Clinical Policy: Evolocumab (Repatha)

Reference Number: PA.CHIP.PHAR.123
Effective Date: 01/2026
Last Review Date: 09/2025

Description
Evolocumab (Repatha®) is a proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor antibody.

FDA Approved Indication(s)
Repatha is indicated:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, myocardial infarction, stroke, unstable angina requiring hospitalization, or coronary revascularization) in adults with established CV disease
- As an adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies in adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia [HeFH]) to reduce LDL-C
- As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH to reduce LDL-C
- As an adjunct to other LDL-C-lowering therapies in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Repatha is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Primary Hyperlipidemia (including HeFH) and Atherosclerotic Cardiovascular Disease (must meet all)**:**

1. Diagnosis of one of the following (a, b, or c):
   a. **HeFH**, and provider's attestation of both of the following (i and ii):
      i. Baseline LDL-C (prior to any lipid-lowering pharmacologic therapy) was one of the following (1 or 2): 1)
         1. If age < 20 years: ≥ 160 mg/dL;
         2. If age ≥ 20 years: ≥ 190 mg/dL;
      ii. HeFH diagnosis is confirmed by one of the following (1 or 2):
         1. World Health Organization (WHO)/Dutch Lipid Network familial hypercholesterolemia diagnostic criteria score of > 8 as determined by requesting provider (see Appendix D);
         2. Definite diagnosis per Simon Broome criteria (see Appendix D);
   b. **Primary hyperlipidemia that is not HeFH**, and both of the following (i and ii):
      i. Provider's attestation of one of the following (1 or 2):

1. Presence of a genetically mediated form of primary hyperlipidemia as evidenced by confirmatory genetic testing results;
2. A diagnosis of secondary hyperlipidemia has been ruled out with absence of all of the following potential causes of elevated cholesterol (a – e):
    a. Poor diet;
    b. Hypothyroidism;
    c. Obstructive liver disease;
    d. Renal disease;
    e. Nephrosis;

ii. Provider's attestation that baseline LDL-C (prior to any lipid-lowering pharmacologic therapy) was ≥ 190 mg/dL;

c. **Atherosclerotic cardiovascular disease (ASCVD)** as evidenced by provider's attestation of a history of any one of the following conditions (i-vii):
   i. Acute coronary syndromes;
   ii. Clinically significant coronary heart disease (CHD) diagnosed by invasive or noninvasive testing (such as coronary angiography, stress test using treadmill, stress echocardiography, or nuclear imaging);
   iii. Coronary or other arterial revascularization;
   iv. Myocardial infarction;
   v. Peripheral arterial disease presumed to be of atherosclerotic origin;
   vi. Stable or unstable angina;
   vii. Stroke or transient ischemic attack (TIA);

2. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
3. Age is one of the following (a or b):
   a. If diagnosis is primary hyperlipidemia (not including HeFH) or ASCVD:≥ 18 years;
   b. If diagnosis is HeFH: ≥ 10 years;
4. Failure of **Praluent**® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Praluent*
5. For members ≥ 18 years old on statin therapy, both of the following (a and b):
   a. Repatha is prescribed in conjunction with a statin at the maximally tolerated dose;
   b. Member has been adherent for at least the last 8 weeks to maximally tolerated doses of one of the following statin regimens (i or ii):
      i. A high intensity statin (*see Appendix E*);
      ii. A moderate or low intensity statin (*see Appendix E*), and member has one of the following (1 or 2):
         1. Previous use of one high-intensity statin (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single-entity or as a combination product]) for a minimum of 8 weeks continuously and LDL-C remained ≥ 70 mg/dL;
         2. Member has tried both rosuvastatin and atorvastatin and has experienced skeletal-muscle related symptoms on both agents which also resolved upon discontinuation;
6. For members ≥ 18 years old <u>not</u> on statin therapy, provider's attestation that

member meets one of the following (a or b):
a. Statin therapy is contraindicated per Appendix F;
b. For members who are statin intolerant, both of the following (i and ii):
   i. Member has tried at least two statins, one of which must be hydrophilic (pravastatin, fluvastatin, or rosuvastatin);
   ii. Member meets one of the following (1 or 2):
      1. Member has statin risk factors (see *Appendix G)*;
      2. Member is statin intolerant due to statin-associated muscle symptoms (SAMS) and meets both of the following (a and b):
         a. Member had intolerable SAMS persisting at least two weeks, which disappeared with discontinuing the statin therapy and recurred with a statin re-challenge;
         b. Previous re-challenge with titration from lowest possible dose and/or intermittent dosing frequency (e.g., 1 to 3 times weekly);

7. Provider's attestation of recent (within the last 60 days) LDL-C of one of the following (a or b):
   a. If member has ASCVD (i or ii):
      i. ≥ 70 mg/dL;
      ii. ≥ 55 mg/dL, and member is at very high risk (see *Appendix I*);
   b. If member has severe primary hyperlipidemia (including HeFH): ≥ 100 mg/dL;
8. Treatment plan does not include coadministration with Juxtapid®, Leqvio®, or Praluent®;
9. Dose does not exceed one of the following (a or b):
   a. 140 mg every 2 weeks;
   b. 420 mg per month.

Approval duration: 6 months or to the member's renewal date

B. Homozygous Familial Hypercholesterolemia (must meet all):
1. Diagnosis of HoFH;
2. Provider's attestation defined as one of the following (a, b, or c):
   a. Genetic mutation indicating HoFH (e.g., mutations in low density lipoprotein receptor [LDLR] gene, PCSK9 gene, apo B gene, low density lipoprotein receptor adaptor protein 1[LDLRAP1] gene);
   b. Treated LDL-C ≥ 300 mg/dL or non-HDL-C ≥ 330 mg/dL;
   c. Untreated LDL-C ≥ 400 mg/dL, and one of the following (i or ii):
      i. Tendinous or cutaneous xanthoma prior to age 10 years;
      ii. Evidence of familial hypercholesterolemia (HeFH or HoFH) in at least one parent (e.g., documented history of elevated LDL-C ≥ 190 mg/dL prior to lipid-lowering therapy);
3. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
4. Member meets one of the following (a or b):
   a. Both of the following (i and ii):
      i. Age ≥ 10 years and < 18 years;

ii. LDL-C ≥ 130 mg/dL within the last 60 days despite statin therapy, unless member has a contraindication (see Appendix F) or history of intolerance to each such therapy;

b. Age ≥ 18 years, and recent (within the last 60 days) LDL-C of one of the following (i or ii):
   i. ≥ 70 mg/dL;
   ii. ≥ 55 mg/dL if member has ASCVD and is at very high risk (see Appendix I);

5. Failure of **Praluent** at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Praluent*
6. For members ≥ 18 years old and on statin therapy, provider's attestation of both of the following (a and b):
   a. Repatha is prescribed in conjunction with a statin at the maximally tolerated dose;
   b. Member has been adherent for at least the last 8 weeks to maximally tolerated doses of one of the following statin regimens (i or ii):
      i. A high intensity statin (*see Appendix E*);
      ii. A moderate or low intensity statin (*see Appendix E*), and member has one of the following (1 or 2):
         1. Previous use of one high-intensity statin (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single-entity or as a combination product]) for a minimum of 8 weeks continuously and LDL-C remained ≥ 70 mg/dL;
         2. Member has tried both rosuvastatin and atorvastatin and has experienced skeletal-muscle related symptoms on both agents which also resolved upon discontinuation;
7. For members ≥ 18 years old and not on statin therapy, provider's attestation that member meets one of the following (a or b):
   a. Statin therapy is contraindicated per Appendix F;
   b. For members who are statin intolerant, both of the following (i and ii):
      i. Member has tried at least two statins, one of which must be hydrophilic (pravastatin, fluvastatin, or rosuvastatin);
      ii. Member meets one of the following (1 or 2):
         1. Member has statin risk factors (see Appendix G);
         2. Member is statin intolerant due to statin-associated muscle symptoms (SAMS) and meets both of the following (a and b):
            a. Member had intolerable SAMS persisting at least two weeks, which disappeared with discontinuing the statin therapy and recurred with a statin re-challenge;
            b. Previous re-challenge with titration from lowest possible dose and/or intermittent dosing frequency (e.g., 1 to 3 times weekly);
8. Treatment plan does not include coadministration with Leqvio, Juxtapid or Praluent;
9. Dose does not exceed one of the following (a or b):
   a. 420 mg per month;
   b. 420 mg every 2 weeks, and member is currently receiving lipid apheresis.

Approval duration: 6 months or to the member's renewal date

C. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. If statin tolerant, provider's attestation of adherence to a statin at the maximally tolerated dose;
3. Member is responding positively to therapy as evidenced by provider's attestation of lab results within the last 3 months showing an LDL-C reduction since initiation of Repatha therapy;
4. Treatment plan does not include coadministration with Leqvio, Juxtapid or Praluent;
5. If request is for a dose increase, new dose does not exceed either of the following (a or b):
   a. Primary hyperlipidemia (including HeFH) or ASCVD: one of the following (i or ii):
      i. 140 mg every 2 weeks;
      ii. ii. 420 mg per month;
   b. HoFH: one of the following (i or ii):
      i. 420 mg every 2 weeks;
      ii. 420 mg every 2 weeks, and either (1 or 2):
         1. Member is currently receiving lipid apheresis;
         2. Provider's attestation that the member did not achieve a clinically meaningful response, defined as not having achieved ≥ 30% reduction in LDL from baseline, with initial dosing.

Approval duration: 6 months or to the member's renewal date

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALT: alanine transaminase
apo B: apolipoprotein B
ASCVD: atherosclerotic cardiovascular disease

CHD: coronary heart disease
CV: cardiovascular
FDA: Food and Drug Administration
FH: familial hypercholesterolemia
HeFH: heterozygous familial hypercholesterolemia
HoFH: homozygous familial hypercholesterolemia
LDL-C: low density lipoprotein cholesterol
LDLR: low density lipoprotein receptor
LDLRAP1: low density lipoprotein receptor adaptor protein 1
PCSK9: proprotein convertase subtilisin
SAMS: statin-associated muscle symptoms
TIA: transient ischemic attack
WHO: World Health Organization

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
atorvastatin (Lipitor®)	40 mg PO QD	80 mg/day
rosuvastatin (Crestor®)	5 - 40 mg PO QD	40 mg/day

Praluent (alirocumab)	**HeFH and ASCVD** Adult: 75mg SC once every 2 weeks or 300 mg SC once every 4 weeks If response to 75 mg every 2 weeks or 300 mg every 4 weeks is inadequate, dose may be increased to 150 mg once every 2 weeks. Pediatrics (HeFH only): Body weight < 50 kg: 150 mg SC every 4 weeks If response is inadequate, dose may be adjusted to 75 mg every 2 weeks Body weight ≥ 50 kg: 300 mg SC every 4 weeks If response is inadequate, dose may be adjusted to 150 mg every 2 weeks **HoFH** 150 mg SC every 2 weeks150 mg SC every 2 weeks	300 mg/month
pravastatin (Pravachol®)	10 - 80 mg PO QD	80 mg/day
fluvastatin (Lescol®)	20 - 80 mg PO QD	80 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity
- Boxed warning(s): none reported

Appendix D: Criteria for Diagnosis of HeFH

- Dutch Lipid Clinic Network criteria for Familial Hypercholesterolemia (FH

FH Criteria	Points	Member's Score†
Family History		
First-degree relative with known premature* coronary and vascular disease	1	Place highest score here
First-degree relative with known LDL-C level above the 95th percentile	1	

First-degree relative with tendinous xanthomata and/or arcus cornealis	2	(0, 1 or 2)
Children aged < 18 years with LDL-C level above the 95th percentile	2	
Clinical History		
Patient with premature* coronary artery disease	2	Place highest score here (0, 1 or 2)
Patient with premature* cerebral or peripheral vascular disease	1	
Physical Examination		
Tendinous xanthomata	6	Place highest score here (0, 4 or 6)
Arcus cornealis prior to age 45 years	4	
Cholesterol Levels - mg/dL (mmol/liter)		
LDL-C ≥ 330 mg/dL (≥ 8.5)	8	Place highest score here (0, 1, 3, 5 or 8)
LDL-C 250 – 329 mg/dL (6.5 – 8.4)	5	
LDL-C 190 – 249 mg/dL (5.0 – 6.4)	3	
LDL-C 155 – 189 mg/dL (4.0 – 4.9)	1	
DNA Analysis		
Functional mutation in the *LDLR, apo B* or *PCSK9* gene	8	Place score here (0 or 8)
TOTAL SCORE	Definite FH: > 8	Place total score here __

*Premature – men < 55 years or women < 60 years
†Choose the highest score from each of the five categories and then add together for a total score. The five categories are 1) Family History, 2) Clinical History, 3) Physical Examination, 4) Cholesterol Levels, and 5) DNA Analysis.

- Simon Broome Register Group Definition of Definite FH (meets 1 and 2):
  1. One of the following (a or b):
     a. Total cholesterol level above 7.5 mmol/l (290 mg/dl) in adults or a total cholesterol level above 6.7 mmol/l (260 mg/dl) for children under 16;
     b. LDL levels above 4.9 mmol/l (190 mg/dl) in adults (4.0 mmol/l in children) (either pre-treatment or highest on treatment);
  2. One of the following (a or b):
     a. Tendinous xanthomas in patient or relative (parent, child, sibling, grandparent, aunt, uncle);
     b. DNA-based evidence of an LDL receptor mutation or familial defective apo B- 100;

Appendix E: High and Moderate Intensity Daily Statin Therapy for Adults

High Intensity Statin Therapy ***Daily dose shown to lower LDL-C, on average, by approximately ≥ 50%***
• Atorvastatin 40-80 mg • Rosuvastatin 20-40 mg

Moderate Intensity Statin Therapy ***Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%***
• Atorvastatin 10-20 mg • Fluvastatin XL 80 mg • Fluvastatin 40 mg BID • Lovastatin 40 mg • Pitavastatin 1-4 mg • Pravastatin 40-80 mg • Rosuvastatin 5-10 mg • Simvastatin 20-40 mg
Low Intensity Statin Therapy ***Daily dose shown to lower LDL-C, on average, by < 30%***
• Simvastatin 10 mg • Pravastatin 10-20 mg • Lovastatin 20 mg • Fluvastatin 20-40 mg

Appendix F: Statin and Ezetimibe Contraindications

Statins
• Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy) • Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment • Pregnancy*, actively trying to become pregnant, or nursing • Immune-mediated hypersensitivity to the HMG-CoA reductase inhibitor drug class (statins) as evidenced by an allergic reaction occurring with at least TWO different statins
Ezetimibe
• Moderate or severe hepatic impairment [Child-Pugh classes B and C] • Hypersensitivity to ezetimibe (e.g., anaphylaxis, angioedema, rash, urticaria)

**In July 2021, the FDA requested removal of the contraindication against use of statins in pregnant women. Because the benefits of statins may include prevention of serious or potentially fatal events in a small group of very high-risk pregnant patients, contraindicating these drugs in all pregnant women is not appropriate.* https://www.fda.gov/safety/medical-product-safety-information/statins-drug-safety-communication-fda-requests-removal-strongest-warning-against-using-cholesterol

Appendix G: Statin Risk Factors

Statin Risk Factors
• Multiple or serious comorbidities, including impaired renal or hepatic function • Unexplained alanine transaminase (ALT) elevations > 3 times upper limit of normal, or active liver disease • Concomitant use of drugs adversely affecting statin metabolism • Age > 75 years, or history of hemorrhagic stroke • Asian ancestry

Appendix H: General Information

- FDA Endocrinologic and Metabolic Drugs Advisory Committee briefing documents for another PCSK-9 inhibitor, Praluent, discuss the questionable determination of statin intolerance, stating: "many patients who are not able to take statins are not truly intolerant of the pharmacological class."
- Patients should remain on concomitant therapy with a statin if tolerated due to the established long term cardiovascular benefits.
- Examples of genetically mediated primary hyperlipidemia include but are not limited to the following:
  - Familial hypercholesterolemia
  - Familial combined hyperlipidemia (FCHL)
  - Polygenic hypercholesterolemia
  - Familial dysbetalipoproteinemia
- The diagnosis of SAMS is often on the basis of clinical criteria. Typical SAMS include muscle pain and aching (myalgia), cramps, and weakness. Symptoms are usually bilateral and involve large muscle groups, including the thigh, buttock, back, and shoulder girdle musculature. In contrast, cramping is usually unilateral and may involve small muscles of the hands and feet. Symptoms may be more frequent in physically active patients. Symptoms often appear early after starting stain therapy or after an increase in dose and usually resolve or start to dissipate within weeks after cessation of therapy, although it may take several months for symptoms to totally resolve. Persistence of symptoms for more than 2 months after drug cessation should prompt a search for other causes or for underlying muscle disease possibly provoked by statin therapy. The reappearance of symptoms with statin rechallenge and their disappearance with drug cessation offers the best evidence that the symptoms are truly SAMS.
- Pravastatin, fluvastatin, and rosuvastatin are hydrophilic statins which have been reported to confer fewer adverse drug reactions than lipophilic statins.

Appendix I: Criteria for Defining Patients at Very High Risk of Future ASCVD Events[2]
Very high risk is defined as having either a history of multiple major ASCVD events **OR** 1 major ASCVD event and multiple high-risk conditions:

- Major ASCVD events:
  - Recent acute coronary syndrome (within the past 12 months)
  - History of myocardial infarction (other than recent acute coronary syndrome event listed above)
  - History of ischemic stroke
  - Symptomatic peripheral artery disease (history of claudication with ankle-brachial index < 0.85 or previous revascularization or amputation)
- High-risk conditions:
  - Age ≥ 65 years
  - HeFH
  - History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
  - Diabetes
  - Hypertension
  - Chronic kidney disease (estimated glomerular filtration rate [eGFR] 15-

59 mL/min/1.73 m^2)
- Current tobacco smoking
- Persistently elevated LDL-C (LDL-C ≥ 100 mg/dL [≥ 2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
- History of congestive heart failure

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Primary hyperlipidemia (including HeFH) or hypercholesterolemia with ASCVD	140 mg SC Q2 weeks or 420 mg SC once monthly	420 mg/month
HoFH	420 mg SC once monthly; Dosage can be increased to 420 mg every 2 weeks if a clinically meaningful response is not achieved in 12 weeks. Patients on lipid apheresis may initiate treatment with 420 mg every 2 weeks to correspond with their apheresis schedule	420 mg/2 weeks

VI. Product Availability
- Prefilled syringe and SureClick autoinjector (not made with latex): 140 mg/mL
- Prefilled syringe and SureClick autoinjector (contains dry natural rubber): 140 mg/mL
- Prefilled cartridge Pushtronex system (on-body infusor): 420 mg/3.5 mL

V. References

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Statin Tolerance

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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics

Reviews, Revisions, and Approvals	Date
Policy created	09/2025