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Pharmacy Solutions

Prior Authorization Protocol

REPATHA™ (evolocumab)

NATL

Coverage of drugs is first determined by the member's pharmacy or medical benefit. Please consult with or refer to the Evidence of Coverage document.

I. FDA Approved Indications:

- 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

II. Health Net Approved Indications and Usage Guidelines:

- Diagnosis of Heterozygous or Homozygous Familial Hypercholesterolemia based on documentation (e.g., medical records, chart notes, laboratory values) of LDL level suggestive of familial hypercholesterolemia (e.g., Adults: baseline LDL >190 mg/dL; Children less than 16 years of age: baseline LDL >155 mg/dL)

OR

- Diagnosis of hypercholesterolemia with history of clinical atherosclerotic cardiovascular disease defined as:
  - LDL≥130 mg/dL

    AND
  - Documented history of one of the following:
    - Acute coronary syndromes
    - Myocardial Infarction
    - Stable or unstable angina
    - Coronary or other arterial revascularization (e.g., percutaneous coronary intervention or coronary artery bypass graft surgery)
    - Stroke
    - Peripheral artery disease presumed to be of atherosclerotic origin
    - Transient ischemic attack (TIA)
    - 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)
    - Carotid artery occlusion >50% without symptoms
    - Renal artery stenosis or renal artery stent procedure

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AND

- Prescribed by or in consultation with a Cardiologist, Endocrinologist, or lipid specialist

AND

- Documentation of concomitant therapy with Zetia in combination with high-intensity statin therapy (atorvastatin 40mg or Crestor® 20 mg or greater) or Vytorin at simvastatin doses of at least 40 mg for a minimum of two months with demonstrated adherence

  OR

- Clinically significant adverse effects to atorvastatin (≥ 40 mg), Crestor (≥ 20 mg) and documentation of concomitant therapy with Zetia in combination with maximally tolerated statin therapy [see General Information section] for a minimum of two months with demonstrated adherence

  OR

- For patients not on statin therapy (Statin Intolerant):
  - Documentation of concomitant therapy with Zetia

    AND
  - Documentation of one of the following:
    1. Statin re-challenge with at least the lowest dose of at least two of the following: pravastatin 10 mg, fluvastatin 20 mg, or rosuvastatin 5 mg, [see General Information section]

       AND

       At least intermittent or alternate dosing frequency (e.g., 1 to 3 times weekly) has been attempted
    2. History of rhabdomyolysis
    3. History of two consecutive abnormal liver function tests (LFT) greater than three times the upper limit of normal (ULN) and experienced symptoms suggesting hepatotoxicity (e.g., jaundice, dark-colored urine, light or clay-colored stools) while taking statin

<u>REAUTHORIZATION REQUESTS:</u>

- Documentation of LDL reduction while on PCSK9 therapy defined as at least 25% LDL reduction from baseline or LDL<70mg/dL for high risk patients or LDL <100mg/DL for moderate risk patients

  AND

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- Confirmation of continued statin therapy at the maximally tolerated dose [see general information] with demonstrated adherence

III. Coverage is Not Authorized For:

- Non-FDA approved indications, which are not listed in the Health Net Approved Indications and Usage Guidelines section, unless there is sufficient documentation of efficacy and safety in the published literature

IV. General Information:

- Maximally tolerated statin dose is defined as the inability to titrate to one of the following statin dosages due to skeletal muscle or hepatic related symptoms, concomitant medications, or medical conditions: rosuvastatin 20 mg, atorvastatin 40 mg, simvastatin 40 mg.
- LDL levels and associated CV risk diagnosis were derived from inclusion criteria defined by the REPATHA clinical trials and recommendations from the 2013 ACC/AHA treatment guidelines.
- Baseline LDL prior to lipid lowering therapy should be used to satisfy the diagnostic criteria for Familial Hypercholesterolemia
- Patients should remain on concomitant therapy with a statin if tolerated due to the established long term cardiovascular benefits.
- Patients with high risk of ASCVD include the following:
  - History of clinical atherosclerotic cardiovascular disease (as defined in section II)
  - Diabetes with an estimated 10-year ASCVD risk ≥7.5% for adults 40-75 years of age
  - Untreated LDL ≥190 mg/dL
- Patients with moderate risk of ASCVD include the following:
  - Diabetes with an estimated 10-year ASCVD risk <7.5% for adults 40-75 years of age
  - Estimated 10-year ASCVD risk ≥5% for adults 40-75 years of age
- The calculator for the 10-year ASCVD risk estimator can be found here: http://tools.cardiosource.org/ASCVD-Risk-Estimator/. Information needed to complete the ASCVD Risk Estimator include: gender, race (white, African American, other), systolic blood pressure, diabetes, age, total cholesterol, HDL-Cholesterol, treatment for hypertension, current smoker
- Statin re-challenge should be performed with pravastatin, fluvastatin or rosuvastatin due to their hydrophilicity which appear to produce less intrinsic muscle toxicity and fewer drug interactions compared to other statins. Re-challenge requires slow titration with lower intensity statins to titrate up to the patient's maximally tolerated statin dose with the goal of high-intensity statin use.
- According to the 2013 AHA/ACC lipid guidelines, rhabdomyolysis is a very rare condition. In adults selected for participation in clinical trials of statin therapy, rhabdomyolysis occurred rarely (<0.06% over a mean 4.8 to 5.1 year treatment period). If rhabdomyolysis occurs, documentation via creatine kinase (CK) levels above >10x ULN is required.

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V. Therapeutic Alternatives:

Drug	Dosing Regimen	Dose/Limit/Maximum Dose
Vytorin (ezetimibe/simvastatin)	10/40 mg PO QD	10/40 mg PO QD (Use of the 10/80 mg dose is restricted to patients who have been taking simvastatin 80 mg for 12 months or more without evidence of muscle toxicity)
atorvastatin (Lipitor)	40 mg PO QD	80 mg PO QD
Crestor (rosuvastatin)	5 - 40 mg PO QD	40 mg PO QD
Praluent	75 to 150 mg SC Q2W	150mg SC Q 2 wks

*Requires Prior Authorization

VI. Recommended Dosing Regimen and Authorization Limit:

Drug	Dosing Regimen	Authorization Limit
Repatha - HeFH or hypercholesterolemia	140 mg SQ Q2 wks or 420mg SQ once monthly	6 months Reauthorization requests require confirmation of continued statin therapy at the maximally tolerated dose with demonstrated adherence (unless contraindicated or statin intolerant) AND documentation of LDL reduction while on Repatha therapy (defined as at least 25% LDL reduction from baseline or LDL<70mg/dL for high risk patients or LDL <100mg/DL for medium risk patients). Continued treatment will be approved for 1 year.
Repatha - HoFH	420 mg SQ once monthly	6 months

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Drug	Dosing Regimen	Authorization Limit
		Reauthorization requests require confirmation of continued statin therapy at the maximally tolerated dose with demonstrated adherence (unless contraindicated or statin intolerant) AND documentation of LDL reduction while on Repatha therapy (defined as at least 25% LDL reduction from baseline or LDL<70mg/dL for high risk patients or LDL <100mg/DL for medium risk patients). Continued treatment will be approved for 1 year.

VII. Product Availability:

140 mg/mL prefilled syringe and SureClick autoinjector
420 mg/3.5 mL prefilled cartridge Pushtronex system (on-body infusor)

VIII. References:

1. Repatha package information. Amgen Inc, Thousand Oaks, CA. July 2016.
2. Food and Drug Administration Center for Drug Evaluation and Research: The Endocrinology and Metabolic Drugs Advisory Committee Meeting Briefing Document BLA 125522 – Repatha (evolocumab) injection. June 10, 2015. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM450072.pdf. Accessed: June 11, 2015.
3. Stone NJ, Robinson JG, Lichtenstein AH, 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. 2014 June 24; 129[suppl 2]: S1-S45.

The materials provided to you are guidelines used by this health plan to authorize, modify, or determine coverage for persons with similar illnesses or conditions. Specific care and treatment may vary depending on individual needs and the benefits covered under your contract.

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