**Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) Inhibitors**

**UTILIZATION MANAGEMENT CRITERIA**

<table>
<thead>
<tr>
<th>DRUG CLASS:</th>
<th>PCSK9 Inhibitor</th>
</tr>
</thead>
</table>
| BRAND (generic) NAMES: | Praluent®1 (alirocumab) 75 mg/mL; 150 mg/mL  
Repatha®1 (evolocumab) 140mg/mL; 420mg/3.5mL |

**FDA-APPROVED INDICATIONS**

**Praluent**

Praluent is a PCSK9 inhibitor antibody indicated as 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-cholesterol (LDL-C).

**Limitations of Use**

The effect of Praluent on cardiovascular morbidity and mortality has not been determined.

**Repatha**

Repatha is a PCSK9 inhibitor antibody indicated as an adjunct to diet and:

- Maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C).
- Other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

**Limitations of Use**

The effect of Repatha on cardiovascular morbidity and mortality has not been determined.

**COVERAGE AUTHORIZATION CRITERIA**

Alirocumab (Praluent®) or evolocumab (Repatha®) may be eligible for coverage when the following criteria are met:

1. The patient has a confirmed diagnosis of homozygous familial hypercholesterolemia (HoFH) through **ONE** of the following **(medical documentation is required)**:
   a. Genetic confirmation of two mutant alleles at the LDLR, Apo-B, PCSK9, or ARH adaptor protein 1/LDLRAP1 gene locus
   b. Untreated LDL-C >500 mg/dL or treated LDL-C ≥300 mg/dL with **ONE** of the following:
      i. Cutaneous or tendon xanthoma before age 10 years
      ii. Untreated elevated LDL-C levels consistent with heterozygous FH in both parents [untreated total cholesterol >290 mg/dL or untreated LDL-C >190 mg/dL

OR
2. The patient has a “definite” diagnosis of heterozygous familial hypercholesterolemia (HeFH), as determined using the Dutch Lipid Clinic Network criteria by a score of 8 or greater (please see chart below). Please provide medical record documentation of ANY of the following where applicable to the patient (medical record documentation is required):
   a. LDLR gene functional mutation
   b. Patient LDL-C level at baseline, prior to the use of all cholesterol lowering medications
   c. Presence of tendon xanthoma
   d. Presence of arcus cornææ at age <45 years
   e. Patient history of coronary artery disease
   f. Patient history of premature cerebral or peripheral vascular disease
   g. First degree relative with tendon xanthoma or arcus cornææ
   h. First degree relative age <18 years with LDL >95th percentile
   i. First degree relative with premature coronary artery disease or LDL-C >95th percentile

OR

3. The patient has clinical atherosclerotic cardiovascular disease (ASCVD) defined as one of the following (medical record documentation is required):
   a. ACS (acute coronary syndrome)
   b. History of MI (myocardial infarction)
   c. Stable or unstable angina
   d. Coronary or other arterial revascularization
   e. Stroke
   f. TIA (transient ischemic attack)
   g. PAD (peripheral arterial disease) presumed to be of the atherosclerotic origin

AND

4. The patient is 18 years of age or older

AND

5. The patient is not pregnant

AND

6. One of the following:
   a. The patient is currently taking and adherent to high-intensity statin therapy, OR
   b. The patient is intolerant to at least 2 different statins

NOTE:
   - Adherence is defined as the proportion of days covered (PDC) to be 80% or greater over the last 6 months
   - High-intensity statin is the equivalent of rosvastatin 20-40mg or atorvastatin 40-80mg
   - Intolerance is defined as (1) the inability to tolerate any dose or (2) the inability to increase the dose above the lowest FDA-approved tablet strength

AND

7. One of the following:
   a. For patients with FH: While on a maximally tolerated conventional lipid lowering regimen, the patient has failed to achieve a 50% reduction in LDL-C from baseline or has a LDL-C ≥100mg/dL (evaluated within the last 6 months) (medical documentation is required), OR
   b. For patients with ASCVD: While on a maximally tolerated conventional lipid lowering regimen, the patient has a LDL-C ≥ 70 mg/dL (evaluated within the last 6 months) (medical documentation is required)

AND
8. If requesting Repatha, the patient has tried/failed treatment with 140mg twice monthly before considering treatment with 420mg once monthly unless the patient has a diagnosis of HoFH;
   AND
9. Praluent and Repatha will not be used concurrently with each other
   AND
10. Praluent and Repatha will not be used concurrently with Juxtapid or Kynamro
    AND
11. Praluent and Repatha has been prescribed by or in consultation with a specialist in cardiology

**Duration of Approval and Continuation Criteria:**
1. Duration of initial approval is 6 months
2. Duration of continued approval is 12 months when the following criteria are met:
   b. The patient has a prior approval for this medication from BCBSNC
   AND
   c. Renewal authorization requires evidence of continued maximally tolerated conventional lipid lowering regimen
   AND
   d. One of the following (medical documentation is required):
      i. While on PCSK9 therapy, the patient has a current LDL-C ≤100mg/dL (evaluated within the last month)
         OR
      ii. While on PCSK9 therapy, the patient was able to achieve 45% reduction in LDL-C from baseline while on PCSK9 therapy
   AND
   e. The patient is currently taking and adherent to PCSK9 therapy. *Adherence is defined as the proportion of days covered (PDC) to be 80% or greater over the last 6 month*
   AND
   f. Praluent and Repatha will not be used concurrently with each other
   AND
   g. If requesting Repatha, the patient has tried/failed treatment with 140mg twice monthly before considering treatment with 420mg once monthly unless the patient has a diagnosis of HoFH
   AND
   h. Praluent will not be used concurrently with Juxtapid®1 or Kynamro®1
   AND
   i. Praluent has been prescribed by or in consultation with a specialist in cardiology
QUANTITY LIMIT EXCEPTION CRITERIA

Quantities above the program set limit may be approved when ONE of the following is met:

1. The quantity (dose) requested is within FDA-approved labeling and the prescribed dose cannot be achieved using a lesser quantity of a higher strength; OR

2. The quantity (dose) requested is greater than the maximum dose recommended in FDA-approved labeling, when specified, or to the safest studied dose per the manufacturer’s product insert and the prescriber has submitted documentation in support of therapy with a higher dose or longer duration for the intended diagnosis.

<table>
<thead>
<tr>
<th>Medication Name/Strength</th>
<th>Quantity Limit per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praluent 75 mg/mL</td>
<td></td>
</tr>
<tr>
<td>Praluent 150 mg/mL</td>
<td>2 mL per 28 days</td>
</tr>
<tr>
<td>Repatha 140 mg/mL</td>
<td></td>
</tr>
<tr>
<td>Repatha 420mg/3.5mL</td>
<td>3.5mL per 28 days</td>
</tr>
</tbody>
</table>

The Dutch Lipid Clinic Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History</td>
<td></td>
</tr>
<tr>
<td>First-degree relative with premature coronary and/or vascular disease (men ≤55 years, women ≤60 years), OR</td>
<td>1</td>
</tr>
<tr>
<td>First-degree relative with known LDL-cholesterol ≥95th percentile for age and sex</td>
<td></td>
</tr>
<tr>
<td>First-degree relative with tendon xanthomata and/or arcus cornealis, OR</td>
<td>2</td>
</tr>
<tr>
<td>Children aged ≤18 years with known LDL-cholesterol ≥95th percentile for age and sex</td>
<td></td>
</tr>
<tr>
<td>Clinical History</td>
<td></td>
</tr>
<tr>
<td>Patient with premature coronary artery disease (age as above)</td>
<td>2</td>
</tr>
<tr>
<td>Patient with premature cerebral or peripheral vascular disease (age as above)</td>
<td>1</td>
</tr>
<tr>
<td>Physical Examination</td>
<td></td>
</tr>
<tr>
<td>Tendon Xanthomas</td>
<td>6</td>
</tr>
<tr>
<td>Arcus cornealis at age ≤45 years</td>
<td>4</td>
</tr>
<tr>
<td>Laboratory Analysis</td>
<td></td>
</tr>
<tr>
<td>LDL-C ≥330</td>
<td>8</td>
</tr>
<tr>
<td>LDL-C 250 – 329</td>
<td>5</td>
</tr>
<tr>
<td>LDL-C 190 – 249</td>
<td>3</td>
</tr>
<tr>
<td>LDL-C 155 – 189</td>
<td>1</td>
</tr>
<tr>
<td>DNA Analysis – functional mutation LDLR, APOB and PCSK9</td>
<td>8</td>
</tr>
<tr>
<td>Total Patient Score</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>A “definite” diagnosis of HeFH requires a patient score ≥8</td>
<td></td>
</tr>
<tr>
<td>A “probable” diagnosis of HeFH requires a patient score 6-7</td>
<td></td>
</tr>
<tr>
<td>A “possible” diagnosis of HeFH requires a patient score 3-5</td>
<td></td>
</tr>
</tbody>
</table>

REFERENCES

© and SM Marks of the Blue Cross and Blue Shield Association. ©1 and ™ Trade names are the intellectual property of their respective owners. Blue Cross and Blue Shield of North Carolina is an independent licensee of the Blue Cross and Blue Shield Association.
POLICY IMPLEMENTATION/UPDATE INFORMATION

May 2017: Clarification of policy in regard to the utilization of Repatha 420mg once monthly in initial approval criteria.

August 2016: Updated criteria to include coverage criteria for ASCVD.

September 2015: Updated criteria to include newest PCSK9 approval, Repatha.

July 2015: Original utilization management criteria issued.

Non-Discrimination and Accessibility Notice

Discrimination is Against the Law

• Blue Cross and Blue Shield of North Carolina (“BCBSNC”) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex.

• BCBSNC does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

BCBSNC:

• Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)

• Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

• If you need these services, contact Customer Service 1-888-206-4697, TTY and TDD, call 1-800-442-7028.

• If you believe that BCBSNC has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:
- BCBSNC, PO Box 2291, Durham, NC 27702, Attention: Civil Rights Coordinator- Privacy, Ethics & Corporate Policy Office, Telephone 919-765-1663, Fax 919-287-5613, TTY 1-888-291-1783
civilrightscoordinator@bcbsnc.com

- You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, Civil Rights Coordinator - Privacy, Ethics & Corporate Policy Office is available to help you.


- This Notice and/or attachments may have important information about your application or coverage through BCBSNC. Look for key dates. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call Customer Service 1-888-206-4697.

ATTENTION: If you speak another language, language assistance services, free of charge, are available to you. Call 1-888-206-4697 (TTY: 1-800-442-7028).


注意：如果您講廣東話或普通話，您可以免費獲得語言援助服務。請致電 1-888-206-4697 (TTY: 1-800-442-7028)。


ملحوظة: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية تتوفر لك بالمجان. اتصل برقم 1-888-206-4697.

ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-888-206-4697 (телетайп: 1-800-442-7028).


注意事項: 日本語を話される場合、無料の言語支援をご利用いただけます。1-888-206-4697（TTY: 1-800-442-7028）まで、お電話にてご連絡ください。

© and SM Marks of the Blue Cross and Blue Shield Association. ®1 and ™ Trade names are the intellectual property of their respective owners. Blue Cross and Blue Shield of North Carolina is an independent licensee of the Blue Cross and Blue Shield Association