Clinical Policy: Evolocumab (Repatha)

Reference Number: CP.PHAR.123
Effective Date: 10/15
Last Review Date: 10/17 Revision Log
Line of Business: Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

Repatha is indicated:

- To reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease
- As an adjunct to alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol (LDL-C)
- As an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-.

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 Centene Corporation® 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, v):
      i. Myocardial infarction;
      ii. Stable or unstable angina;
      iii. Nonhemorrhagic stroke or transient ischemic attack;

iv. Coronary or other arterial revascularization;
v. Peripheral arterial disease presumed to be of atherosclerotic origin;

4. Recent (within the last 30 days) low-density lipoprotein cholesterol (LDL-C) ≥ 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 ≥ 300 mg/dL or non-HDL-C ≥ 330 mg/dL;
   c. Untreated LDL-C ≥ 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 ≥ 190 mg/dL prior to lipid-lowering therapy);
3. Meets a or b:
   a. Age is < 18 years and LDL-C ≥ 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 ≥ 18 years and recent (within the last 30 days) low-density lipoprotein cholesterol (LDL-C) ≥ 70mg/dL;

4. If member is ≥ 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 ≥ 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 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 Centene benefit or member has previously met all initial approval criteria;
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 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 – CP.PHAR.57 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

apoB: apolipoprotein B
ACC/AHA: American College of Cardiology/American Heart Association
ALT: alanine transaminase
CVD: cardiovascular disease
FDA: Food and Drug Administration
FH: familial hypercholesterolemia
HDL-C: high-density lipoprotein cholesterol
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 kexin 9

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 95th percentile	1	
First-degree relative with tendinous xanthomata and/or arcus cornealis	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.

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 ≥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.
7. Zetia Prescribing Information. Whitehouse Station, NJ: Merck and Company, Inc.; August 2013. Available at http://www.merck.com/product/usa/pi_circulars/z/zetia/zetia_pi.pdf. Accessed May 10, 2017.
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
Policy created	09/15	10/15
Converted policy to new template. HoFH criteria: Signs changed from ">" to "≥" for following criteria: Treated LDL-C ≥ *300 mg/dL* or *non-HDL-C ≥ 330 mg/dL*; *Untreated LDL-C ≥ 500 mg/dL*, and one of the following (i or ii): Evidence of HeFH in both parents (e.g., documented history of elevated *LDL-C ≥ 190 mg/dL* prior to lipid-lowering therapy); Added "statin intolerance" criteria statement for HoFH members < 18 years of age under requirement for statin therapy; Added examples of Zetia intolerance; Added Repatha dosage for ASCVD, HeFH, and	10/16	10/16

Reviews, Revisions, and Approvals	Date	Approval Date
HoFH per PI. Incorpoated ASCVD, HoFH, TLC appendices into the criteria. Combined Zetia and statin contraindications (App D) and added nursing as a contraindication. Added scoring instructions to the Dutch criteria appendix. Statin risk factors are listed at App E. Modified renewal duration to 12 months. Added requirement for the use of statin and zetia therapy for the last 4 months to ensure that LDL-C submitted reflect the full effect of statin/zetia use after a full 12 weeks of therapy		
Policy converted to new template. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. References updated.	09/17	10/17
Modified definition of ASCVD to include nonhemorrhagic stroke or transient ischemic attack.	11/17	
No clinical changes Added new indication to reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease to the FDA approved indication section.	12.14.17	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.