Clinical Policy: Alirocumab (Praluent)

Reference Number: PA.CP.PHAR.124
Effective Date: 01/2018
Last Review Date: 10/2016 Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for alirocumab injection (Praluent®).

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that 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 is ≥ 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, or v):
      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. Ischemic cerebrovascular disease such as stroke or TIA
4. Recent (within the last 30 days) low-density lipoprotein cholesterol (LDL-C) ≥ 70mg/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);

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;
10. Member has no known history of serious hypersensitivity reaction to Praluent (e.g., hypersensitivity vasculitis or hypersensitivity reactions requiring hospitalization).

Approval duration: 3 months

B. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Heterozygous Familial Hypercholesterolemia and Atherosclerotic Cardiovascular Disease Primary Hyperlipidemia (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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;
3. Member has no known history of serious hypersensitivity reaction to Praluent (e.g., hypersensitivity vasculitis or hypersensitivity reactions requiring hospitalization).

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 Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or
2. Refer to PA.CP.PHAR.57 - 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:

- 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
HeFH: heterozygous familial hypercholesterolemia
HoFH: homozygous 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)

FH Criteria	Points	Member's Score†
Family History		
First-degree relative with known premature* coronary and vascular disease	1	Place highest score here (0, 1 or 2)
First-degree relative with known LDL-C level above the 95th percentile	1	
First-degree relative with tendinous xanthomata and/or arcus cornealis	2	
Children aged < 18 years with LDL-C level above the 95th percentile	2	
Clinical History		
Patient with premature* coronary artery disease	2	Place highest score here (0, 1 or 2)
Patient with premature* cerebral or peripheral vascular disease	1	
Physical Examination		
Tendinous xanthomata	6	Place highest score here
Arcus cornealis prior to age 45 years	4	

		(0, 4 or 6)
Cholesterol Levels - mg/dL (mmol/liter)		
LDL-C ≥330 mg/dL (≥8.5)	8	Place highest score here (0, 1, 3, 5 or 8)
LDL-C 250 – 329 mg/dL (6.5 – 8.4)	5	
LDL-C 190 – 249 mg/dL (5.0 – 6.4)	3	
LDL-C 155 – 189 mg/dL (4.0 – 4.9)	1	
DNA Analysis		
Functional mutation in the *LDLR, apo B* or *PCSK9* gene	8	Place highest score here (0 or 8)
TOTAL SCORE	Definite FH: >8	Place score total here __

*Premature – men < 55 years or women < 60 years
†Choose the highest score from each of the five categories and then add together for a total score. The five categories are 1) Family History, 2) Clinical History, 3) Physical Examination, 4) Cholesterol Levels, and 5) DNA Analysis.

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 10-20mg
  - 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 m

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;
- 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	Date	Approval Date

References

1. Praluent Prescribing Information. Bridgewater, NJ: Sanofi-Eventis U.S. LLC; October 2015. Available at http://products.sanofi.us/praluent/praluent.pdf. Accessed on August 29, 2016.
2. Llyod-Jones DM, Morris PB, Ballantyne CM, et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk. *J Am Coll Cardiol*. 2016; 68(1): 92-125.
3. Stone NJ, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* November 2013. DOI: 10.1161/01.cir.0000437738.63853.7a
4. Jacobson TA, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 – full report. *Journal of Clinical Lipidology*. March-April 2015; 9(2): 129-169. http://dx.doi.org/10.1016/j.jacl.2015.02.003
5. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. *Journal of Clinical Lipidology.* June 2011; 5(3S): 1-15.
6. Jacobson TA. National Lipid Association Task Force on Statin Therapy – 2014 update. *Journal of Clinical Lipidology.* 2014; 8(S1-S4): 1-81.
7. Zetia Prescribing Information. Whitehouse Station, NJ: Merck and Company, Inc.; August 2013. Available at http://www.merck.com/product/usa/pi_circulars/z/zetia/zetia_pi.pdf. Accessed August 29, 2016.
8. Al-Rasadi K, Al-Waili K, Al-Sabti HA, et al. Criteria for diagnosis of familial hypercholesterolemia: A comprehensive analysis of the different guidelines, appraising their suitability in the Omani Arab population. *Oman Medical Journal.* 2014; 29(2): 85–91. http://doi.org/10.5001/omj.2014.22