

Clinical Policy: Evolocumab (Repatha)

Reference Number: PA.CP.PHAR.123

Effective Date: 01/18

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Line of Business: Medicaid

[Revision Log](#)

Description

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

FDA Approved Indication(s)

Repatha is indicated as an adjunct to diet and:

- Maximally tolerated statin therapy for 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).
- Other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

Limitation of use: the effect of Repatha on cardiovascular morbidity and mortality has not been determined.

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Repatha is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Heterozygous Familial Hypercholesterolemia and Atherosclerotic Cardiovascular Disease (must meet all):

1. Prescribed by or in consultation with a cardiologist, endocrinologist or lipid specialist;
2. Age is ≥ 18 years;
3. Diagnosis of one of the following (a or b):
 - a. HeFH defined as a World Health Organization (WHO)/Dutch Lipid Network familial hypercholesterolemia diagnostic criteria score of > 8 as determined by requesting provider (Appendix B);
 - b. Atherosclerotic cardiovascular disease as evidenced by a history of any of the following conditions (i, ii, iii, iv, or v):
 - i. Myocardial infarction;
 - ii. Stable or unstable angina;
 - iii. Coronary or other arterial revascularization;
 - iv. Peripheral arterial disease presumed to be of atherosclerotic origin;
 - v. Ischemic cerebrovascular disease such as stroke and TIA;

4. Recent (within the last 30 days) low-density lipoprotein cholesterol (LDL-C) \geq 70mg/dL;
5. Member has received a high intensity statin (Appendix C) adherently for at least the last 4 months, unless one of the following applies (a, b, or c):
 - a. Statin therapy is contraindicated per Appendix D;
 - b. Member has received a moderate intensity statin (Appendix C) adherently for at least the last 4 months due to (i or ii):
 - i. Intolerance to two high intensity statins;
 - ii. A statin risk factor (Appendix E);
 - c. Member is unable to take a high or moderate intensity statin due to (i or ii):
 - i. Intolerance to two high and two moderate intensity statins;
 - ii. A statin risk factor (Appendix E) and history of intolerance to two moderate intensity statins;
6. Member has received Zetia therapy adherently for at least the last 4 months, unless contraindicated per Appendix D or a history of Zetia intolerance (e.g., associated diarrhea or upper respiratory tract infection);
7. Member has received counseling on therapeutic lifestyle changes (i.e., heart healthy diet; regular exercise; avoidance of tobacco products; maintenance of a healthy weight);
8. Request is for Repatha 140 mg every 2 weeks or 420 mg once monthly;
9. Member has no known history of serious hypersensitivity reaction to Repatha (e.g., rash, urticaria);
10. Treatment plan does not include coadministration with Juxtapid (lomitapid), Kynamro (mipomersen), or Praluent (alirocumab).

Approval duration: 3 months

B. Homozygous Familial Hypercholesterolemia (must meet all):

1. Prescribed by or in consultation with a cardiologist, endocrinologist or lipid specialist;
2. Diagnosis of HoFH defined as one of the following (a, b or c):
 - a. Genetic mutation indicating HoFH (LDLR, PCSK9, apolipoprotein B , LDLRAP1);
 - b. Treated LDL-C \geq 300 mg/dL or non-HDL-C \geq 330 mg/dL;
 - c. Untreated LDL-C \geq 500 mg/dL, and one of the following (i or ii):
 - i. Tendinous or cutaneous xanthoma prior to age 10 years;
 - ii. Evidence of HeFH in both parents (e.g., documented history of elevated LDL-C \geq 190 mg/dL prior to lipid-lowering therapy);
3. Meets a or b:
 - a. Age is $<$ 18 years and LDL-C \geq 130 mg/dL within the last 30 days despite statin and Zetia therapy unless a contraindication (Appendix D) or history of intolerance to each such therapy;
 - b. Age is \geq 18 years and recent (within the last 30 days) low-density lipoprotein cholesterol (LDL-C) \geq 70mg/dL;
4. If member is \geq 18 years, has received a high intensity statin (Appendix C) adherently for at least the last 4 months, unless one of the following applies (a, b, or c):
 - a. Statin therapy is contraindicated per Appendix D;

- b. Member has received a moderate intensity statin (Appendix C) adherently for at least the last 4 months due to (i or ii):
 - i. Intolerance to two high intensity statins;
 - ii. A statin risk factor (Appendix E);
- c. Member is unable to take a high or moderate intensity statin due to (i or ii):
 - i. Intolerance to two high and two moderate intensity statins;
 - ii. A statin risk factor (Appendix E) and history of intolerance to two moderate intensity statins;
5. If member \geq 18 years, has received Zetia therapy adherently for at least the last 4 months, unless contraindicated per Appendix D or a history of Zetia intolerance (e.g., associated diarrhea or upper respiratory tract infection);
6. Member has received counseling on therapeutic lifestyle changes (i.e., heart healthy diet; regular exercise; avoidance of tobacco products; maintenance of a healthy weight);
7. Treatment plan does not include coadministration with Juxtapid (lomitapid), Kynamro (mipomersen), or Praluent (evolocumab);
8. Request is for Repatha 420 mg once monthly.

Approval duration: 3 months

C. Other diagnoses/indications

1. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Lab results within the last 3 months are submitted showing an LDL-C reduction since initiation of Repatha therapy;
3. Request does not exceed (a or b):
 - a. HeFH: Repatha 140 mg every 2 weeks or 420 mg once monthly;
 - b. HoFH: Repatha 420 mg once monthly.

Approval duration: 12 months

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

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – PA.CP.PHAR.57 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

apoB: apolipoprotein B	HeFH: heterozygous familial hypercholesterolemia
ACC/AHA: American College of Cardiology/American Heart Association	HoFH: homozygous familial hypercholesterolemia
ALT: alanine transaminase	LDL-C: low density lipoprotein cholesterol
CVD: cardiovascular disease	LDLR: low density lipoprotein receptor
FDA: Food and Drug Administration	LDLRAP1: low density lipoprotein receptor adaptor protein 1
FH: familial hypercholesterolemia	PCSK9: proprotein convertase subtilisin kexin 9
HDL-C: high-density lipoprotein cholesterol	

Appendix B: 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 (0, 1 or 2)
First-degree relative with known LDL-C level above the 95 th percentile	1	
First-degree relative with tendinous xanthomata and/or arcus cornealis	2	
Children aged < 18 years with LDL-C level above the 95 th 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 <i>LDLR</i> , <i>apo B</i> or <i>PCSK9</i> 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.

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

- High Intensity Statin Therapy
Daily dose shown to lower LDL-C, on average, by approximately $\geq 50\%$
 - 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 10-20mg
 - Fluvastatin XL 80 mg
 - Fluvastatin 40 mg 2x/day
 - Lovastatin 40 mg
 - Pitavastatin 2-4 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
 - Pitavastatin 1 m

Appendix D: Statin and Zetia 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;
- Zetia
 - Moderate or severe hepatic impairment [Child-Pugh classes B and C];
 - Hypersensitivity to Zetia (e.g., anaphylaxis, angioedema, rash, urticaria).

Appendix E: Statin Risk Factors

- Multiple or serious comorbidities, including impaired renal or hepatic function;
- Unexplained ALT elevations > 3 times ULN, or active liver disease;
- Concomitant use of drugs adversely affecting statin metabolism;
- Age > 75 years, or history of hemorrhagic stroke;
- Asian ancestry.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
HeFH or hypercholesterolemia	140 mg SQ Q2 weeks or 420mg SQ once monthly	420mg per month
HoFH	420 mg SQ once monthly	420mg per month

VI. Product Availability

Prefilled syringe and SureClick autoinjector: 140 mg/mL

Prefilled cartridge Pushtronex system (on-body infusor): 420 mg/3.5 mL

VII. References

1. Repatha Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; July 2016. Available at http://pi.amgen.com/united_states/repatha/repatha_pi_hcp_english.pdf. Accessed on May 10, 2017.
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3. 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*. November 2013. DOI: 10.1161/01.cir.0000437738.63853.7a
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5. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. *Journal of Clinical Lipidology*. June 2011; 5(3S): 1-15.
6. Jacobson TA. National Lipid Association Task Force on Statin Therapy – 2014 update. *Journal of Clinical Lipidology*. 2014; 8(S1-S4): 1-81.
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8. Al-Rasadi K, Al-Waili K, Al-Sabti HA, et al. Criteria for diagnosis of familial hypercholesterolemia: A comprehensive analysis of the different guidelines, appraising their suitability in the Omani Arab population. *Oman Medical Journal*. 2014; 29(2): 85–91. <http://doi.org/10.5001/omj.2014.22>

Reviews, Revisions, and Approvals	Date	Approval Date