Pharmacy Policy

PCSK9 Inhibitors

Policy Number: 9.059
Version Number: 3.0
Version Effective Date: 09/07/2017

Product Applicability □ All Plan* Products

Well Sense Health Plan
- New Hampshire Medicaid
- NH Health Protection Program

Boston Medical Center HealthNet Plan
- MassHealth
- Qualified Health Plans/ConnectorCare/Employer Choice Direct
- Senior Care Options

Note: Disclaimer and audit information is located at the end of this document.

Policy Summary

The Plan may authorize coverage of Praluent™ and Repatha™ when appropriate criteria are met.

Description of Item or Service

Familial hypercholesterolemia (FH) is a genetic disorder that causes significant increases in low-density lipoprotein (LDL) cholesterol and total cholesterol (TC). There are two forms of FH; heterozygous FH occurring in approximately 1 case per 500 persons, and homozygous FH occurring in 1 case per 1 million persons (United States data). There is no known cure for homozygous FH; patients are managed with lipid apheresis, lipid lowering therapies, and when available, liver transplantation. According to the Simon Broome diagnostic criteria, heterozygous FH is characterized by:

- LDL-C > 155mg/dL or TC > 260mg/dL in children, LDL-C >190mg/dL or TC >290mg/dL in adults; and
- Tendon xanthomas or evidence of this in a first or second degree relative; or
- DNA evidence of an LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation.

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A high level of LDL cholesterol is correlated with mortality from cardiovascular disease and it is the key modifiable risk factor for cardiovascular disease. The National Cholesterol Education Program (NCEP) – Adult Treatment Panel III recommends statins as first-line drugs when LDL-lowering drugs are indicated to achieve LDL-C treatment goals. The 2013 American College of Cardiology and the American Heart Association (ACC/AHA) clinical practice guideline for the treatment of blood cholesterol levels to reduce atherosclerotic cardiovascular disease (ASCVD) risk in adults establishes recommendations for the management of cholesterol. According to the guideline, there is no evidence to support continued use of specific LDL-C and/or non-high-density lipoprotein cholesterol (non-HDL-C) treatment targets. Rather, the appropriate intensity of statin therapy should be used to reduce risk in those most likely to benefit.

This guideline recommends moderate- or high-intensity statin therapy for 4 groups: 1) Patients who have clinical ASCVD(i.e. coronary heart disease, stroke, peripheral arterial disease, all of presumed atherosclerotic origin) without New York Heart Association (NYHA) class II-IV heart failure or receiving hemodialysis; 2) patients with an LDL-C of 190 mg/dL or higher; 3) patients with type 1 or type 2 diabetes who are between 40 and 75 years of age and an LDL-C 70-189 mg/dL without ASCVD; and 4) patients with an estimated 10-year risk of ASCVD 7.5% or higher (using the Pooled Cohort Equations) and an LDL-C 70-189 mg/dL who are between 40 and 75 years of age without clinical ASCVD or diabetes. Use of high intensity statin therapy (atorvastatin 80mg or rosuvastatin 20mg) is expected to reduce LDL-C by at least 50% which correlates with reduced risk for ASCVD and mortality. The guideline also emphasizes the importance of adopting a heart-healthy lifestyle to prevent and control high blood cholesterol.

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are a new class of drugs for the management hypercholesterolemia. PCSK9 inhibitors are monoclonal antibodies that exert their effect by targeting and inactivating hepatic PCSK9 which is involved in the degradation of LDL-C receptors in the liver. The increased LDL-C receptors in the liver leads to increased clearance of LDL cholesterol from the bloodstream which ultimately results in lower LDL-C levels.

Praluent™ (alirocumab) is indicated as an 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 low-density lipoprotein (LDL) cholesterol. Praluent™ was approved based on results from five prospective, randomized, double-blind, placebo controlled trials with 3499 patients (36% with Heterozygous FH, and 54% with ASCVD). All patients were receiving a maximally tolerated dose of statin, with or without other lipid modifying therapies. The trials were at least 52 weeks in duration with a primary efficacy endpoint of “mean percent change in LDL-C from baseline” measured at 24 weeks. All studies met their primary efficacy endpoint at 24 weeks. Patients had an average reduction in LDL cholesterol ranging from 36 to 59 percent, compared to placebo. The recommended dosing for Praluent™ is 75mg subcutaneous injection once every two weeks, if LDL-C response is inadequate; this can be increased to a maximum dose of 150mg every two weeks. LDL-C reduction occurs within 2 weeks after initiation of treatment with Praluent™. The most commonly occurring adverse reaction with Praluent™ was influenza, injection site reactions and nasopharyngitis. Long-term safety data are still pending.

Repatha™ (evolocumab) is indicated as an 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 low-density lipoprotein (LDL) cholesterol; and other LDL-
lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C. Repatha™ was approved based on the results from one 52-week placebo-controlled trial and eight 12-week placebo-controlled trials in patients with primary hyperlipidemia, including two that specifically enrolled patients with HeFH and one that enrolled participants with HoFH. In one of the 12-week studies, 329 patients with HeFH, who required additional lowering of LDL cholesterol despite statins with or without other lipid-lowering therapies, were randomized to receive Repatha™ or placebo for 12 weeks. Participants taking Repatha™ had an average reduction in LDL cholesterol of approximately 60 percent, compared to placebo. The recommend dosing for HeFH or clinical ASCVD is 140mg every 2 weeks or 420mg subcutaneous injection once monthly, and for HoFH, 420mg once monthly. The most common side effect reported with Repatha™ includes nasopharyngitis, upper respiratory tract infection, flu, back pain, and injection site reactions. Long-term safety has not been determined.

Recommendation for the use of PCSK9 inhibitors have not been addressed in pertinent cholesterol management guidelines at this time. Despite, significant LDL-C lowering effect, the effect of Praluent™ and Repatha™ on cardiovascular morbidity and mortality has not been determined.

Policy

The Plan may approve coverage of Praluent™ or Repatha™ for members meeting the following criteria:

Prior Authorization

A prior authorization request will be required for all prescriptions for Praluent™ or Repatha™. These requests will be approved when the following criteria are met:

Initial therapy (Duration of Approval – Maximum of 6 months)

Documentation of the following (must be documented in medical records):

1. One of the following:
   a. Age is 18 years or older and member has a diagnosis of heterozygous familial hypercholesterolemia (Confirmed via genotype or using WHO/Dutch Lipid Network or Simon Broome criteria); or
   b. If requesting Repatha, member age is 13 year or older and has a diagnosis of homozygous familial hypercholesterolemia (Confirmed via genotype or using WHO/Dutch Lipid Network or Simon Broome criteria); AND

2. Either of the following:
   a. Inadequate LDL reduction while adherent to a minimum of 90 day continuous use of atorvastatin 80mg or rosuvastatin 40mg in combination with Zetia evidenced by:
      i. Current LDL-C greater than or equal to 100mg/dl; AND
      ii. Less than a 50 percent reduction in LDL-C from baseline; OR

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b. Inability to tolerate a high intensity statin (atorvastatin 80mg or rosuvastatin 40mg); AND Inadequate response while adherent to a minimum of 90 day continuous use of a maximum tolerated dose of a non-high intensity statin and Zetia evidenced by:
   i. Current LDL-C greater than or equal to 100mg/dl; AND

3. Current statin at maximum tolerated dose will be continued with Praluent™ or Repatha™; AND

4. Medication is prescribed by, or in collaboration with, a cardiologist, endocrinologist, or lipid specialist; AND

5. Appropriate lifestyle modifications have been implemented, including an appropriate lipid-lowering diet that will continue during treatment (including but not limited to the following):
   - Total dietary fat < 35% of total calories
   - Weight loss in overweight patients
   - Aerobic exercise
   - Diet rich in fruits and vegetables

Re-authorization of Therapy (Duration of Approval – Maximum of 12 months)

Prior Authorization is required for all prescriptions for continued treatment beyond the initial approval duration. These requests will be approved when the following criteria are met:

1. Initial criteria were previously met; AND
2. Medical records documenting LDL-C reduction while on Praluent™ or Repatha™ therapy; AND
3. Continued use of statin at highest tolerated dose; AND
4. Member has received counseling regarding cholesterol lowering diet.

Quantity Limitations Apply - see appendix 1

Limitations

The Plan will not approve coverage of Praluent™ or Repatha™ in the following instances:

1. When the criteria above has not been met.
2. When Praluent™ is requested for the treatment of homozygous familial hypercholesterolemia.
3. When member is currently taking Kynamro or Juxtapid.
4. When member is unable to use any statin therapy.

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Clinical Background Information and References


Appendix 1: Quantity Limitations

<table>
<thead>
<tr>
<th>Medication Name</th>
<th>Quantity Limitation</th>
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</thead>
<tbody>
<tr>
<td>Praluent 75mg or 150mg pen</td>
<td>2 prefilled pens per 28 days</td>
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<tr>
<td>Repatha 140mg</td>
<td>3 injections per 28 days</td>
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<tr>
<td>Repatha 420mg</td>
<td>1 infusor per 30 days</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Original Approval Date</th>
<th>Original Effective Date</th>
<th>Policy Owner</th>
<th>Approved by</th>
</tr>
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<tbody>
<tr>
<td>09/10/2015</td>
<td>10/05/2015 (BMCHP); 11/04/2015 (Well Sense)</td>
<td>Pharmacy Services</td>
<td>Pharmacy &amp; Therapeutics (P&amp;T) Committee</td>
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Policy Revisions History

<table>
<thead>
<tr>
<th>Review Date</th>
<th>Summary of Revisions</th>
<th>Revision Effective Date</th>
<th>Approved by</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/12/2016</td>
<td>P&amp;T Annual Review, no changes required</td>
<td>09/15/2016</td>
<td>P&amp;T Committee</td>
</tr>
<tr>
<td>05/11/2017</td>
<td>P&amp;T Annual Review, changed Repatha age restriction from 18 years or older to 13 years or older for homozygous FH, criteria changed to no longer require providers to submit chart notes documenting that member has tried lifestyle modification in past, specified repatha 140mg QL as 3 injections per 28 days, added QL for 420mg infusor</td>
<td>09/07/2017</td>
<td>P&amp;T Committee</td>
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Next Review Date

05/10/2018

Other Applicable Policies

9.002 Mandatory Generic Substitution Policy
9.015 Quantity Limitation Policy
OCA 3.14 Medically Necessary Policy

Reference to Applicable Laws and Regulations, If Any

Disclaimer Information

Medical Policies are the Plan’s guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member’s benefit document, and when appropriate, coordinates with the Member’s health care Providers to consider the individual Member’s health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan’s service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member’s benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

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The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.

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