Commercial/Healthcare Exchange PA Criteria

Effective: May 4, 2016

Prior Authorization: Repatha (evolocumab)

Products Affected:
Repatha (evolocumab) Subcutaneous Solution (Prefilled Syringe)
Repatha (evolocumab) Pushtronex System Subcutaneous Solution (Cartridge)
Repatha (evolocumab) SureClick Subcutaneous Solution (Auto-injector)

Medication Description:

Evolocumab (Repatha) is a human monoclonal IgG2 directed against human proprotein convertase subtilisin kexin 9 (PCSK9). Evolocumab binds to PCSK9 and inhibits circulating PCSK9 from binding to the low density lipoprotein (LDL) receptor (LDLR), preventing PCSK9-mediated LDLR degradation and permitting LDLR to recycle back to the liver cell surface. By inhibiting the binding of PCSK9 to LDLR, evolocumab increases the number of LDLRs available to clear LDL from the blood, thereby lowering LDL-C levels.

Repatha is indicated as an adjunct to diet and maximally tolerated statin therapy for the 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). Repatha is also indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

Covered Uses:

- Hyperlipidemia in Patients with Clinical Atherosclerotic Cardiovascular Disease (ASCVD)
- Heterozygous Familial Hypercholesterolemia (HeFH)
- Homozygous Familial Hypercholesterolemia (HoFH)
- Primary hypercholesterolemia

Exclusion Criteria:

Repatha has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Concurrent use of Repatha with Praluent (alirocumab injection for SC use), Juxtapid (lomitapide capsules) or Kynamro (mipomersen injection). Praluent is another PCSK9 inhibitor and should not be used with Repatha. Juxtapid and Kynamro are agents indicated as an adjunct to lipid-lowering medications and diet to modify lipid parameters (e.g., reduce LDL-C levels) in patients with HoFH.28-29. The efficacy and safety of using Praluent, Juxtapid and Kynamro in combination with Repatha have not been established.

2. Coverage is not recommended for conditions not listed in the **"Other Criteria"**. Criteria will be updated as new published data are available.

Required Medical information;

- Information
- Diagnosis
- Current LDL-C (within the past 90 days)
- Previous trial of high dose statins: rosuvastatin 40mg and atorvastatin 80mg
- Confirmation that a medication reconciliation has been performed, by the prescriber, to identify any potential drug interactions that could cause elevated statin levels

Age Restrictions:

1. **Hyperlipidemia in Patients with Clinical Atherosclerotic Cardiovascular Disease (ASCVD)**
   - The patient is aged ≥ 18 years
2. **Heterozygous Familial Hypercholesterolemia [HeFH]**
   - The patient is aged ≥ 18 years
3. **Homozygous Familial Hypercholesterolemia [HoFH]**
   - The patient is aged ≥ 13 years
4. **Primary hypercholesterolemia**
   - The patient is aged ≥ 18 years

Prescriber Restrictions: Prescribed by, or in consultation with, a cardiologist, endocrinologist, or a physician who focuses in the treatment of CV risk management and/or lipid disorders.

Coverage Duration:

- Initial Prior Authorization: 12 weeks
- Continuation of Therapy: 12 months

Other Criteria:

1. **Hyperlipidemia in Patients with Clinical Atherosclerotic Cardiovascular Disease (ASCVD).***
   Approve Repatha if the patient meets the following criteria (A, B, C, D and E):
   A) The patient is aged ≥ 18 years; **AND**
   B) The patient meets the following criteria (i and ii):
      i. The patient has a current low-density lipoprotein cholesterol (LDL-C) level ≥ 70 mg/dL within the past 90 days (after treatment with antihyperlipidemic agents but prior to PCSK9 inhibitor therapy such as Praluent [alirocumab injection for SC use] or Repatha) [documentation required]; **AND**
      ii. The patient has had one of the following conditions or diagnoses (a, b, c, d, or e):
         a) The patient has had a previous myocardial infarction (MI) or has a history of an acute coronary syndrome (ACS) [documentation required]; **OR**
         b) The patient has a diagnosis of angina (stable or unstable) [documentation required]; **OR**
         c) The patient has a past history of stroke or transient ischemic attack (TIA) [documentation required]; **OR**
         d) The patient has peripheral arterial disease (PAD) [documentation required]; **OR**
         e) The patient has undergone a coronary or other arterial revascularization procedure in the past (e.g., coronary artery bypass graft [CABG], percutaneous coronary intervention [PCI], angioplasty, coronary stent procedure) [documentation required]; **AND**

C) The patient meets one of the following criteria (i or ii):
- **i.** The patient has tried 2 high-intensity statin therapies (i.e., atorvastatin 80 mg daily AND rosuvastatin 40 mg daily) FOR 8-12 continuous weeks[documentation required]; **AND** the LDL-C level remains ≥ 70 mg/dL [documentation required]; **OR**
- **ii.** The patient has been determined to be statin intolerant by meeting one of the following criteria (a or b):
  - **a)** The patient experienced statin-related rhabdomyolysis (statin-induced muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness, acute renal failure and/or elevated creatine kinase [CK] levels [e.g., greater or equal to 10 times the upper limit of normal]) [documentation required]; **OR**
  - **b)** The patient experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) and meets both of the following criteria [(1) and (2)]:
    - **(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) [documentation required]; **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); AND

D) Repatha is prescribed by, or in consultation with, a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders; **AND**

E) If able to tolerate statins, the patient continues to receive the maximum tolerated dose of a statin while receiving Repatha therapy.

2. Heterozygous Familial Hypercholesterolemia [HeFH].[†*]

Approve Repatha if the patient meets the following criteria (A, B, C, D and E):

A) The patient is aged ≥ 18 years; **AND**

B) The patient meets the following criteria (i and ii):
- **i.** The patient has a current low-density lipoprotein cholesterol (LDL-C) level ≥ 100 mg/dL within the past 90 days; **AND**
- **ii.** The patient's diagnosis of HeFH is defined by WHO/Dutch Lipid group criteria **OR** Simon-Broome Criteria **OR** genetic testing; **AND**

C) The patient meets one of the following criteria (i or ii):
- **i.** The patient has tried 2 high-intensity statin therapies (i.e., atorvastatin 80 mg daily AND rosuvastatin 40 mg daily) for 8-12 continuous weeks [documentation required]; AND the LDL-C level remains ≥ 100 mg/dL [documentation required]; **OR**
- **ii.** The patient has been determined to be statin intolerant by meeting one of the following criteria (a or b):
  - **a)** The patient experienced statin-related rhabdomyolysis (statin-induced muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness, acute renal failure and/or elevated creatine kinase [CK] levels [e.g., greater or equal to 10 times the upper limit of normal]) [documentation required]; **OR**

b) The patient experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) and meets both of the following criteria [(1) and (2)]:

(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) [documentation required]; **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); **AND**

D) Repatha is prescribed by, or in consultation with, a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders; **AND**

E) If able to tolerate statins, the patient continues to receive the maximum tolerated dose of a statin while receiving Repatha therapy.

3. Homozygous Familial Hypercholesterolemia [HoFH].

Approve Repatha if the patient meets the following criteria (A, B, C, D, and E):

A) The patient is aged ≥ 13 years; **AND**

B) The patient meets the following criteria (i and ii):

i. The patient has a current low-density lipoprotein cholesterol (LDL-C) level ≥ 100 mg/dL within the past 90 days; **AND**

ii. The patient has genetic confirmation of two mutant alleles at the low-density lipoprotein receptor (LDLR), apolipoprotein B (APOB), proprotein convertase subtilisin kexin type 9 (PCSK9) or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene locus [documentation required]; **AND**

C) The patient meets one of the following criteria (i OR ii):

i. The patient has tried 2 high-intensity statin therapies (i.e., atorvastatin 80 mg daily AND rosuvastatin 40mg daily) for 8-12 continuous weeks [documentation required] AND the LDL-C level remains ≥ 100 mg/dL [documentation required]; **OR**

ii. The patient has been determined to be statin intolerant by meeting one of the following criteria (a or b):

a) The patient experienced statin-related rhabdomyolysis (statin-induced muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness, acute renal failure and/or elevated creatine kinase [CK] levels [e.g., ≥ 10 times the upper limit of normal]) [documentation required]; **OR**

b) The patient experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) and meets both of the following criteria [(1) and (2)]:

(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) [documentation required]; **AND**

(2) When receiving separate trials of both atorvastatin and rosuvastatin the skeletal-related muscle symptoms (e.g., myopathy, myalgia) resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); A**ND**

D) Prescribed by, or in consultation with, a cardiologist, endocrinologist, or a physician who focuses in the treatment of CV risk management and/or lipid disorders; **AND**

E) The patient continues to receive the maximum tolerated dose of a statin while receiving Repatha, if able to tolerate statins.

4. **Primary hypercholesterolemia**

Approve Repatha if the patient meets the following criteria (A, B, C, D, and E):

A) The patient is aged ≥ 18 years; **AND**

B) The patient has a current LDL-C level equal to or greater than 100 mg/dL within the past 90 days; **AND**

C) The patient meets one of the following criteria (i OR ii):

i. The patient has tried 2 high-intensity statin therapies (i.e., atorvastatin 80 mg daily AND rosuvastatin 40mg daily) for 8-12 continuous weeks [documentation required] AND the LDL-C level remains ≥ 100 mg/dL [documentation required]; **AND**

ii. The patient has been determined to be statin intolerant by meeting one of the following criteria (a or b):

a) The patient experienced statin-related rhabdomyolysis (statin-induced muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness, acute renal failure and/or elevated creatine kinase [CK] levels [e.g., ≥ 10 times the upper limit of normal]) [documentation required]; **OR**

b) The patient experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) and meets both of the following criteria [(1) and (2)]:

(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) [documentation required]; **AND**

(2) When receiving separate trials of both atorvastatin and rosuvastatin the skeletal-related muscle symptoms (e.g., myopathy, myalgia) resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); A**ND**

D) Repatha is prescribed by, or in consultation with, a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders; **AND**

E) If able to tolerate statins, the patient continues to receive the maximum tolerated dose of a statin while receiving Repatha therapy.

Renewal Criteria:

1. **Hyperlipidemia in Patients with Clinical Atherosclerotic Cardiovascular Disease (ASCVD)**
   - Lipid panel showing ≥ 40% reduction in LDL-C from baseline.
   - Continued adherence to maximally tolerated statin dose.
2. **Heterozygous Familial Hypercholesterolemia [HeFH]**
   - Lipid panel showing ≥ 40% reduction in LDL-C from baseline.
   - Continued adherence to maximally tolerated statin dose.
3. **Homozygous Familial Hypercholesterolemia [HoFH]**
   - Lipid panel showing ≥ 20% reduction in LDL-C from baseline.
   - Continued adherence to maximally tolerated statin dose.
4. **Primary hypercholesterolemia**
   - Lipid panel showing ≥ 40% reduction in LDL-C from baseline.
   - Continued adherence to maximally tolerated statin dose.

References:

1. Repatha [package insert]. Thousand Oaks, CA; Amgen; August 2015.
2. Robinson et al. Effect of evolocumab or ezetimibe added to moderate- or high-intensity statin therapy on LDL-C lowering in patients with hypercholesterolemia: the LAPLACE-2 randomized clinical trial. JAMA. 2014 May 14;311(18):1870-82.
3. Blom et al. A 52-week placebo-controlled trial of evolocumab in hyperlipidemia. N Engl J Med. 2014 May 8;370(19):1809-19.
4. Raal et al. PCSK9 inhibition with evolocumab (AMG 145) in heterozygous familial hypercholesterolemia (RUTHERFORD-2): a randomized, double-blind, placebo-controlled trial. Lancet. 2015 Jan 24;385(9965):331-40.
5. Raal et al. Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolemia (TESLA Part B): a randomized, double-blind, placebo-controlled trial. Lancet. 2015 Jan 24;385(9965):341-50.
6. FDA Briefing Information: Evolocumab. The Endocrinologic and Metabolic Drugs Advisory Committee Meeting. FDA Center for Drug Evaluation and Research.2015 June 10. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM450072.pdf. Accessed August 31, 2015.
7. Stone NJ, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation, 2014; 129(25 Suppl 2): S1-45.
8. Jacobson et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1 – executive summary. Journal of Clinical Lipidology. 2014. Available at: http://www.sciencedirect.com/science/article/pii/S1933287414002748. Accessed August 31, 2015
9. FDA approves Repatha to treat certain patients with high cholesterol. FDA News Release. 27 August 2015. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm460082.htm

Policy Revision history

Rev #	Type of Change	Summary of Change	Sections Affected	Date
1	New Policy	New Policy	All	01/13/2016
2	Clinical Update	Clarification of covered uses, renewal criteria removed	Covered Uses, Other criteria	03/01/2016
3	Additional criteria	Medication reconciliation requirement	Required Medical Information	12/12/2017

4	Update Criteria	Clinical criteria updated	Other Criteria	5/23/2018
5	Update Criteria	New Indication	Other Criteria, Age Restriction, Covered Uses	07/20/2018
6	Policy	ConnectiCare adoption of Policy	All	7/25/18