Clinical Policy: Alirocumab (Praluent)
Reference Number: ERX.SPMN.183
Effective Date: 01/2017
Last Review Date:

See Important Reminder at the end of this policy for important regulatory and legal information.

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that alirocumab injection (Praluent®) is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Heterozygous Familial Hypercholesterolemia and Atherosclerotic Cardiovascular Disease (must meet all):
      1. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
      2. Age ≥ 18 years;
      3. Diagnosis of one of the following (a or b):
         a. Heterozygous familial hypercholesterolemia (HeFH) defined as a World Health Organization (WHO)/Dutch Lipid Network familial hypercholesterolemia diagnostic criteria score of > 8 as determined by requesting provider (Appendix B);
         b. Atherosclerotic cardiovascular disease (ASCVD) as evidenced by a history of any of the following conditions (i, ii, iii, iv, v, or vi):
            i. Myocardial infarction;
            ii. Stable or unstable angina;
            iii. Coronary or other arterial revascularization;
            iv. Peripheral arterial disease presumed to be of atherosclerotic origin;
            v. Acute coronary syndromes;
            vi. Stroke or transient ischemic attack (TIA);
      4. Recent (within the last 30 days) low-density lipoprotein cholesterol (LDL-C) ≥ 70 mg/dL;
      5. Member has received a high intensity statin (Appendix C) adherently for at least the last 4 months, unless one of the following applies (a, b, or c):
         a. Statin therapy is contraindicated per Appendix D;
         b. Member has received a moderate intensity statin (Appendix C) adherently for at least the last 4 months due to (i or ii):
            i. Intolerance to two high intensity statins;
            ii. A statin risk factor (Appendix E);
         c. Member is unable to take a high or moderate intensity statin due to (i or ii):
            i. Intolerance to two high and two moderate intensity statins;
            ii. A statin risk factor (Appendix E) and history of intolerance to two moderate intensity statins;
      6. Member has received Zetia therapy adherently for at least the last 4 months, unless contraindicated per Appendix D or a history of Zetia intolerance (e.g., associated diarrhea or upper respiratory tract infection);
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7. Member has received counseling on therapeutic lifestyle changes (i.e., heart healthy diet; regular exercise; avoidance of tobacco products; maintenance of a healthy weight);
8. Treatment plan does not include coadministration with Juxtapid (lomitapid), Kynamro ( mipomersen), or Repatha ( evolocumab);
9. Request is for Praluent 75 mg every 2 weeks.

Approval duration: 3 months

B. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy.

II. Continued Approval
A. Heterozygous Familial Hypercholesterolemia and Atherosclerotic Cardiovascular Disease Primary Hyperlipidemia (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Meets (a or b):
      a. Request is for 75 mg every 2 weeks and lab results within the last 3 months are submitted showing an LDL-C reduction since initiation of Praluent therapy;
      b. Request is for 150 mg every 2 weeks and (i or ii):
         i. If request represents a new dose increase, member has demonstrated adherence to Praluent and, if applicable, Zetia and/or statin therapies, and lab results within the last 3 months are submitted showing an LDL-C > 70 mg/dL after a minimum of 8 weeks of Praluent therapy at 75 mg;
         ii. If request represents a continuation of Praluent 150 mg, lab results within the last 3 months are submitted showing an LDL-C reduction since initiation of the Praluent dose increase.

Approval duration: 12 months (3 months if request is for dose increase)

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
   2. Refer to ERX.SPMN.16 - Global Biopharm Policy.

Background

Description/Mechanism of Action:
Alirocumab is a human monoclonal antibody (IgG1 isotype) directed against proprotein convertase subtilisin kexin 9 (PCSK9). Alirocumab binds to PCSK9 and inhibits circulating PCSK9 from binding to the LDL receptor (LDLR) preventing PCSK9-mediated LDLR degradation and permitting LDLR to recycle back to the liver cell surface. By inhibiting the binding of PCSK9 to LDLR, alirocumab increases the number of LDLRs available to clear LDL from the blood, thereby lowering LDL-C levels. Alirocumab is produced by recombinant DNA technology in Chinese hamster ovary cell suspension culture.
Formulations:
Praluent 75 mg/mL or 150 mg/mL solution for subcutaneous injection in a single-dose pre-filled pen or single-dose pre-filled syringe; sterile, preservative free, latex free.

FDA Approved Indications:
Praluent is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody/subcutaneous injectable formulation 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, who require additional lowering of LDL-C.

Limitations of use:
- The effect of Praulent on cardiovascular morbidity and mortality has not been determined.

Appendices

Appendix A: Abbreviation Key

- apoB: apolipoprotein B
- ACC/AHA: American College of Cardiology/American Heart Association
- ALT: Alanine transaminase
- ASCVD: atherosclerotic cardiovascular disease
- CVD: cardiovascular disease
- FH: familial hypercholesterolemia
- HDL-C: high-density lipoprotein cholesterol
- HoFH: homozygous familial hypercholesterolemia
- HfFH: heterozygous familial hypercholesterolemia
- LDL-C: low density lipoprotein cholesterol
- LDLR: low density lipoprotein receptor
- LDLRAP1: low density lipoprotein receptor adaptor protein 1
- PCSK9: proprotein convertase subtilisin kexin 9
- TC: total cholesterol
- TLC: therapeutic lifestyle changes
- ULN: upper limit of normal

Appendix B: Dutch Lipid Clinic Network criteria for Familial Hypercholesterolemia (FH)

<table>
<thead>
<tr>
<th>FH Criteria</th>
<th>Points</th>
<th>Member’s Score†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family History</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First-degree relative with known premature* coronary and vascular disease</td>
<td>1</td>
<td>Place highest score here (0, 1 or 2)</td>
</tr>
<tr>
<td>First-degree relative with known LDL-C level above the 95th percentile</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>First-degree relative with tendinous xanthomata and/or arcus cornealis</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Children aged &lt; 18 years with LDL-C level above the 95th percentile</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical History</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient with premature* coronary artery disease</td>
<td>2</td>
<td>Place highest score here (0, 1 or 2)</td>
</tr>
<tr>
<td>Patient with premature* cerebral or peripheral vascular disease</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Physical Examination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tendinous xanthomata</td>
<td>6</td>
<td>Place highest score here (0, 4 or 6)</td>
</tr>
<tr>
<td>Arcus cornealis prior to age 45 years</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td><strong>Cholesterol Levels - mg/dL (mmol/liter)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL-C ≥330 mg/dL (≥8.5)</td>
<td>8</td>
<td>Place highest score here</td>
</tr>
<tr>
<td>LDL-C 250 – 329 mg/dL (6.5 – 8.4)</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
### Appendix C: High and Moderate Intensity Daily Statin Therapy for Adults

- **High Intensity Statin Therapy**
  - *Daily dose shown to lower LDL-C, on average, by approximately ≥50%*
    - Atorvastatin 40-80 mg
    - Rosuvastatin 20-40 mg

- **Moderate Intensity Statin Therapy**
  - *Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%*
    - Atorvastatin 10-20 mg
    - Fluvastatin XL 80 mg
    - Fluvastatin 40 mg 2x/day
    - Lovastatin 40 mg
    - Pitavastatin 2-4 mg
    - Pravastatin 40-80 mg
    - Rosuvastatin 5-10 mg
    - Simvastatin 20-40 mg

- **Low Intensity Statin Therapy**
  - *Daily dose shown to lower LDL-C, on average, by <30%*
    - Simvastatin 10 mg
    - Pravastatin 10–20 mg
    - Lovastatin 20 mg
    - Fluvastatin 20–40 mg
    - Pitavastatin 1 mg

### Appendix D: Statin and Zetia Contraindications

- **Statins**
  - Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy);
  - Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment;
  - Pregnancy, actively trying to become pregnant, or nursing;
  - Immune-mediated hypersensitivity to the HMG-CoA reductase inhibitor drug class (statins) as evidenced by an allergic reaction occurring with at least TWO different statins;

- **Zetia**
  - Moderate or severe hepatic impairment [Child-Pugh classes B and C];
  - Hypersensitivity to Zetia (e.g., anaphylaxis, angioedema, rash, urticaria).

### Appendix E: Statin Risk Factors

- Multiple or serious comorbidities, including impaired renal or hepatic function;
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- Unexplained ALT elevations > 3 times ULN, or active liver disease;
- Concomitant use of drugs adversely affecting statin metabolism;
- Age > 75 years, or history of hemorrhagic stroke;
- Asian ancestry.

Reviews, Revisions, and Approvals

| Policy created. | 11/16 | 12/16 |

References

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional
medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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