



## FORMULARY EXCEPTION POLICY

**POLICY:** PCSK9 Inhibitors – Repatha® and Repatha® authorized alternative (evolcumab 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

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**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  $\geq 18$  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  $\geq 40$  mg daily; rosuvastatin tablets  $\geq 20$  mg daily [as a single-entity or as a combination product])\* for  $\geq 8$  continuous weeks **[documentation required]** AND the LDL-C level after this treatment regimen remains  $\geq 70$  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  $\geq$  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 (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  $\geq$  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  $\geq$  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  $\geq 100$  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  $\geq 40$  mg daily; rosuvastatin tablets  $\geq 20$  mg daily [as a single-entity or as a combination product])\* for  $\geq 8$  continuous weeks **[documentation required]**; AND the LDL-C level after this treatment regimen remains  $\geq 70$  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  $\geq 0.5$  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 (and if patient meets criteria A through E). If neither the Repatha nor Repatha authorized alternative is formulary, approve.

**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  $\geq 13$  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  $\geq$  300 mg/dL (after treatment with antihyperlipidemic agents but prior to agents such as Repatha, Kynamro<sup>®</sup> [mipomersen injection] or Juxtapid<sup>®</sup> [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  $\geq$  40 mg daily; rosuvastatin tablets  $\geq$  20 mg daily [as a single-entity or as a combination product])\* for  $\geq$  8 continuous weeks **[documentation required]** AND the low-density lipoprotein cholesterol (LDL-C) level after this treatment regimen remains  $\geq$  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  $\geq$  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.
- 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  $\geq$  18 years; AND
  - B) The patient has a coronary artery calcium or calcification (CAC) score  $\geq$  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  $\geq$  40 mg daily; rosuvastatin tablets  $\geq$  20 mg daily [as a single-entity or as a combination product])<sup>\*</sup> AND Zetia<sup>®</sup> (ezetimibe tablets, generic) [as a single-entity or as a combination product] for  $\geq$  8 continuous weeks **[documentation required]**; AND the LDL-C level after this treatment regimen remains  $\geq$  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  $\geq$  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

Type of Revision	Summary of Changes	Date
New policy	--	07/01/2018
Selected revision	Added Repatha authorized alternative to the policy with related criteria changes.	01/01/2019
DEU selected revision	Selected revision to be effective 04/05/2019 to remove auto-approvals for Praluent.	04/03/2019

DEU – Drug Evaluation Unit.