Utilization Management Policy Name:  Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) Inhibitors – Enhanced and Essential Formularies

Restricted Products:
- Praluent® (alirocumab)
- Repatha® (evolocumab)

FDA Approved Use:

Praluent is a PCSK9 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).

Repatha is a PCSK9 inhibitor antibody indicated:
- to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease.
- as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol (LDL-C).
- as an adjunct to diet 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.

Rationale:

Praluent and Repatha can be used in attempts to treat conditions that have not been validated by the FDA. Other products, such as statins, treat the same condition at a lower cost for members. Quantity limits have been added to ensure safe and effective use.

Criteria Summary:

FDA approved use/medical necessity; trial of effective and lower cost agent; exception to quantity limitation

Criteria for Approval of Restricted Product(s):

1. The patient is 18 years of age or older; AND
2. The patient has a confirmed diagnosis of homozygous familial hypercholesterolemia (HoFH) through ONE of the following:
   a. Genetic confirmation of two mutant alleles at the LDLR, Apo-B, PCSK9, or ARH adaptor protein 1/LDLRAP1 gene locus
   b. Untreated LDL-C >500 mg/dL or treated LDL-C ≥300 mg/dL with ONE of the following:
i. Cutaneous or tendon xanthoma before age 10 years
   ii. Untreated elevated LDL-C levels consistent with heterozygous FH in both parents [untreated total cholesterol >290 mg/dL or untreated LDL-C >190 mg/dL; OR

3. The patient has a “definite” diagnosis of heterozygous familial hypercholesterolemia (HeFH), as determined using the Dutch Lipid Clinic Network criteria by a score of 8 or greater (please see chart on pages 4-5). Please confirm there is medical record documentation of ANY of the following where applicable to the patient:
   a. LDLR gene functional mutation
   b. Patient LDL-C level at baseline, prior to the use of all cholesterol lowering medications
   c. Presence of tendon xanthoma
   d. Presence of arcus corneae at age <45 years
   e. Patient history of coronary artery disease
   f. Patient history of premature cerebral or peripheral vascular disease
   g. First degree relative with tendon xanthoma or arcus corneae
   h. First degree relative age <18 years with LDL >95th percentile
   i. First degree relative with premature coronary artery disease or LDL-C >95th percentile; OR

4. The patient has clinical atherosclerotic cardiovascular disease (ASCVD) defined as one of the following:
   a. ACS (acute coronary syndrome)
   b. History of MI (myocardial infarction)
   c. Stable or unstable angina
   d. Coronary or other arterial revascularization
   e. Stroke
   f. TIA (transient ischemic attack)
   g. PAD (peripheral arterial disease) presumed to be of the atherosclerotic origin; OR

5. The patient has been diagnosed with primary hyperlipidemia and is at moderate to high risk for atherosclerotic disease per American College of Cardiology risk categories; AND

6. The patient is not pregnant; AND

7. One of the following:
   a. The patient is currently taking and adherent to high-intensity statin therapy, OR
   b. The patient is intolerant to at least 2 different statins

NOTE:
- Adherence is defined as the proportion of days covered (PDC) to be 80% or greater over the last 3 months
- High-intensity statin is the equivalent of rosvuastatin 20-40mg, atorvastatin 40-80mg, or simvastatin 80mg
- Intolerance is defined as (1) the inability to tolerate any dose or (2) the inability to increase the dose above the lowest FDA-approved tablet strength; AND

8. For patients with ASCVD or primary hyperlipidemia: While on a maximally tolerated conventional lipid lowering regimen, the patient has a LDL-C ≥ 70 mg/dL (evaluated within the last 3 months); AND

9. If requesting Repatha, the patient has tried/failed treatment with 140mg twice monthly before considering treatment with 420mg once monthly unless the patient has a diagnosis of HoFH; AND

10. Praluent and Repatha will not be used concurrently with each other or with Juxtapid / Kynamro; AND

11. If requesting Praluent, the patient has tried and failed or has a clinical contraindication to Repatha; AND

12. Praluent or Repatha has been prescribed by or in consultation with a specialist in cardiology AND

13. For formularies that exclude (non-formulary) the requested medication, Non-formulary Exception Criteria applies (outlined below)*

Duration of Approval: 12 months

Continuation Criteria:

1. The patient has a prior approval for this medication from Blue Cross NC; AND

2. There is evidence of continued maximally tolerated conventional lipid lowering regimen; AND

3. For patients with ASCVD or Primary hyperlipidemia, they must have one of the following:
   a. While on PCSK9 therapy, the patient has a current LDL-C < 70mg/dL (evaluated within the last month); OR
   b. While on PCSK9 therapy, the patient was able to achieve 45% reduction in LDL-C from baseline; AND

4. The patient is currently taking and adherent to PCSK9 therapy. Adherence is defined as the proportion of days covered (PDC) to be 80% or greater over the last 3 month; AND

5. Praluent and Repatha will not be used concurrently with each other or with Juxtapid / Kynamro; AND

6. If requesting Repatha, the patient has tried/failed treatment with 140mg twice monthly before considering treatment with 420mg once monthly unless the patient has a diagnosis of HoFH; AND

7. Praluent or Repatha has been prescribed by or in consultation with a specialist in cardiology

Duration of Approval: 12 months
Quantity Limitations: quantity limitations apply to brand and associated generic products.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Quantity per Day (unless specified)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praluent 75 mg/mL</td>
<td>2 mL per 28 days</td>
</tr>
<tr>
<td>Praluent 150 mg/mL</td>
<td></td>
</tr>
<tr>
<td>Repatha 140 mg/mL</td>
<td></td>
</tr>
<tr>
<td>Repatha 420mg/3.5mL</td>
<td>3.5mL per 28 days</td>
</tr>
</tbody>
</table>

Quantity Limit Exception Criteria:

1. The quantity (dose) requested is for documented titration purposes at the initiation of therapy (authorization for a 90 day titration period); **AND**
2. The prescribed dose cannot be achieved using a lesser quantity of a higher strength; **AND**
3. The quantity (dose) requested does not exceed the maximum FDA labeled dose, when specified, or to the safest studied dose per the manufacturer’s product insert; **OR**
4. If the quantity (dose) requested exceeds the maximum FDA labeled dose, when specified, or to the safest studied dose per the manufacturer’s product insert, then the prescriber must submit documentation in support of therapy with a higher dose for the intended diagnosis (submitted documentation may include medical records OR fax form which reflects medical record documentation that shows the length of time the requested dose has been used, and what other medications and doses have been tried and failed).

**The Dutch Lipid Clinic Criteria**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family History</strong></td>
<td></td>
</tr>
<tr>
<td>First-degree relative with premature coronary and/or vascular disease (men ≤55 years, women ≤60 years), OR</td>
<td>1</td>
</tr>
<tr>
<td>First-degree relative with known LDL-cholesterol ≥95th percentile for age and sex</td>
<td></td>
</tr>
<tr>
<td>First-degree relative with tendon xanthomata and/or arcus cornealis, OR</td>
<td>2</td>
</tr>
<tr>
<td>Children aged ≤18 years with known LDL-cholesterol ≥95th percentile for age and sex</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical History</strong></td>
<td></td>
</tr>
<tr>
<td>Patient with premature coronary artery disease (age as above)</td>
<td>2</td>
</tr>
<tr>
<td>Patient with premature cerebral or peripheral vascular disease (age as above)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Physical Examination</strong></td>
<td></td>
</tr>
<tr>
<td>Tendon Xanthomas</td>
<td>6</td>
</tr>
<tr>
<td>Arcus cornealis at age ≤45 years</td>
<td>4</td>
</tr>
<tr>
<td><strong>Laboratory Analysis</strong></td>
<td></td>
</tr>
<tr>
<td>LDL-C ≥330</td>
<td>8</td>
</tr>
<tr>
<td>LDL-C 250 – 329</td>
<td>5</td>
</tr>
<tr>
<td>LDL-C 190 – 249</td>
<td>3</td>
</tr>
<tr>
<td>LDL-C 155 – 189</td>
<td>1</td>
</tr>
<tr>
<td>DNA Analysis – functional mutation LDLR, APOB and PCSK9</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total Patient Score</strong></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>A “definite” diagnosis of HeFH requires a patient score ≥8</td>
<td></td>
</tr>
<tr>
<td>A “probable” diagnosis of HeFH requires a patient score 6-7</td>
<td></td>
</tr>
<tr>
<td>A “possible” diagnosis of HeFH requires a patient score 3-5</td>
<td></td>
</tr>
</tbody>
</table>

*Non-formulary Exception Criteria*

Non-Formulary Exception criteria applies on formularies which exclude requested product(s). Satisfactory completion of criteria points (above) may satisfy some, or all, portions of the Non-Formulary Exception Criteria. This criteria is summarized as:

a) Request must be for an FDA approved indication; **AND**

b) Patient must have a trial and failure of up to **TWO** formulary medications or a clinical contraindication/intolerance to those medications not tried.

**References:** all information referenced is from FDA package insert unless otherwise noted below.

**Policy Implementation/Update Information:** Originated: July 2015; Last updated: August 2018

August 2018: Updated statin trial and approval duration requirements

July 2018: Updated criteria to change medical record requirements and clarify preferred product
May 2018: Updated criteria to include coverage for primary hyperlipidemia
May 2017: Clarification of policy in regard to the utilization of Repatha 420mg once monthly in initial approval criteria.
August 2016: Updated criteria to include coverage criteria for ASCVD.
September 2015: Updated criteria to include newest PCSK9 approval, Repatha.
July 2015: Original utilization management criteria issued.

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- If you need these services, contact Customer Service 1-888-206-4697, TTY and TDD, call 1-800-442-7028.

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