1. Background:

Repatha™ (evolocumab) is a PCSK9 (proprotein convertase subtilisin kexin type 9) 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

2. Coverage Criteria: 

A. Primary Hyperlipidemia

1. Initial Therapy

   a. Repatha will be approved based on all of the following criteria:

      (1) Submission of medical records (e.g., chart notes, laboratory values) documenting one of the following diagnoses:

      (a) Heterozygous familial hypercholesterolemia (HeFH) as confirmed by both of the following:

         i. Pre-treatment LDL-C greater than 190 mg/dL (greater than 155 mg/dL if less than 16 years of age)
         ii. Pre-treatment LDL-C greater than 190 mg/dL in adult first- or second-degree relative

         -OR-

         (b) Atherosclerotic cardiovascular disease (ASCVD) as confirmed by one of the following:

         i. Acute coronary syndromes
         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 presumed to be of atherosclerotic origin
Submission of medical records (e.g., chart notes, laboratory values) documenting one of the following [prescription claims history may be used in conjunction as documentation of medication use, dose, and duration]:

(a) Patient has been receiving at least 12 consecutive weeks of high-intensity statin therapy and will continue to receive high-intensity statin [i.e. atorvastatin 40-80 mg, Crestor (rosuvastatin) 20-40 mg] at maximally tolerated dose

-OR-

(b) Both of the following:
   i. Patient is unable to tolerate high-intensity statin as evidenced by one of the following intolerable and persistent (i.e. more than 2 weeks) symptoms:
      • Myalgia (muscle symptoms without CK elevations)
      • Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

-AND-

ii. Patient has been receiving at least 12 consecutive weeks of moderate-intensity statin therapy and will continue to receive a moderate-intensity statin [i.e. atorvastatin 10-20 mg, Crestor (rosuvastatin) 5-10 mg, simvastatin ≥ 20 mg, pravastatin ≥ 40 mg, lovastatin 40 mg, Lescol XL (fluvastatin XL) 80 mg, fluvastatin 40 mg twice daily or Livalo (pitavastatin) ≥ 2 mg] at maximally tolerated dose

-OR-

(c) Both of the following:
   i. Patient is unable to tolerate moderate- and high-intensity statin as evidenced by one of the following intolerable and persistent (i.e. more than 2 weeks) symptoms:
      • Myalgia (muscle symptoms without CK elevations)
      • Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

-AND-

ii. Patient has been receiving at least 12 consecutive weeks of low-intensity statin therapy and will continue to receive a low-intensity statin [i.e. simvastatin 10 mg, pravastatin 10-20 mg,
lovastatin 20 mg, fluvastatin 20-40 mg, or Livalo (pitavastatin) 1 mg] at maximally tolerated dose

-OR-

(d) Patient is unable to tolerate low-, moderate-, and high-intensity statins as evidenced by both of the following:

i. One of the following intolerable and persistent (i.e. more than 2 weeks) symptoms for low-, moderate-, and high-intensity statins:
   • Myalgia (muscle symptoms without CK elevations)
   • Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

-AND-

ii. Patient has undergone a trial of statin rechallenge with another low-intensity statin with documented reappearance of muscle symptoms

-OR-

(e) Patient has a labeled contraindication to all statins as documented in medical records

-OR-

(f) Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN

-AND-

(3) Submission of medical record (e.g., chart notes, laboratory values) documenting one of the following [prescription claims history may be used in conjunction as documentation of medication use, dose, and duration]:

(a) Patient has been receiving at least 12 consecutive weeks of Zetia (ezetimibe) therapy as adjunct to maximally tolerated statin therapy and will continue to receive Zetia

-OR-

(b) Patient has a history of contraindication, or intolerance to Zetia

-AND-

(4) Submission of medical record (e.g., laboratory values) documenting one of the following LDL-C values while on maximally tolerated lipid lowering therapy
within the last 30 days:

(a) LDL-C ≥ 100 mg/dL with ASCVD

(b) LDL-C ≥ 130mg/dL without ASCVD

-AND-

(5) Used as an adjunct to a low-fat diet and exercise

-AND-

(6) Prescribed by one of the following:

(a) Cardiologist

(b) Endocrinologist

(c) Lipid specialist

-AND-

(7) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

-AND-

(8) One of the following as documented by prescription claims history or medical record:

(a) History of failure after 12 consecutive weeks of Praluent at FDA maximum labeled dosing of 150 mg every 2 weeks

(b) History of intolerance to Praluent therapy

*Results of prior genetic testing can be submitted as confirmation of diagnosis of HeFH, however please note that UnitedHealthcare does not currently cover genetic testing for evidence of an LDL-receptor mutation, familial defective apo B-100 or a PCSK9 mutation.

Authorization will be issued for 6 months

2. Reauthorization

a. Repatha will be approved based on all of the following criteria:

(1) Patient continues to receive statin at maximally tolerated dose (unless patient
has documented inability to take statins)

-AND-

(2) Patient continues to receive Zetia as an adjunct to maximally tolerated statin therapy (unless patient has documented inability to take Zetia)

-AND-

(3) Patient is continuing a low-fat diet and exercise regimen

-AND-

(4) Prescribed by one of the following:
   (a) Cardiologist
   (b) Endocrinologist
   (c) Lipid specialist

-AND-

(5) Submission of medical records (e.g. chart notes, laboratory values) documenting LDL-C reduction while on Repatha therapy

-AND-

(6) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

**Authorization will be issued for 12 months**

**B. Homozygous Familial Hypercholesterolemia**

1. **Initial Therapy**

   a. **Repatha** will be approved based on all of the following criteria:
      (1) Diagnosis of homozygous familial hypercholesterolemia (HoFH) as confirmed by submission of medical records (e.g., chart notes, laboratory values) documenting both of the following:*  
         (a) One of the following:  
            i. Pre-treatment LDL-C greater than 500 mg/dL
            ii. Treated LDL-C greater than 300 mg/dL
-AND-

(b) One of the following:
   i. Xanthoma before 10 years of age
   ii. Evidence of heterozygous familial hypercholesterolemia (HeFH) in both parents

-AND-

(2) Used as an adjunct to a low-fat diet and exercise

-AND-

(3) Patient is receiving other lipid-lowering therapy (e.g., statin, ezetimibe, LDL apheresis)

-AND-

(4) Prescribed by one of the following:
   (a) Cardiologist
   (b) Endocrinologist
   (c) Lipid specialist

-AND-

(5) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

-AND-

(6) Not used in combination with Juxtapid (lomitapide)

-AND-

(7) Not used in combination with Kynamro (mipomersen)

*Results of prior genetic testing can be submitted as confirmation of diagnosis of HoFH, however please note that UnitedHealthcare does not currently cover genetic testing for evidence of an LDL-receptor mutation, familial defective apo B-100 or a PCSK9 mutation.

Authorization will be issued for 6 months.
2. **Reauthorization**

   a. *Repatha* will be approved based on **all** of the following criteria:

      (1) Patient is continuing a low-fat diet and exercise regimen

      -AND-

      (2) Patient continues to receive other lipid-lowering therapy (e.g., statin, LDL apheresis)

      -AND-

      (3) Submission of medical records (e.g. chart notes, laboratory values) documenting LDL-C reduction while on Repatha therapy

      -AND-

      (4) Prescribed by **one** of the following:

         (a) Cardiologist

         (b) Endocrinologist

         (c) Lipid specialist

         --AND--

      (5) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

      -AND-

      (6) Not used in combination with Juxtapid (lomitapide)

      -AND-

      (7) Not used in combination with Kynamro ( mipomersen)

**Authorization will be issued for 12 months.**

\(^a\) For Maryland, requests for continuation of therapy may also be approved if the provider confirms the patient has been on the medication in the past 180 days and that the medication is effective in treating the patient’s condition. Please see Maryland Continuation of Care guideline.

\(^b\) For Indiana (effective 7/1/16) and West Virginia (effective 1/1/17), step therapy
3. Additional Clinical Rules:

Supply Limits may be in place.

4. References:


<table>
<thead>
<tr>
<th>Program</th>
<th>Prior Authorization/Medical Necessity - Repatha™ (evolocumab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/2015</td>
<td>New program.</td>
</tr>
<tr>
<td>5/2015</td>
<td>Added examples of atherosclerotic cardiovascular disease.</td>
</tr>
<tr>
<td>9/2015</td>
<td>Revised clinical criteria to include combination use of high-intensity statin or documented intolerance to high-, moderate- and low intensity statin therapy to achieve the maximally tolerated statin therapy.</td>
</tr>
<tr>
<td>11/2015</td>
<td>Added step therapy requirement language for Primary Hyperlipidemia</td>
</tr>
<tr>
<td>1/2016</td>
<td>Removed continuation of therapy criterion.</td>
</tr>
<tr>
<td>8/2016</td>
<td>Add requirement of Praluent failure at maximum labeled dosing. Added MD, IN, and WV coverage information. Updated reference.</td>
</tr>
<tr>
<td>11/2016</td>
<td>Added California coverage information.</td>
</tr>
<tr>
<td>12/2016</td>
<td>Modified medical record criteria to include review of prescription claims history. Updated references.</td>
</tr>
</tbody>
</table>