FORMULARY EXCEPTION POLICY

POLICY: PCSK9 Inhibitors – Repatha® and Repatha® authorized alternative (evolocumab injection for subcutaneous use – Amgen)

Repatha – NDCs 55513076001, 55513076002, 55513075001, 55513077001
Repatha authorized alternatives – NDCs 72511076001, 72511076002, 72511075001

DATE EFFECTIVE: 01/01/2019; selected revision 04/03/2019

Documentation: Documentation is required where noted in the criteria as [documentation required]. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts and/or other information.

Approval Duration: All approvals are provided for 1 year.

Note: For the indications of atherosclerotic cardiovascular disease (ASCVD) and heterozygous familial hypercholesterolemia (HeFH), a trial of Praluent therapy is required, if Praluent is formulary.

CRITERIA
Coverage of Repatha or Repatha authorized alternative is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Atherosclerotic Cardiovascular Disease (ASCVD) [Clinical]. Approve Repatha or Repatha authorized alternative for 1 year if the patient meets the following criteria (A, B, C, D and E PLUS one of F or G):
   A) The patient is aged ≥ 18 years; AND
   B) The patient has had one of the following conditions or diagnoses (i, ii, iii, iv or v):
      i. The patient has had a previous myocardial infarction (MI) or has a history of an acute coronary syndrome (ACS) [documentation required]; OR
      ii. The patient has a diagnosis of angina (stable or unstable) [documentation required]; OR
      iii. The patient has a past history of stroke or transient ischemic attack (TIA) [documentation required]; OR
      iv. The patient has peripheral arterial disease (PAD) [documentation required]; OR
      v. 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 one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin tablets ≥ 20 mg daily [as a single-entity or as a combination product])∗ for ≥ 8 continuous weeks [documentation required] AND the LDL-C level after this treatment regimen 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 (Note: Statin-induced muscle breakdown that is usually associated with markedly elevated creatine kinase [CK] levels [at least 10 times the upper limit of normal], along with evidence of end organ damage which can include signs of acute renal injury [noted by substantial increases in serum creatinine {Scr} levels {a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr}] and/or myoglobinuria [myoglobin present in urine]) [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 rosvastatin (as single-entity or as combination products) [documentation required]; AND

(2) 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); 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) The patient is not concurrently using Repatha with Praluent, Juxtapid, or Kynamro: AND

F) If Praluent is formulary: The patient meets both of the criteria below (i and ii):

i. The patient has tried Praluent® (alirocumab injection for SC use) [documentation required]; AND

ii. The patient has had unacceptable toxicity and/or suboptimal efficacy to Praluent according to the prescribing physician; OR

G) If Praluent is non-formulary: Approve Repatha or Repatha authorized alternative, whichever is formulary (and if patient meets criteria A through E). If neither the Repatha nor Repatha authorized alternative is formulary, approve.

2. Heterozygous Familial Hypercholesterolemia [HeFH]. Approve Repatha or Repatha authorized alternative for 1 year if the patient meets the following criteria (A, B, C, D and E PLUS one of F or G):

A) The patient is aged ≥ 18 years; AND

B) The patient meets one of the following criteria (i, ii, iii, iv or v):

i. The patient has an untreated LDL-C ≥ 190 mg/dL (prior to treatment with antihyperlipidemic agents) [documentation required]; OR

ii. The patient has genetic confirmation of HeFH by mutations in 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 [documentation required]; OR

iii. The patient has been diagnosed with HeFH meeting one of the following diagnostic criteria thresholds (a or b):

a) The prescriber used the Dutch Lipid Network criteria and the patient has a score > 5 [documentation required]; OR

b) The prescriber used the Simon Broome criteria and the patient met the threshold for “definite” or “possible” familial hypercholesterolemia [documentation required]; OR
iv. The patient has clinical manifestations of HeFH (e.g., cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas or xanthelasma) [documentation required]; OR
v. 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 such as Praluent® [alirocumab injection for SC use] or Repatha) [documentation required]; AND

C) The patient meets one of the following criteria (i or ii):
   i. The patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin tablets ≥ 20 mg daily [as a single-entity or as a combination product])’ for ≥ 8 continuous weeks [documentation required]; AND the LDL-C level after this treatment regimen 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 (Note: Statin-induced muscle breakdown that is usually associated with markedly elevated creatine kinase [CK] levels [at least 10 times the upper limit of normal], along with evidence of end organ damage which can include signs of acute renal injury [noted by substantial increases in serum creatinine {Scr} levels {a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr}] and/or myoglobinuria [myoglobin present in urine]) [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) The patient is not concurrently using Repatha with Praluent, Juxtapid, or Kynamro: AND

F) If Praluent is formulary: The patient meets both of the criteria below (i and ii):
   i. The patient has tried Praluent® (alirocumab injection for SC use) [documentation required]; AND
   ii. The patient has had unacceptable toxicity and/or suboptimal efficacy to Praluent according to the prescribing physician; OR

G) If Praluent is non-formulary: Approve Repatha or Repatha authorized alternative, whichever is formulary (if neither Repatha nor Repatha authorized alternatives is formulary, approve whichever product is being requested).

3. **Homozygous Familial Hypercholesterolemia [HoFH].** Approve Repatha or Repatha authorized alternative, whichever is formulary (if neither Repatha nor Repatha authorized alternatives is formulary, approve whichever product is being requested), for 1 year 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 one of the following (i, ii, iii or iv):
      i. 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]; OR

ii. The patient has an untreated low-density lipoprotein (LDL-C) level > 500 mg/dL (prior to treatment with antihyperlipidemic agents) [documentation required]; OR

iii. The patient has a treated low-density lipoprotein cholesterol (LDL-C) level ≥ 300 mg/dL (after treatment with antihyperlipidemic agents but prior to agents such as Repatha, Kynamro® [ mipomersen injection] or Juxtapid® [lomitapide capsules]) [documentation required]; OR

iv. The patient has clinical manifestations of HoFH (e.g., cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas or xanthelasma) [documentation required]; AND

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

i. The patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosvastatin tablets ≥ 20 mg daily [as a single-entity or as a combination product])* for ≥ 8 continuous weeks [documentation required] AND the low-density lipoprotein cholesterol (LDL-C) level after this treatment regimen 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 (Note: Statin-induced muscle breakdown that is usually associated with markedly elevated creatine kinase [CK] levels [at least 10 times the upper limit of normal], along with evidence of end organ damage which can include signs of acute renal injury [noted by substantial increases in serum creatinine {Scr} levels {a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr}] and/or myoglobinuria [myoglobin present in urine]) [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 rosvastatin (as single-entity or as combination products) [documentation required]; AND

      (2) 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); 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) The patient is not concurrently using Repatha with Praluent, Juxtapid, or Kynamro.

4. Primary Hyperlipidemia (not associated with ASCVD, HeFH, or HoFH). [Note: This may be referred to as combined hyperlipidemia, hypercholesterolemia {pure, primary}, dyslipidemia, increased/elevated LDL-C]. Approve Repatha or Repatha authorized alternative, whichever is formulary, (if neither Repatha nor Repatha authorized alternatives is formulary, approve whichever product is being requested) for 1 year 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 coronary artery calcium or calcification (CAC) score ≥ 300 Agatston units [documentation required]; AND

C) The patient meets one of the following criteria (i or ii):
i. The patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin tablets ≥ 20 mg daily [as a single-entity or as a combination product]) AND Zetia® (ezetimibe tablets, generic) [as a single-entity or as a combination product] for ≥ 8 continuous weeks [documentation required]; AND the LDL-C level after this treatment regimen 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 (Note: Statin-induced muscle breakdown that is usually associated with markedly elevated creatine kinase [CK] levels [at least 10 times the upper limit of normal], along with evidence of end organ damage which can include signs of acute renal injury [noted by substantial increases in serum creatinine {Scr} levels {a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr}] and/or myoglobinuria [myoglobin present in urine]) [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) The patient is not concurrently using Repatha with Praluent, Juxtapid, or Kynamro.

### HISTORY

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
<th>Date</th>
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<tbody>
<tr>
<td>New policy</td>
<td></td>
<td>07/01/2018</td>
</tr>
<tr>
<td>Selected revision</td>
<td>Added Repatha authorized alternative to the policy with related criteria changes.</td>
<td>01/01/2019</td>
</tr>
<tr>
<td>DEU selected revision</td>
<td>Selected revision to be effective 04/05/2019 to remove auto-approvals for Praluent.</td>
<td>04/03/2019</td>
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DEU – Drug Evaluation Unit.