
         |-------------|-------------------------------------------|
         | < 18        | 220 (155)                                 |
         | 20-29       | 240 (170)                                 |
         | 30-39       | 270 (190)                                 |
         | ≥ 40        | 290 (205)                                 |

   C. ONE of the following:
      1. Inadequate response to one of the following medications in combination with ezetimibe:
         a. simvastatin (daily dose ≥ 40mg)
         b. atorvastatin (daily dose ≥ 20mg)
         c. rosuvastatin (Crestor) (daily dose ≥ 10mg)
      2. Member has experienced ONE of the following:
         a. Rhabdomyolysis or muscle symptoms with creatine kinase (CK) elevations >10 times upper limit of normal on any statin OR
         b. Myalgia (muscle symptoms without CK elevations) or myositis (muscle symptoms with CK elevations <10 times upper limit of normal with TWO stations within the past year

Authorization duration: 6 months
Re-authorization criteria: evolocumab (Repatha) is re-approved when there is a reduction in LDL-C of at least 25% since initiation of therapy
Re-authorization duration: 12 months

I. Hypercholesterolemia - Alirocumab (Praluent) and evolocumab (Repatha) are approved with documentation is provided of ALL of the following:

   A. ONE of the following:
      1. Diagnosis of heterozygous familial hypercholesterolemia by ONE of the following:
         a. Genetic confirmation of a mutation at the LDL receptor, Apo B, PCSK9; or
         b. Untreated LDL cholesterol greater than or equal to 190mg/dL in members 18 years of age and older or greater than or equal to 155 mg/dL in members less than 18 years of age and one of the following:
            i. Tendon xanthomas in the member, first degree relative (parent, sibling, child), or second degree relative (grandparent, aunt, uncle)
            ii. Family history of elevated total cholesterol greater than 290 mg/dl in a first degree relative (parent, sibling, child) or second degree relative (grandparent, aunt, uncle)
            iii. Family history of coronary disease in first degree relative (parent, sibling, child) less than 60 years of age or second degree relative (grandparent, aunt, uncle) less than 50 years of age
      2. Clinical atherosclerotic cardiovascular disease and BOTH of the following:
         a. ONE of the following:
i. Diagnosed by stress test, angiography (cardiac, peripheral, cerebral), CT angiography

ii. History of an atherosclerotic event (e.g. myocardial infarction, angina, stroke, claudication, carotid stenosis)

iii. Arterial intervention for atherosclerotic cardiovascular disease (e.g. coronary stent, peripheral artery stent, carotid endarterectomy, carotid stent)

b. LDL-C ≥ 70 mg/dL

B. ONE of the following:

1. Inadequate response to a minimum 8-week trial of ezetimibe in combination with ONE high intensity statin (e.g. atorvastatin ≥ 40mg, rosuvastatin ≥ 20mg, etc)

2. Member has experienced ONE of the following:

   a. Rhabdomyolysis or muscle symptoms with CK elevations >10 times upper limit of normal on any statin; or
   
   b. Myalgia (muscle symptoms without CK elevations) or myositis (muscle symptoms with CK elevations <10 times upper limit of normal with TWO statins
   
   c. Hepatotoxicity secondary to statins defined as increased transaminases > 3 times upper limit of normal
   
   d. Concurrent liver disease documented by ONE of the following:

      i. Child Pug A or worse
      ii. Persistent elevation in transaminases (> 3 times upper limit of normal) for at least 6 weeks

C. Inadequate response or inability to tolerate alirocumab (Praluent) -applies to evolocumab

Authorization duration: 6 months
Re-authorization criteria: evolocumab (Repatha) and alirocumab (Praluent) are re-approved when there is a sustained reduction in LDL-C of at least 25% since initiation of therapy
Re-authorization duration: 12 months

**Black Box Warning:**
N/A

**Guidelines:**
Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

**BENEFIT APPLICATION**

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the pharmacy benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

**References:**


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<tr>
<th>Applicable Drugs:</th>
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<tr>
<td>Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.</td>
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<table>
<thead>
<tr>
<th>Brand Name</th>
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<tbody>
<tr>
<td>Praluent</td>
<td>alirocumab</td>
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<tr>
<td>Policy Version Number: 8.00</td>
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<tr>
<td>P&amp;T Approval Date: January 12, 2017</td>
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<td>Policy Effective Date: March 01, 2017</td>
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<td>Next Required Review Date: January 12, 2018</td>
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