I. Medication Description

PCSK9 inhibitors are human monoclonal IgG2 antibodies that binds 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 with supporting clinical documentation for every request.

III. Policy

Coverage is available for those 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), 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 Heterozygous Familial Hypercholesterolemia (HeFH):
    - The patient is aged ≥ 18 years AND
    - The patient has a low-density lipoprotein cholesterol (LDL-C) level ≥ 160 mg/dL (after treatment with antihyperlipidemic agents but prior to PCSK9 inhibitor therapy)
  - For Homozygous Familial Hypercholesterolemia (HoFH):
    - Repatha is the prescribed medication AND
    - The patient is aged ≥ 13 years AND
    - The patient meets 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

The patient has a treated low-density lipoprotein cholesterol (LDL-C) level ≥ 300 mg/dL (after treatment with antihyperlipidemic agents but prior to agents such as Repatha, Kynamro® [mipomersen injection] or Juxtapid® [lomitapide capsules]) OR

The patient has clinical manifestations of HoFH (e.g., cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas or xanthelasma)

**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 another antihyperlipidemic agent concomitantly 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:

- Stabilization of disease or in 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).

VIII. **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

IX. **References**


The Plan fully expects that only appropriate and medically necessary services will be rendered. ThePlan 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.