SPECIALTY GUIDELINE MANAGEMENT

REPATHA (evolocumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

A. Repatha is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of low density lipoprotein cholesterol (LDL-C).

B. Repatha is indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Clinical atherosclerotic cardiovascular disease (ASCVD)

Authorization of 12 months may be granted for members who meet ALL of the criteria listed below:

1. Member has a history of clinical ASCVD (See Appendix A).
2. Member meets at least ONE of the following requirements [a or b]:
   a. Member has a current LDL-C level ≥ 70 mg/dL after at least three months of treatment with a high-intensity statin dose (e.g., atorvastatin ≥ 40 mg or rosuvastatin ≥ 20 mg daily) plus ezetimibe 10 mg daily. If the member is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose (e.g., atorvastatin 20 mg or equivalent) may be used.
   b. Member has a current LDL-C level ≥ 70 mg/dL with contraindication or intolerance to statins (See Appendix B and C).

B. Heterozygous Familial Hypercholesterolemia (HeFH)

Authorization of 12 months may be granted for members who meet ALL of the criteria listed below:

1. Member has a diagnosis of familial hypercholesterolemia (See Appendix D).
2. Member meets at least ONE of the following requirements [a, b, c or d]:
   a. With ASCVD: See Section A.
   b. Without ASCVD: Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose (i.e., atorvastatin ≥ 40 mg or rosuvastatin ≥ 20 mg daily) plus ezetimibe 10 mg daily.
   c. Member has a current LDL-C level ≥ 100 mg/dL with contraindication or intolerance to statins (See Appendices B and C) and is taking ezetimibe 10mg daily.
   d. Member has a current LDL-C level ≥ 100 mg/dL and contraindication to both statins and ezetimibe (See Appendix C).

c. **Homozygous Familial Hypercholesterolemia FH**
Authorization for 12 months may be granted for members who meet ALL of the applicable criteria listed below:
1. Member has a diagnosis of homozygous FH confirmed by genetic analysis or clinical criteria (See Appendix E).
2. Member meets at least ONE of the following requirements [a, b, c, d, e or f]:
   a. With ASCVD: See Section A.
   b. Without ASCVD: Member has a current LDL-C level ≥ 100 mg/dL after at least three months of treatment with a high-intensity statin dose (i.e., atorvastatin ≥ 40 mg or rosuvastatin ≥ 20 mg daily) plus ezetimibe 10 mg daily.
   c. Member has a current LDL-C level ≥ 100 mg/dL with a contraindication or intolerance to statins (See Appendices B and C) and is receiving ezetimibe 10 mg daily.
   d. Member has a current LDL-C level ≥ 100 mg/dL and a contraindication to both statins and ezetimibe (See Appendix C).
   e. Member has received Juxtapid or Kynamro through a prior authorization process of a pharmacy or medical benefit.
   f. Member has been treated regularly with lipid apheresis within the previous 3 months.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members who have received Repatha through a pharmacy or medical benefit and who achieve or maintain an LDL-C reduction (e.g., LDL-C is now at goal, robust lowering of LDL-C).

IV. APPENDICES

APPENDIX A. Clinical ASCVD
- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary angioplasty [PTCA], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease of presumed atherosclerotic origin (e.g., carotid artery stenosis)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)

APPENDIX B. Statin-associated muscle symptoms (SAMS) and statin re-challenge
- Intolerable SAMS persisting at least two weeks, which subsided when the medication was discontinued, and reemerged with a statin re-challenge.
  NOTE: Re-challenge must be with a different statin.
- Statin-associated elevation in CK level ≥ 10 times upper limit of normal (ULN)
  NOTE: Statin re-challenge is NOT required for members who have experienced an elevation of CK level greater than or equal to 10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

APPENDIX C. Contraindications to statins and ezetimibe
- Contraindications to statins
  - Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
  - Women who are pregnant or may become pregnant
  - Nursing mothers

- Contraindication to ezetimibe
  - Hypersensitivity reactions (e.g., anaphylaxis, angioedema, rash and urticaria)

APPENDIX D: Diagnosis of familial hypercholesterolemia (FH)

A diagnosis of FH is made when one of the following diagnostic criteria is met:

- Genetic confirmation
  - An LDL-receptor mutation, familial defective apo B-100, or a PCSK9 gain-of-function mutation
- Simon-Broome Diagnostic Criteria for FH
  - Total cholesterol > 290 mg/dL or LDL-C > 190 mg/dL in patients over 16 years of age or total cholesterol > 260 mg/dl or LDL-C > 155 mg/dl in patients less than 16 years of age and one of the following
    - Tendon xanthomas in the patient, first (parent, sibling or child) or second degree relative (grandparent, uncle or aunt)
    - Family history of myocardial infarction in a first degree relative before the age of 60 or in a second degree relative before the age of 50
    - Total cholesterol greater than 290 mg/dl in an adult first or second degree relative
    - Total cholesterol greater than 260 mg/dl in a child, brother, or sister aged younger than 16 years
- Dutch Lipid Clinic Network Criteria for FH
  - Total score > 5 points

APPENDIX E. Diagnosis of Homozygous FH

- Genetic confirmation
  - Mutations in both alleles at LDL receptor, ApoB, PCSK9 or LDL receptor adaptor protein gene locus
- Clinical diagnosis
  - Untreated LDL-C > 500 mg/dL OR unknown untreated LDL-C with treated LDL-C > 300 mg/dL **plus**
  - One of the following:
    - Tendon or cutaneous xanthomas at age 10 or younger
    - Diagnosis of FH by Simon-Broome Diagnostic Criteria or Dutch Lipid Clinic Network Criteria (See Appendix D) in both parents
    - Evidence of FH in both parents with a history including any of the following:
      - Total cholesterol ≥ 310 mg/dL
      - Premature ASCVD (before 55 years in men and 60 years in women)
      - Tendon xanthoma
      - Sudden premature cardiac death

V. REFERENCES

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