I. Medication Description

PCSK9 inhibitors are human monoclonal IgG2 antibodies that bind to and inhibit proprotein convertase subtilisin/kexin type 9 (PCSK9) binding to low-density lipoprotein receptors (LDLR). PCSK9 binds to LDLR on the hepatocyte surface to promote LDLR degradation within the liver. LDLR is the primary receptor that clears circulating LDL; with evolocumab inhibiting the binding of PCSK9 to LDLR, the number of LDLRs available to clear LDL increases, thereby lowering LDL-C concentrations.

II. Position Statement

Coverage is determined through a prior authorization process for all requests.

III. Policy

Coverage is available for members who meet all of the following criteria:

- One of the following, dependent upon the diagnosis:
  - For hyperlipidemia in clinical Atherosclerotic Cardiovascular Disease (ASCVD):
    - The patient is aged ≥ 18 years AND
    - The patient has a low-density lipoprotein cholesterol (LDL-C) level ≥ 70 mg/dL (after treatment with antihyperlipidemic agents but prior to PCSK9 inhibitor therapy) AND
    - The patient has had one of the following conditions or diagnoses: previous myocardial infarction (MI), a history of acute coronary syndrome (ACS), angina (stable or unstable), history of stroke or transient ischemic attack (TIA), peripheral arterial disease (PAD) including aortic aneurysm, or has undergone a coronary or other arterial revascularization procedure in the past (e.g., coronary artery bypass graft [CABG], percutaneous coronary intervention [PCI], angioplasty, coronary stent procedure)
  - For Primary (familial) Hyperlipidemia (including Heterozygous Familial Hypercholesterolemia [HeFH]):
    - The patient is aged ≥ 18 years AND
    - One of the following:
      - WHO/Dutch Lipid Network Criteria score of greater than eight points OR
      - Definite diagnosis according to Simon-Broome criteria AND
      - Baseline LDL-C level has been provided
  - For Homozygous Familial Hypercholesterolemia (HoFH):
    - Repatha is the prescribed medication AND
    - The patient is aged ≥ 13 years AND
- Member has a confirmed diagnosis of homozygous familial hypercholesterolemia (HoFH) by one of the following:
  - The patient has genetic confirmation of two mutant alleles at the low-density lipoprotein receptor (LDLR), apolipoprotein B (APOB), proprotein convertase subtilisin kexin type 9 (PCSK9) or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene locus OR
  - The patient has an untreated low-density lipoprotein (LDL-C) level > 500 mg/dL (prior to treatment with antihyperlipidemic agents) or treated LDL-C ≥ 300 mg/dL (after treatment with antihyperlipidemic agents but prior to agents such as Repatha, Kynamro® [mipomersen injection] or Juxtapid® [lomitapide capsules]) with either:
    - Cutaneous or tendonous xanthoma before age 10 years OR
    - Elevated LDL cholesterol levels before lipid-lowering therapy consistent with heterozygous familial hypercholesterolemia in both parents

AND
- The medication is prescribed by (or in consultation with) a cardiologist, endocrinologist, or a physician who has obtained additional education/certification in cardiovascular risk management and/or the treatment of lipid disorders AND
- The patient meets one of the following:
  - The patient has tried one high-intensity statin therapy (atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily) AND ezetimibe concomitantly (unless the addition of ezetimibe is contraindicated) for ≥ 8 continuous weeks and the LDL-C level remains ≥ 70 mg/dL OR
  - The patient has been determined to be statin-intolerant by meeting one of the following criteria:
    - The patient experienced statin-related rhabdomyolysis (statin-induced muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness, acute renal failure and/or elevated creatine kinase [CK] levels [e.g., greater or equal to 10 times the upper limit of normal]) OR
    - The patient experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) and meets both of the following criteria:
      - The skeletal-related muscle symptoms (e.g., myopathy or myalgia) occurred while receiving separate trials of both atorvastatin and rosuvastatin AND
      - When receiving separate trials of both atorvastatin and rosuvastatin the skeletal-related muscle symptoms (e.g., myopathy, myalgia) resolved upon discontinuation of each respective statin therapy

AND
- If able to tolerate statins, the patient continues to receive the maximum-tolerated dose of a statin while receiving PCSK9 Inhibitor therapy.
IV. Quantity Limitations

- Coverage of Praluent will be limited to 2 pre-filled pens/syringes every 4 weeks.
- Coverage of Repatha will be limited to 3 pre-filled syringes/autoinjectors or one 3.5mL injector every 4 weeks.

V. Coverage Duration

Coverage is available for 12 months and may be renewed.

VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Clinically significant LDL-C reduction has been shown with treatment AND
- Stabilization of disease or absence of disease progression AND
- Absence of unacceptable toxicity from the drug.

VII. Billing/Coding Information

- Praluent is available as 75mg/mL and 150mg/mL pre-filled pens and pre-filled syringes.
- Repatha is available as 140mg/mL prefilled syringes, 2-pack 140mg/mL prefilled SureClick® autoinjectors and 420mg/3.5mL single-use Pushtronex™ system (on-body infuser with prefilled cartridge).

IX. Summary of Policy Changes

- 10/9/15: new policy
- 6/15/16: no policy changes
- 4/5/17: package sizes updated; quantity limits updated to reflect changes in package sizes
- 5/1/18: no policy changes
- 5/15/19: updated coverage criteria for primary (familial) and homozygous hyperlipidemia
- 11/15/19: updated Praluent coverage criteria to include heterozygous familial hypercholesterolemia
- 5/1/20: added aortic aneurysm to ASCVD definition according to 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol; updated renewal criteria

X. References

3. Robinson JG, Nedergaard BS, Rogers WJ, et al, for the LAPLACE-2 Investigators. Effect of evolocumab or ezetimibe added to moderate- or high-intensity statin therapy on LDL-C lowering in patients with


The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary agent will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.