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

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Repatha is the preferred product.

This is a FlexRx standard and GenRx standard prior authorization program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

**FDA INDICATIONS AND DOSING**

<table>
<thead>
<tr>
<th>Agents</th>
<th>Indications</th>
<th>Strength(s)</th>
<th>Dosing and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praluent® (alirocumab)</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 150 mg/mL prefilled pen and syringe</td>
<td>75 mg SC 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>Praluent® (alirocumab)</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 cholesterol</td>
<td>75 mg/mL prefilled pen and syringe 150 mg/mL prefilled pen and syringe</td>
<td>75 mg SC 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>Repatha® (evolocumab)</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 420 mg/3.5 mL Pushtronex system (infusor with pre-filled cartridge)</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 HoFH: 420 mg SC once monthly</td>
</tr>
<tr>
<td>Repatha® (evolocumab)</td>
<td>Adjunct to diet, alone or in combination with other lipid lowering therapies (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia (HeFH) to reduce low-density lipoprotein cholesterol</td>
<td>140 mg/mL prefilled pen and autoinjector 420 mg/3.5 mL Pushtronex system (infusor with pre-filled cartridge)</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 HoFH: 420 mg SC once monthly</td>
</tr>
</tbody>
</table>
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

* 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. A probable diagnosis can be made in patients with 6-8 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>
<tr>
<td>Group 5: Molecular genetic testing (DNA analysis)</td>
<td>Points</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>--------</td>
</tr>
<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

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**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 to 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.

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**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/APH/AASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol states the following regarding PCSK9 therapy:\(^9\)

- 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 \(\geq 70\) mg/dL \((\geq 1.8\) mmol/L\) or higher or a non-HDL-C level of 100 mg/dL \((\geq 2.6\) 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/APH/AASPC/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>Statins</td>
<td>≥50%</td>
<td>30%-49%</td>
<td>&lt;30%</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td></td>
<td></td>
<td>Simvastatin 10 mg</td>
</tr>
<tr>
<td>40-80 mg</td>
<td></td>
<td></td>
<td>Pravastatin 10-20 mg</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td></td>
<td></td>
<td>Lovastatin 20 mg</td>
</tr>
<tr>
<td>20-40 mg</td>
<td></td>
<td></td>
<td>Fluvastatin 20-40 mg</td>
</tr>
<tr>
<td>Simvastatin 20-40 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pravastatin 40-80 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovastatin 40-80 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvastatin XL 80 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvastatin 40 mg twice daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pitavastatin 1-4 mg</td>
<td></td>
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</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** \((\geq 40\%\) 10-year ASCVD risk on maximally tolerated statin therapy) with LDL-C \(\geq 70\) 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 \(\geq 40\%\) stenosis in \(\geq 2\) 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 \(\geq 100\) 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 $\geq 220$ mg/dL are an additional group of extremely high-risk patients, with $\geq 45\%$ 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 $\geq 100$ mg/dL and the following:
  - Less-extensive clinical ASCVD (i.e., no polyvascular ASCVD, no clinical peripheral arterial disease, a prior ASCVD event $\geq 2$ years prior, and no coronary artery bypass grafting)
  - Adverse or poorly controlled cardiometabolic risk factor(s) including age $\geq 65$ years, current smoking, chronic kidney disease, lipoprotein(a) $\geq 37$ 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 $\geq 130$ mg/dL and either of the following:
  - 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)
  - Primary prevention patients with HeFH or SH LDL-C $\geq 220$ mg/dL and have the following:
    - No clinical ASCVD or CAC $< 100$ Agatston units
    - Poorly controlled cardiometabolic risk factor

CAC Agatston score in non-contrast CT can be used for patient risk classification for coronary heart disease:\(^{11,12}\)

- 0 CAC = no CAC, very low risk,
- 1-99 CAC = mild CAC, mildly increased risk
- 100 - 299 CAC = moderate CAC, moderately increased risk
- $\geq 300$ CAC = moderate to severely increased risk

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

TARGET AGENTS

Preferred Agent
Repatha® (evolocumab)

Non-Preferred Agent
Praluent® (alirocumab)

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><strong>Praluent (alirocumab)</strong></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></td>
<td>Allowed NDCs: 72733-5901-**</td>
<td></td>
<td></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></td>
<td>Allowed NDCs: 72733-5902-**</td>
<td></td>
<td></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><strong>Repatha (evolocumab)</strong></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></td>
<td></td>
<td></td>
<td></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) AND ONE of the following:
            a. Genetic confirmation of one mutant allele at the **LDLR, Apo-B, PCSK9**, or **1/LDLRAP1** gene
            OR
            b. History of LDL-C >190 mg/dL (>4.9 mmol/L) (pretreatment)
c. The patient has clinical manifestations of HeFH (e.g. cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthoma, or xanthelasma)

OR

d. The patient has “definite” or “possible” familial hypercholesterolemia as defined by the Simon Broome criteria

OR

e. The Patient has a Dutch Lipid Clinic Network Criteria score of greater than 5

OR

f. The patient has a treated low-density lipoprotein cholesterol (LDL-C) level ≥ 100 mg/dL after treatment with antihyperlipidemic agents but prior to PCSK9 inhibitor therapy

OR

2. A diagnosis of homozygous familial hypercholesterolemia (HoFH) AND ONE of the following:
   a. Genetic confirmation of two mutant alleles at the LDLR, Apo-B, PCSK9, or LDLRAP1 gene

   OR

   b. History of untreated LDL-C >500 mg/dL (>13 mmol/L) or treated LDL-C ≥300 mg/dL (≥7.76 mmol/L)

   OR

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

OR

3. A diagnosis of clinical atherosclerotic cardiovascular disease (ASCVD) AND BOTH of the following:
   a. ONE of the following:
      A. The patient is 18 years of age or greater

   OR

   B. The prescriber has provided information in support of use for those less than 18 years of age

   AND

   b. The patient has 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

OR

4. The patient has primary hyperlipidemia AND BOTH of the following:
   a. ONE of the following:
      i. The patient is 18 years of age or greater
ii. The prescriber has provided information in support of use for those less than 18 years of age

**AND**

b. ONE of the following:
   i. The patient has a coronary artery calcium or calcification (CAC) score ≥300 Agatston units
   **OR**
   ii. 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:
      i. LDL-C ≥70 mg/dL while on maximally tolerated statin therapy
      **AND**
      ii. ONE of the following:
         A. 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**
         B. 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**
         C. Patients with ASCVD and LDL-C ≥220 mg/dL with ≥45% 10-year ASCVD risk despite statin therapy
   **OR**
   b. The patient has 30-39% 10-year ASCVD risk AND ALL of the following:
i. LDL-C ≥ 100 mg/dL while on maximally tolerated statin therapy
   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:
   i. LDL-C ≥ 130 mg/dL while on maximally tolerated statins
   AND
   ii. ONE of the following:
      A. 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)
      OR
      B. The use is for primary prevention with LDL-C ≥ 220 mg/dL AND BOTH of the following:
         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 has been adherent to high-intensity statin therapy (i.e. rosvuastatin ≥ 20 mg daily, atorvastatin ≥ 40 mg) for ≥ 8 continuous weeks AND ONE of the following:
      a. The patient’s LDL-C level after this treatment regimen remains ≥ 70 mg/dL
      OR
      b. The patient has not achieved a 50% reduction in LDL-C from baseline after this treatment regimen
      OR
      c. If the patient has ASCVD, the patient’s non HDL-C level after this treatment regimen remains ≥ 100 mg/dL

OR
2. The patient has been determined to be statin intolerant by meeting one of the following criteria:
   a. The patient experienced statin-related rhabdomyolysis
      OR
   b. The patient experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) and BOTH of the following:
      i. The skeletal-related muscle symptoms (e.g., myopathy or myalgia) occurred while receiving separate trials of both atorvastatin and rosvastatin (as single-entity or as combination products)
      AND
      ii. When receiving separate trials of both atorvastatin and rosvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms (e.g., myopathy, myalgia) resolved upon discontinuation of each respective statin therapy (atorvastatin and rosvastatin);
      OR
   c. The patient experienced elevations in hepatic transaminase while receiving separate trials of both atorvastatin and rosvastatin (as single-entity or as combination products)
   OR
3. The patient has a hypersensitivity to atorvastatin and rosvastatin
   OR
4. The patient has an FDA labeled contraindication to atorvastatin and rosvastatin
   OR
5. The patient’s medication history includes use of high intensity atorvastatin or rosvastatin therapy in the past 999 days
   OR
6. BOTH of the following:
   a. The prescriber has stated that the patient has tried high intensity atorvastatin or rosvastatin therapy
      AND
   b. High intensity atorvastatin or rosvastatin was discontinued due to lack of effectiveness or an adverse event
   OR
7. 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

8. The prescriber has provided documentation that atorvastatin and rosuvastatin 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

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 agent was prescribed by, or in consultation with, a cardiologist, an endocrinologist, and/or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders

AND

3. The patient will NOT be using the requested agent in combination with another PCSK9 agent for the requested indication

AND

4. The patient does not have any FDA labeled contraindications to the requested agent

AND

5. ONE of the following:
   a. The request is for a preferred agent
   OR
   b. The request is for a non-preferred agent AND 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 or hypersensitivity to the preferred agent
      OR
      iii. The patient has an FDA labeled contraindication to ALL preferred agents
      OR
      iv. The patient is currently being treated with the requested agent as indicated by ALL of the following:
         1. A statement by the prescriber that the patient is currently taking the requested agent
         AND
         2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
         AND
         3. The prescriber states that a change in therapy is expected to be ineffective or cause harm
      OR
      v. The prescriber has provided documentation that the preferred agent 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

AND

6. ONE of the following:
c. The requested quantity (dose) does NOT exceed the program quantity limit
   **OR**

d. **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

**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 the plan’s prior authorization process
   **AND**

2. **ONE** of the following:
   a. The request is for a preferred agent
      **OR**
   b. The request is for a non-preferred agent
      i. The patient has tried and had an inadequate response to the preferred agent
         **OR**
      ii. The patient has an intolerance or hypersensitivity to the preferred agent
         **OR**
      iii. The patient has an FDA labeled contraindication to ALL preferred agents
         **OR**
      iv. The patient is currently being treated with the requested agent as indicated by **ALL** of the following:
         1. A statement by the prescriber that the patient is currently taking the requested agent
            **AND**
         2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
            **AND**
         3. The prescriber states that a change in therapy is expected to be ineffective or cause harm
            **OR**
      v. The prescriber has provided documentation that ALL preferred agents 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
         **AND**

3. The patient has shown clinical benefit with PCSK9
   **AND**
4. The patient is currently adherent to therapy with a PCSK9
   AND
5. If the patient has cardiovascular disease OR hyperlipidemia, then ONE of the
   following:
      a. The patient is currently adherent to high-intensity statin therapy (i.e.
         rosvastatin ≥20 mg, atorvastatin ≥40 mg)
      OR
      b. The patient has been determined to be statin intolerant by meeting one of
         the following criteria:
            i. The patient experienced statin-related rhabdomyolysis
            OR
            ii. The patient experienced skeletal-related muscle symptoms (e.g.,
                myopathy [muscle weakness] or myalgia [muscle aches, soreness,
                stiffness, or tenderness]) and BOTH of the following:
                1. The skeletal-related muscle symptoms (e.g., myopathy or
                   myalgia) occurred while receiving separate trials of both
                   atorvastatin and rosuvastatin (as single-entity or as
                   combination products)
                   AND
                2. When receiving separate trials of both atorvastatin and
                   rosuvastatin (as single-entity or as combination products) the
                   skeletal-related muscle symptoms (e.g., myopathy, myalgia)
                   resolved upon discontinuation of each respective statin
                   therapy (atorvastatin and rosuvastatin);
                   OR
            iii. The patient experienced elevations in hepatic transaminase while
                receiving separate trials of both atorvastatin and rosuvastatin (as
                single-entity or as combination products)
                OR
      c. The patient has a hypersensitivity to atorvastatin and rosuvastatin
      OR
      d. The patient has an FDA labeled contraindication to atorvastatin and
         rosuvastatin
      OR
      e. The patient’s medication history includes use of high intensity atorvastatin
         or rosuvastatin therapy in the past 999 days
      OR
      f. BOTH of the following:
         i. The prescriber has stated that the patient has tried high intensity
            atorvastatin or rosuvastatin therapy
            AND
         ii. High intensity atorvastatin or rosuvastatin was discontinued due to
             lack of effectiveness or an adverse event
         OR
      g. The patient is currently being treated with the requested agent as indicated
         by ALL of the following:
         ii. A statement by the prescriber that the patient is currently taking the
             requested agent
             AND
         iii. A statement by the prescriber that the patient is currently receiving a
             positive therapeutic outcome on requested agent
             AND
iv. The prescriber states that a change in therapy is expected to be ineffective or cause harm

**OR**

h. The prescriber has provided documentation that atorvastatin and rosuvastatin 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

**AND**

6. The agent was prescribed by, or in consultation with, a cardiologist, an endocrinologist, and/or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders **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

**Length of approval:** 12 months

<table>
<thead>
<tr>
<th>Agent(s)</th>
<th>Contraindication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praluent (alirocumab)</td>
<td>History of a serious hypersensitivity reaction to Praluent (alirocumab)</td>
</tr>
<tr>
<td>Repatha (evolocumab)</td>
<td>History of a serious hypersensitivity reaction to Repatha (evolocumab)</td>
</tr>
</tbody>
</table>
Step Therapy Supplement
Program Summary

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

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. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

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