Repatha

**Description**

Repatha (evolocumab)

**Background**

Repatha is used in addition to diet and maximally tolerated statin therapy in adult patients with heterozygous familial hypercholesterolemia (HeFH), homozygous familial hypercholesterolemia (HoFH) or patients with clinical atherosclerotic cardiovascular disease such as heart attacks or strokes, who require additional lowering of LDL cholesterol. HeFH is an inherited condition that causes high levels of low-density lipoprotein (LDL) cholesterol. Repatha provides another treatment option for patients with known cardiovascular disease who have not been able to lower their LDL cholesterol enough on statins. A high level of LDL cholesterol (known as “bad” cholesterol) in the blood is linked to cardiovascular disease. Heart disease is the number one cause of death for Americans, both men and women (1).

Repatha is an antibody that targets a specific protein, called PCSK9, which works by reducing the number of receptors on the liver that remove LDL cholesterol from the blood. By blocking PCSK9’s ability to work, more receptors are available to get rid of LDL cholesterol from the blood and, as a result, lower LDL cholesterol levels (1).

**Regulatory Status**

FDA Indicated for: Repatha is a PCSK9 (Proprotein Convertase Subtilisin Kexin Type 9) inhibitor antibody indicated as adjunct to diet and maximally tolerated statin therapy for the treatment of: (2)
1. Maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who requires additional lowering of low density lipoprotein cholesterol (LDL-C).

2. 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 (2).

The safety and effectiveness of REPATHA have not been established in pediatric patients with HoFH who are younger than 13 years old. The safety and effectiveness of REPATHA have not been established in pediatric patients with primary hyperlipidemia or HeFH (2).

Physicians often measure CK in patients about to begin statins or already on statins. Many physicians will not start or continue statins to lower LDLC in asymptomatic patients with high CK because of concern about possible statin-induced myositis-rhabdomyolysis. No patients during follow-up on statins developed CK more than 10 times the UNL (2500 IU/L) High pretreatment CK, predominantly 1 to 5 times the UNL, as in the current report, should not be an impediment to start or continue statins to lower LDLC (3).

Related policies
Juxtapid, Kynamro, Praluent

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Repatha may be considered medically necessary in patients 13 years of age or older for the treatment of homozygous familial hypercholesterolemia (HoFH). Repatha may be considered medically necessary in patients 18 years of age or older heterozygous familial hypercholesterolemia (HeFH) or for patients that have atherosclerotic cardiovascular disease if the conditions indicated below are met.

Repatha is considered investigational in patients who are less than 13 years of age and in patients who do not have a confirmed diagnosis of homozygous familial hypercholesterolemia. Repatha is considered investigational in patients who are less than 18 years of age and in patients who do not have a confirmed diagnosis heterozygous familial hypercholesterolemia (HeFH) or atherosclerotic cardiovascular disease.
Prior-Approval Requirements

Diagnoses

Patient must have ONE of the following:

1. Homozygous familial hypercholesterolemia (HoFH)

   AND ALL of the following:
   a. 13 years and older
   b. Provided documentation (medical records, patient’s chart) of confirmed diagnosis by LDL-R DNA Sequencing Test or APOB (hypercholesterolemia) Mutation Analysis
   c. Genetic confirmation of two mutant alleles at the LDLR, Apo-B, PCSK9, ARH adaptor protein 1/LDLRAP1 gene locus

2. Heterozygous familial hypercholesterolemia (HeFH)
   a. 18 years and older

   AND ONE of the following:
   1) Provided documentation (医疗 records, patient’s chart) of confirmed diagnosis by LDL-R DNA Sequencing Test or APOB (hypercholesterolemia) Mutation Analysis
   2) Dutch Lipid Clinic Network Criteria score > 8
   3) Simon-Broome Diagnostic Criteria for definite familial hypercholesterolemia

   AND ALL of the following for HeFH and HoFH:
   1) Provided documentation (medical records, laboratory reports) of baseline and/or current LDL-C level \( \geq 100 \text{ mg/dL} \) in the past 60 days
   2) Documented 3 months prior therapy with at least ONE high intensity statin in combination with Zetia (ezetimibe)

3. Atherosclerotic cardiovascular disease (ASCVD)

   AND ONE of the following for ASCVD:
   a. Documented history of ONE of the following atherosclerotic cardiovascular disease (ASCVD) or cardiovascular events:
      i. Acute coronary syndrome
      ii. Myocardial infarction
iii. Stable or unstable angina
iv. Coronary or other arterial revascularization procedure (such as PTCA, CABG)
v. Transient ischemic attack (TIA)
vi. Peripheral arterial disease presumed to be of atherosclerotic origin
vii. Findings from CT angiogram or catheterization consistent with clinical ASCVD

b. At high risk for atherosclerotic cardiovascular disease (ASCVD) or cardiovascular event based on 10-year risk score used by ONE of the following tools:
   1. ASCVD Pooled Cohort Risk Assessment—score greater than or equal to 15% (Calculator is available at http://tools.cardiosource.org/ASCVD-Risk-Estimator/)
   2. Framingham Risk Score—score greater than or equal to 20% (available at http://cvdrisk.nhlbi.nih.gov/)

AND ALL of the following for ASCVD:
   1. 18 years and older
   2. Laboratory report or medical records of LDL-C 100 mg/dL or greater in the past 60 days:
   3. Documented 3 months prior therapy with at least ONE high intensity statin in combination with Zetia (ezetimibe)

OR ONE of the following:

a. Intolerance to a statin
   1) Provide medical records of documentation of the following intolerable adverse reactions with ONE of the following:
      a) Intolerable and persistent (ie: more than 2 weeks) muscle symptoms (eg., muscle pain, weakness, cramps) with ONE of the following:
         i. Patient has taken at least ONE high intensity statin in combination with Zetia (ezetimibe) and re-challenge with ONE low to moderate intensity statin in combination with Zetia (ezetimibe) with a documented reappearance of the muscle symptoms
         ii. Documentation provided indicated creatinine kinase (CK) levels greater than 5 times upper normal limit
and/or rhabdomyolysis with CK levels greater than 2,500 IU/L)

b) Intolerable and persistent hepatotoxicity with ALL of the following:
   i. Documentation indicating persistent elevations (>3 times the upper limit of normal occurring on 2 more occasions) of serum transaminases or the presence of jaundice
   ii. Secondary causes of elevations in hepatic transaminase levels have been ruled out (eg., infection, medications, herbal supplements)

b. Inadequate response to a high intensity statin
   1) Laboratory results within the past 60 days indicating:
      a) LDL-C 100 mg/dL or greater
   2) Patient has undergone 3 months of prior therapy with at least TWO trials of different statins in combination with Zetia (ezetimibe).

c. Contraindication to a high intensity statin must have ONE of the following:
   1) Currently pregnant or may become pregnant
   2) Nursing mother

   AND ALL of the following for HeFH, HoFH and ASCVD:
   a. Patient will be assessed for response (ie., LDL-C reduction) and adherence to the prescribed lipid lowering regimen after 3 months
   b. Prescribed or recommended by cardiologist, endocrinologist, or lipidologist
   c. NO dual therapy with another proprotein convertase subtilisin/kexin type 9 inhibitor, Juxtagapid, or Kynamro

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

Prior – Approval Renewal Requirements

Diagnoses
   Patient must have ONE of the following:
1. Heterozygous familial hypercholesterolemia (HeFH)
2. Homozygous familial hypercholesterolemia (HoFH)
3. Atherosclerotic cardiovascular disease (ASCVD)

AND ALL of the following:
a. Documentation has been provided indicating the reduction in LDL-C (i.e., chart notes, medical record, and/or laboratory reports) of ONE of the following:
   i. Percentage reduction of LDL-C level is greater than or equal to (≥) 40%, compared to the level immediately prior to starting a PCSK9 inhibitor
   ii. Absolute LDL-C is less than (<) 100mg/dL

b. Patient will be assessed for adherence to the prescribed lipid lowering regimen
c. NO dual therapy with another proprotein convertase subtilisin/kexin type 9 inhibitor, Juxtapid, or Kynamro

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

<table>
<thead>
<tr>
<th>High-intensity statin therapy</th>
<th>Moderate-intensity statin therapy</th>
<th>Low-intensity statin therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin (Lipitor) 40 - 80 mg a day</td>
<td>Atorvastatin (Lipitor) 10 - 20mg a day Simvastatin (Zocor ) 20 - 40mg a day</td>
<td>Simvastatin (Zocor ) 10mg a day Pravastatin (Pravachol ) 10 - 20mg a day</td>
</tr>
<tr>
<td>Rosuvastatin (Crestor) 20 - 40mg a day</td>
<td>Rosuvastatin (Crestor ) 5 - 10mg a day Pravastatin (Pravachol ) 40 - 80mg a day</td>
<td>Pravastatin (Pravachol ) 20mg a day</td>
</tr>
<tr>
<td></td>
<td>Lovastatin (Mevacor ) 40mg a day Fluvastatin XL (Lescol XL ) 80mg a day</td>
<td>Lovastatin (Mevacor ) 20mg a day</td>
</tr>
<tr>
<td></td>
<td>Fluvastatin (Lescol ) 40mg twice a day Pitavastatin (Livalo ) 2 - 4mg a day</td>
<td>Fluvastatin (Lescol ) 20 - 40mg a day</td>
</tr>
</tbody>
</table>

Policy Guidelines
**Section:** Prescription Drugs  
**Effective Date:** January 1, 2017  
**Subsection:** Cardiovascular Agents  
**Original Policy Date:** September 9, 2015  
**Subject:** Repatha  
**Page:** 7 of 8

### Pre - PA Allowance

None

### Prior - Approval Limits

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Repatha 140mg</th>
<th>9 syringes per 90 days OR 420mg</th>
<th>3 syringes per 90 days</th>
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**Duration** 3 months

### Prior – Approval *Renewal* Limits

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**Duration** 12 months

### Rationale

**Summary**

Repatha is used in addition to diet and maximally tolerated statin therapy in adult patients with homozygous familial hypercholesterolemia (HoFH), heterozygous familial hypercholesterolemia (HeFH) or patients with clinical atherosclerotic cardiovascular disease such as heart attacks or strokes, who require additional lowering of LDL cholesterol. Repatha is an antibody that targets a specific protein, called PCSK9, which works by reducing the number of receptors on the liver that remove LDL cholesterol from the blood. By blocking PCSK9’s ability to work, more receptors are available to get rid of LDL cholesterol from the blood and, as a result, lower LDL cholesterol levels. The safety and efficacy of Repatha in pediatric patients 18 years or less have not been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Repatha while maintaining optimal therapeutic outcomes.

**References**
Section: Prescription Drugs  Effective Date: January 1, 2017
Subsection: Cardiovascular Agents Original Policy Date: September 9, 2015
Subject: Repatha Page: 8 of 8


Policy History

<table>
<thead>
<tr>
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| September 2015 | Addition to PA  
Annual review and change of active liver disease from the contraindications to intolerance section.  
Addition of “Current utilization, including samples, does not guarantee approval of coverage,” to the criteria |
| December 2015 | Annual review                                                                                                                         |
| July 2016   | Addition of 420mg syringe and documentation in the past 60 days for LDL levels                                                           |
| September 2016 | Policy number change from 5.16.08 to 5.40.08                                                                                   |
|             | Annual editorial review and reference update                                                                                           |
|             | Change in intolerable and persistent (ie: more than 2 weeks) muscle symptoms (eg., muscle pain, weakness, cramps) with ALL of the following- |
|             | to ONE of the following                                                                                                             |
|             | Change from documentation provided indicated creatinine kinase (CK) levels greater than 10 times upper normal limit and/or rhabdomyolysis with CK levels greater than 10,000 IU/L – to 5 times and 2,500 IU/L |
| December 2016 | Annual review                                                                                                                         |

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 2, 2016 and is effective on January 1, 2017.

Deborah M. Smith, MD, MPH