Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) Inhibitors Prior Authorization with Quantity Limit Program Summary - Through Preferred Agent(s)

This program applies to Medicaid.

Preferred products are:
- Praluent:
  - NDC 72733-5901-01
  - NDC 72733-5901-02
  - NDC 72733-5902-02
- Repatha:
  - NDC 72511-0750-01
  - NDC 72511-0760-01
  - NDC 72511-0760-02
  - NDC 72511-0770-01

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

**FDA INDICATIONS AND DOSING**¹,²

<table>
<thead>
<tr>
<th>Agents</th>
<th>Indications</th>
<th>Strength(s)</th>
<th>Dosing and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Praluent®</strong></td>
<td>To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease</td>
<td>75 mg/mL prefilled pen and syringe</td>
<td>75 mg SC³ once every 2 weeks. An alternative dosage for patients who prefer less frequent dosing is 300 mg once every 4 weeks (monthly). May increase dose up to 150 mg SC every 2 weeks if the LDL-C response is inadequate. For patients with HeFH undergoing LDL apheresis: 150 mg once every 2 weeks.</td>
</tr>
<tr>
<td>(alirocumab) Injection</td>
<td>As adjunct to diet alone or in and maximally tolerated statins for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease who require additional lowering of LDL cholesterol⁷</td>
<td>150 mg/mL prefilled pen and syringe</td>
<td></td>
</tr>
<tr>
<td><strong>Repatha®</strong></td>
<td>To reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease</td>
<td>140 mg/mL prefilled pen and autoinjector</td>
<td>Adults with established cardiovascular disease or Primary hyperlipidemia with CVD or HeFH: 140 mg SC every 2 weeks or 420 mg SC monthly</td>
</tr>
<tr>
<td>(evolocumab) Injection</td>
<td>Adjunct to diet, alone or in combination with other lipid lowering therapies (e.g., statins, ezetimibe), for treatment of adults</td>
<td>420 mg/3.5 mL Pushtronom system (infusor with pre-filled cartridge)</td>
<td></td>
</tr>
</tbody>
</table>
with primary hyperlipidemia (including heterozygous familial hypercholesterolemia (HeFH) to reduce low-density lipoprotein cholesterol

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

| HoFH: 420 mg SC^ once monthly |

^ Subcutaneous

**CLINICAL RATIONALE**

**Heterozygous familial hypercholesterolemia (HeFH)**

Criteria have been developed to aid in diagnosing HeFH. These include the Simon Broome Register criteria and Dutch Lipid clinic Network criteria. Definitive diagnosis of HeFH according to Simon Broome diagnostic criteria requires the patient has one of the following:

- Total cholesterol greater than 6.7 mmol/L or low-density lipoprotein cholesterol (LDL-C) greater than 4.0 mmol/L in a child aged younger than 16 years, or greater than 7.5 mmol/L or LDL-C greater than 4.9 mmol/L in an adult (levels either pre-treatment or highest on treatment) plus tendon xanthomas in the patient, or in first-degree relative (parent, sibling or child), or in second-degree relative (e.g. grandparent, uncle or aunt)

**Or**

- DNA-based evidence of an LDL receptor mutation, familial defective Apo B-100, or a PCSK9 mutation

The Dutch Lipid Clinic Network criteria assign points based on cholesterol levels, family history of hyperlipidemia or cardiovascular disease, clinical presentation, and/or presence of identified genetic mutation affecting plasma LDL-C. A definitive diagnosis of HeFH can be made in patients with greater than 8 points.

**Dutch Lipid Clinic Network criteria for diagnosis of heterozygous familial hypercholesterolemia**

<table>
<thead>
<tr>
<th>Group 1: Family history</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-degree relative with known premature (&lt;55 years, men; &lt;60 years, women) coronary heart disease (CHD)</td>
<td>1</td>
</tr>
<tr>
<td>First-degree relative with known LDL cholesterol &gt;95th percentile by age and gender for country</td>
<td>1</td>
</tr>
<tr>
<td>First-degree relative with tendon xanthoma and/or corneal arcus</td>
<td>2</td>
</tr>
<tr>
<td>Children &lt;18 years with LDL cholesterol &gt;95th percentile by age and gender for country</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2: Clinical history</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject has premature (&lt;55 years, men; &lt;60 years, women) CHD</td>
<td>2</td>
</tr>
<tr>
<td>Subject has premature (&lt;55 years, men; &lt;60 years, women) cerebral or peripheral vascular disease</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 3: Physical examination</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendon xanthoma</td>
<td>6</td>
</tr>
<tr>
<td>Corneal arcus in a person &lt;45 years</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 4: Biochemical results (LDL-C)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;8.5 mmol/L (&gt;325 mg/dL)</td>
<td>8</td>
</tr>
<tr>
<td>6.5–8.4 mmol/L (251–325 mg/dL)</td>
<td>5</td>
</tr>
<tr>
<td>5.0–6.4 mmol/L (191–250 mg/dL)</td>
<td>3</td>
</tr>
<tr>
<td>4.0–4.9 mmol/L (155–190 mg/dL)</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 5: Molecular genetic testing (DNA analysis)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causative mutation shown in the LDLR, APOB, or PCSK9 genes</td>
<td>8</td>
</tr>
</tbody>
</table>
Use and Interpretation

Assign only one score, the highest applicable, per group then add the points from each group to achieve the total score

- Definitive FH diagnosis: > 8 points
- Probable FH diagnosis: 6 to 8 points
- Possible FH diagnosis: 3 to 5 points
- Unlikely FH diagnosis: 0 to 2 points

Homozygous familial hypercholesterolemia (HoFH)

Guidelines advise that diagnosis of HoFH can be made on the basis of genetic or clinical criteria. Genetic confirmation of the HoFH includes confirmation of two mutant alleles at the LDL-R, APOB, PCSK9, or LDLRAP1 genes. While genetic testing may provide a definitive diagnosis of HoFH, it is recognized that in some patients, genetic confirmation remains elusive, despite exhaustive investigation; indeed, the existence of additional FH genes cannot be excluded. Historically, HoFH has been most commonly diagnosed on the basis of either an untreated LDL-C plasma concentration >13 mmol/L (>500 mg/dL), or a treated LDL-C concentration of ≥8 mmol/L (≥300 mg/dL), accompanied by the presence of cutaneous or tendon xanthomas before the age of 10 years, or the presence of untreated elevated LDL-C levels consistent with HeFH in both parents.

According the American Heart Association (AHA), initial treatment for FH should include a high intensity statin. If the LDL-C is not at goal after 3 months of therapy with the high intensity statin and the patient has been adherent, AHA recommends the addition of ezetimibe. For patients who do not respond to this two drug regimen within 3 months, AHA recommends addition of a PCKS9, a bile acid sequestrant, or niacin. Patients with HoFH who require additional therapy despite treatment with the three drug regimen, AHA recommends addition of Juxtapid or Kynamro and LDL apheresis.

Atherosclerotic Cardiovascular Disease (ASCVD) – Secondary Prevention

The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHa/ASPC/NLA/PCNA guideline lists the following as clinical ASCVD:

- Acute coronary syndrome (ACS)
- Myocardial infarction (MI)
- Stable or unstable angina or coronary or other arterial revascularization
- Stroke
- Transient ischemic attack (TIA) or peripheral artery disease (PAD) including aortic aneurysm

Management

The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHa/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol states the following regarding PCSK9 therapy:

- Severe hypercholesterolemia (LDL-C ≥190 mg/dL [≥4.9 mmol/L])
  - In patients 30-75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL (≥2.6 mmol/L) or higher while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered
  - In patients 40-75 years of age with a baseline LDL-C level of 220 mg/dL (≥5.7 mmol/L) or higher while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered

The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHa/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol states the following regarding PCSK9 therapy:

- Secondary atherosclerotic cardiovascular disease (ASCVD) prevention
  - In patients with clinical ASCVD who are judged to be very high risk and considered for PCSK9 inhibitor therapy, maximally tolerated LDL-C lowering therapy should include maximally tolerated statin therapy and ezetimibe
  - In patients with clinical ASCVD who are judged to be very high risk and who are on maximally tolerated LDL-C lowering therapy with LDL-C 70 mg/dL (≥1.8 mmol/L) or higher
or a non-HDL-C level of 100 mg/dL (≥2.6 mmol/L) or higher, it is reasonable to add PCSK9 inhibitor following a clinical-patient discussion about the net benefit, safety, and cost.

The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline categorizes the following statin intensities:9

<table>
<thead>
<tr>
<th>LDL-C Lowering</th>
<th>High Intensity</th>
<th>Moderate Intensity</th>
<th>Low Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥50%</td>
<td>Atorvastatin 40-80 mg</td>
<td>Atorvastatin 10-20 mg</td>
<td>Simvastatin 10 mg</td>
</tr>
<tr>
<td>30%-49%</td>
<td>Rosuvastatin 20-40 mg</td>
<td>Rosuvastatin 5-10 mg</td>
<td>Pravastatin 10-20 mg</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>Simvastatin 20-40 mg*</td>
<td>Pravastatin 40-80 mg</td>
<td>Lovastatin 20 mg</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin 10-20 mg</td>
<td>Lovastatin 40-80 mg</td>
<td>Fluvastatin 20-40 mg</td>
</tr>
<tr>
<td></td>
<td>Rosuvastatin 5-10 mg</td>
<td>Fluvastatin XL 80 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simvastatin 20-40 mg*</td>
<td>Fluvastatin 40 mg twice daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pravastatin 40-80 mg</td>
<td>Pitavastatin 1-4 mg</td>
<td></td>
</tr>
</tbody>
</table>

* Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA because of the risk of myopathy, including rhabdomyolysis.

The National Lipid Association (NLA) 2019 consensus statement identifies the following patients, who are already on maximally tolerated statin therapy, as most likely to benefit from PCSK9 therapy.10

- Extreme high-risk (≥40% 10-year ASCVD risk on maximally tolerated statin therapy) with LDL-C ≥70 mg/dL and either of the following:
  - Extensive or active burden of ASCVD (i.e., polyvascular ASCVD, which affects all 3 vascular beds—coronary, cerebrovascular, and peripheral arterial; clinical peripheral arterial disease in addition to coronary and/or cerebrovascular disease; a clinical ASCVD event with multivessel coronary artery disease defined as ≥40% stenosis in ≥2 large vessels; or recurrent myocardial infarction within 2 years of the initial event) in the presence of adverse or poorly controlled cardiometabolic risk factors.
  - Extremely high-risk elevations in cardiometabolic factors with less-extensive ASCVD (i.e., HeFH, diabetes, LDL-C ≥100 mg/dL, less than high-intensity statin therapy, chronic kidney disease, poorly controlled hypertension, high-sensitivity C-reactive protein >3 mg/L, or metabolic syndrome, usually occurring with other extremely high-risk or very-high-risk characteristics), usually with other adverse or poorly controlled cardiometabolic risk factors present. Patients with ASCVD and HeFH or severe hyperlipidemia (SH) LDL-C ≥220 mg/dL are an additional group of extremely high-risk patients, with ≥45% 10-year ASCVD risk despite statin therapy. Statin-treated HeFH patients with coronary artery calcium (CAC) score >100 Agatston units also have about a 45% 10-year ASCVD risk despite statin therapy.

- Very high-risk (30-39% 10-year ASCVD risk on maximally tolerated statin therapy) with LDL-C ≥100 mg/dL and the following:
  - Less-extensive clinical ASCVD (i.e., no polyvascular ASCVD, no clinical peripheral arterial disease, a prior ASCVD event ≥2 years prior, and no coronary artery bypass grafting)
  - Adverse or poorly controlled cardiometabolic risk factor(s) including age ≥65 years, current smoking, chronic kidney disease, lipoprotein(a) ≥37 nmol/L, high-sensitivity C-reactive protein 1–3 mg/L, metabolic syndrome with a history of myocardial infarction, ischemic stroke, or symptomatic peripheral arterial disease, usually in the presence of other adverse or poorly controlled cardiometabolic risk factors.
• High-risk (20-29% 10-year ASCVD risk on maximally tolerated statin therapy) with LDL-C ≥130 mg/dL and either of the following:
  o High-risk patients with ASCVD who have the following:
    ▪ Less-extensive ASCVD
    ▪ Well-controlled cardiometabolic risk factors (i.e., no diabetes, nonsmoker, on high-intensity statin with LDL-C <100 mg/dL, blood pressure <140/90 mm Hg, and C-reactive protein <1 mg/dL)
  o Primary prevention patients with HeFH or SH LDL-C ≥220 mg/dL and have the following:
    ▪ No clinical ASCVD or CAC <100 Agatston units
    ▪ Poorly controlled cardiometabolic risk factor

REFERENCES
Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) Inhibitors
Prior Authorization with Quantity Limit—Through Preferred Agent(s) - Medicaid

TARGET AGENTS
Praluent® (alirocumab)
Repatha® (evolocumab)

PRIOR AUTHORIZATION AND QUANTITY LIMIT TARGET DRUGS—RECOMMENDED LIMITS

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praluent (alirocumab)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75 mg/mL pre-filled pen</td>
<td>3935001000D520</td>
<td>M, N, O, or Y</td>
<td>1 package of 2 pens/28 days</td>
</tr>
<tr>
<td>75 mg/mL pre-filled syringe</td>
<td>3935001000E520</td>
<td>M, N, O, or Y</td>
<td>1 package of 2 syringes/28 days</td>
</tr>
<tr>
<td>150 mg/mL pre-filled pen</td>
<td>3935001000D530</td>
<td>M, N, O, or Y</td>
<td>1 package of 2 pens/28 days</td>
</tr>
<tr>
<td>150 mg/mL pre-filled syringe</td>
<td>3935001000E530</td>
<td>M, N, O, or Y</td>
<td>1 package of 2 syringes/28 days</td>
</tr>
<tr>
<td>Repatha (evolocumab)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>140 mg/mL pre-filled syringe</td>
<td>3935002000E520</td>
<td>M, N, O or Y</td>
<td>2 syringes/28 days</td>
</tr>
<tr>
<td>140 mg/mL pre-filled autoinjector</td>
<td>3935002000D520</td>
<td>M, N, O or Y</td>
<td>2 pens/28 days</td>
</tr>
<tr>
<td>420 mg/3.5 mL single-use Pushtronex system (infusor with pre-filled cartridge)</td>
<td>3935002000E230</td>
<td>M, N, O or Y</td>
<td>1 Pushtronex system/30 days</td>
</tr>
</tbody>
</table>

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Target Agents will be approved when ALL of the following are met:
1. ONE of the following:
   A. ALL of the following:
      i. The patient has ONE of the following:
         1. A diagnosis of heterozygous familial hypercholesterolemia (HeFH) confirmed by ONE of the following:
            a. Genetic confirmation of one mutant allele at the LDLR, Apo-B, PCSK9, or ARH adaptor protein 1/LDLRAP1 gene locus
               OR
            b. BOTH of the following:
               i. ONE of the following:
                  1. History of total cholesterol > 290 mg/dL (>7.5 mmol/L) (pretreatment or highest level while on treatment)
                  OR
                  2. History of LDL-C > 190 mg/dL (>4.9 mmol/L) (pretreatment or highest level while on treatment)
                  AND
               ii. History of tendon xanthomas in ONE of the following:
                  1. The patient
                  OR
                  2. The patient’s first degree relative (i.e. parent, sibling, or child)
                  OR
3. The patient’s second degree relative (e.g. grandparent, uncle, or aunt)

OR

C. The patient has a Dutch Lipid Clinic Network Criteria score of greater than 8 (see scoring algorithm in Table 2 below)

OR

2. A diagnosis of homozygous familial hypercholesterolemia (HoFH) confirmed by 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

OR

b. History of untreated LDL-C >500 mg/dL (>13 mmol/L) or treated LDL-C ≥300 mg/dL (≥7.76 mmol/L) with ONE of the following:
   i. The patient had cutaneous or tendon xanthoma before age 10 years

OR

   ii. Untreated elevated cholesterol levels consistent with heterozygous FH in both parents [untreated LDL-C >190 mg/dL (>4.9 mmol/L) or untreated total cholesterol greater than 290 mg/dL (>7.5 mmol/L)]

OR

3. BOTH of the following:
   a. A diagnosis of clinical atherosclerotic cardiovascular disease (ASCVD) defined as having ONE of the following:
      i. Acute coronary syndrome
      ii. History of myocardial infarction
      iii. Stable or unstable angina
      iv. Coronary or other arterial revascularization
      v. Stroke
      vi. Transient ischemic attack
      vii. Peripheral arterial disease, including aortic aneurysm, presumed to be of atherosclerotic origin

   AND

   b. The patient has very high risk for future ASCVD events

OR

4. The patient has primary hyperlipidemia AND ALL of the following:
   a. The patient is 40-75 years of age
   AND
   b. The patient has an LDL-C level ≥ 220 mg/dL (≥5.7 mmol/L) while receiving maximally tolerated statin and ezetimibe therapy

OR

5. The patient has ≥20% 10-year ASCVD risk AND ONE of the following:
   a. The patient has ≥40% 10-year ASCVD risk AND BOTH of the following (medical records required):
      i. LDL-C ≥70 mg/dL while on maximally tolerated statin therapy
      (medical records required)
   AND
   
   ii. ONE of the following:
      1. The patient has extensive or active burden of ASCVD (i.e., polyvascular ASCVD, which affects all 3 vascular beds—coronary, cerebrovascular, and peripheral arterial; clinical peripheral arterial disease in addition to coronary and/or cerebrovascular disease; a clinical ASCVD event with multivessel coronary artery disease defined as ≥40% stenosis in ≥2 large vessels; or recurrent myocardial infarction within 2 years of the
initial event) in the presence of adverse or poorly controlled cardiometabolic risk factors

OR

2. Extremely high-risk elevations in cardiometabolic factors with less-extensive ASCVD (i.e., diabetes, LDL-C ≥100 mg/dL, less than high-intensity statin therapy, chronic kidney disease, poorly controlled hypertension, high-sensitivity C-reactive protein >3 mg/L, or metabolic syndrome, usually occurring with other extremely high-risk or very-high-risk characteristics), usually with other adverse or poorly controlled cardiometabolic risk factors present

OR

3. Patients with ASCVD and LDL-C ≥220 mg/dL with ≥45% 10-year ASCVD risk despite statin therapy (medical records required)

OR

b. The patient has 30-39% 10-year ASCVD risk AND ALL of the following (medical records required):
   i. LDL-C ≥100 mg/dL while on maximally tolerated statin therapy (medical records required)
   AND
   ii. Less-extensive clinical ASCVD (i.e., no polyvascular ASCVD, no clinical peripheral arterial disease, a prior ASCVD event ≥2 years prior, and no coronary artery bypass grafting)
   AND
   iii. Adverse or poorly controlled cardiometabolic risk factor(s) including age ≥65 years, current smoking, chronic kidney disease, lipoprotein(a) ≥37 nmol/L, high-sensitivity C-reactive protein 1–3 mg/L, metabolic syndrome with a history of myocardial infarction, ischemic stroke, or symptomatic peripheral arterial disease, usually in the presence of other adverse or poorly controlled cardiometabolic risk factors

OR

c. The patient has 20-29% 10-year ASCVD risk AND BOTH of the following (medical records required):
   i. LDL-C ≥130 mg/dL while on maximally tolerated statins (medical records required)
   AND
   ii. ONE of the following:
      1. The patient has less extensive ASCVD and well-controlled cardiometabolic risk factors (i.e., no diabetes, nonsmoker, on high-intensity statin with LDL-C <100 mg/dL, blood pressure <140/90 mm Hg, and C-reactive protein <1 mg/dL [medical records required for LCL-C, blood pressure, C-reactive protein])
      OR
      2. The use is for primary prevention with LDL-C ≥220 mg/dL AND BOTH of the following (medical records required for LDL-C):
         a. No clinical ASCVD or CAC <100 Agatston units
         AND
         b. Poorly controlled cardiometabolic risk factor

   AND
   ii. ONE of the following:
1. The patient is currently adherent^ (for the past 90 days) to high-intensity statin therapy (i.e. rosuvastatin 20-40 mg, atorvastatin 40-80 mg, or simvastatin 80 mg) (medical records required)
   OR
2. BOTH of the following:
   a. The patient has tried and is intolerant* to high-intensity statin therapy (i.e. rosuvastatin 20-40 mg and atorvastatin 40–80mg)
      AND
   b. The patient is currently adherent^ (for the past 90 days) to low or moderate intensity statin therapy (medical records required)
   OR
3. The patient has an intolerance* to TWO different statins
   OR
4. The patient has an FDA labeled contraindication to a statin
   AND
   iii. ONE of the following:
       1. The patient has not achieved a 50% reduction in LDL-C from baseline while on a maximally tolerated statin
          OR
       2. The patient has an LDL-C ≥70 mg/dL (≥ 1.81 mmol/L) evaluated within the past 90 days
          OR
       3. The patient has ASCVD AND a non-HDL-C level of ≥100 mg/dL (≥2.6 mmol/L) evaluated within the past 90 days
          OR
           B. The patient has another indication that is supported in compendia [AHFS, or DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use] for the requested agent and route of administration
           AND
2. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. cardiologist, endocrinologist, or lipid specialist) or has the prescriber consulted with a specialist in the area of the patient’s diagnosis
   AND
3. If the client has a preferred agent, ONE of the following:
   A. The requested agent is the preferred agent
      OR
   B. ONE of the following:
      i. The patient has tried and had an inadequate response to the preferred agent
      OR
      ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agent that is not expected to occur with the requested agent
      AND
4. The patient will NOT be using the requested agent in combination with another PCSK9 agent for the requested
   AND
5. The patient does not have any FDA labeled contraindications to the requested agent
   AND
6. ONE of the following:
   A. The requested quantity (dose) does not exceed the program quantity limit
      OR
   B. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         AND
      ii. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication
         AND
iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

^Adherence is defined as filling ≥80% of therapy as prescribed in the past 90 days
*intolerance is defined as inability to tolerate the lowest FDA approved starting dose of a statin

**Length of Approval:** 12 months

**Renewal Evaluation**

**Target Agents** will be approved for renewal when ALL of the following criteria are met:

1. The patient has been previously approved for therapy for PCSK9 inhibitors through Prime Therapeutics PA process
   AND
2. If the client has a preferred agent, ONE of the following:
   a. The requested agent is the preferred agent
   OR
   b. ONE of the following:
      i. The patient has tried and had an inadequate response to the preferred agent
      OR
      ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agent that is not expected to occur with the requested agent
   AND
3. The patient has shown clinical benefit with PCSK9s (medical records required)
   AND
4. The patient is currently adherent^ (for the past 90 days) to therapy with a PCSK9 (medical records required)
   AND
5. IF the patient has cardiovascular disease OR hyperlipidemia, then BOTH of the following:
   a. ONE of the following:
      i. The patient is currently adherent^ (for the past 90 days) to high-intensity statin therapy (i.e. rosuvastatin 20-40 mg, atorvastatin 40-80 mg, or simvastatin 80 mg) (medical records required)
      OR
      ii. BOTH of the following:
         1. The patient has tried and is intolerant* to high-intensity statin therapy (i.e. rosuvastatin 20-40 mg and atorvastatin 40-80mg)
         AND
         2. The patient is currently adherent^ (for the past 90 days) to low or moderate intensity statin therapy (medical records required)
      OR
   b. The patient has an intolerance* to TWO different statins
   OR
   c. The patient has an FDA labeled contraindication to a statin
   AND
6. The prescriber is a specialist in the area of the patient’s diagnosis (e.g. cardiologist, endocrinologist, lipid specialist) or has the prescriber has consulted with a specialist in the area of the patient’s diagnosis
   AND
7. The patient will NOT be using the requested agent in combination with another PCSK9 agent for the requested indication
   AND
8. The patient does not have any FDA labeled contraindications to the requested agent
   AND
9. ONE of the following:
   a. The requested quantity (dose) does not exceed the program quantity limit
   OR
   b. ALL of the following:
i. The requested quantity (dose) is greater than the program quantity limit  
**AND**  
ii. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication  
**AND**  
iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit  

^Adherence is defined as filling ≥80% of therapy as prescribed in the past 90 days  
*intolerance is defined as inability to tolerate the lowest FDA approved starting dose of a statin

**Length of approval: 12 months**

**Table 2: Dutch Lipid Clinic Network criteria for diagnosis of heterozygous familial hypercholesterolemia**

<table>
<thead>
<tr>
<th>Group 1: Family history</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-degree relative with known premature (&lt;55 years, men; &lt;60 years, women) coronary heart disease (CHD)</td>
<td>1</td>
</tr>
<tr>
<td>First-degree relative with known LDL cholesterol &gt;95th percentile by age and gender for country</td>
<td>1</td>
</tr>
<tr>
<td>First-degree relative with tendon xanthoma and/or corneal arcus</td>
<td>2</td>
</tr>
<tr>
<td>Children &lt;18 years with LDL cholesterol &gt;95th percentile by age and gender for country</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 2: Clinical history</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject has premature (&lt;55 years, men; &lt;60 years, women) CHD</td>
<td>2</td>
</tr>
<tr>
<td>Subject has premature (&lt;55 years, men; &lt;60 years, women) cerebral or peripheral vascular disease</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 3: Physical examination</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendon xanthoma</td>
<td>6</td>
</tr>
<tr>
<td>Corneal arcus in a person &lt;45 years</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 4: Biochemical results (LDL-C)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;8.5 mmol/L (&gt;325 mg/dL)</td>
<td>8</td>
</tr>
<tr>
<td>6.5–8.4 mmol/L (251–325 mg/dL)</td>
<td>5</td>
</tr>
<tr>
<td>5.0–6.4 mmol/L (191–250 mg/dL)</td>
<td>3</td>
</tr>
<tr>
<td>4.0–4.9 mmol/L (155–190 mg/dL)</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group 5: Molecular genetic testing (DNA analysis)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causative mutation shown in the LDLR, APOB, or PCSK9 genes</td>
<td>8</td>
</tr>
</tbody>
</table>

**Use and Interpretation**

Assign only one score, the highest applicable, per group then add the points from each group to achieve the total score

Definitive FH diagnosis: > 8 points  
Probable FH diagnosis: 6 to 8 points  
Possible FH diagnosis: 3 to 5 points  
Unlikely FH diagnosis: 0 to 2 points
Step Therapy Supplement Program Summary

This program applies to Medicaid.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

   OR

2. BOTH of the following
   a. The patient’s medication history includes the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following:
      i. Evidence of a paid claim(s) within the past 999 days
      OR
      ii. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days
   AND
   b. ONE of the following:
      i. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
      OR
      ii. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)

   OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria