Pharmacy Medical Necessity Guidelines: PCSK9 Inhibitor Therapy

Effective: February 1, 2024

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM
These pharmacy medical necessity guidelines apply to the following: ☒ Tufts Health RITogether – A Rhode Island Medicaid Plan		**Fax Numbers:** RXUM: 617.673.0939	

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Repatha (evolocumab) is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody indicated:

- **Prevention of cardiovascular events**
  To reduce the risk of myocardial infarction, stroke, and coronary revascularization in adults with established cardiovascular disease
- **Primary hyperlipidemia (including heterozygous familial hypercholesterolemia)**
  As an adjunct to diet, alone or in combination with other lipid-lowering therapies, for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C)
- **Heterozygous familial hypercholesterolemia**
  As an adjunct to diet and other lipid-lowering therapies in pediatric patients 10 years of age and older with HeFH, to reduce LDL-C
- **Homozygous familial hypercholesterolemia**
  As an adjunct to diet and other LDL-lowering therapies for the treatment of adults and pediatric patients 10 years of age and older with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C

Praluent (alirocumab) is another PCSK9 inhibitor indicated reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with cardiovascular disease and as an adjunct to diet, alone or in combination with other lipid-lowering therapies (e.g., statins, ezetimibe), for the treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) who require additional lowering of LDL cholesterol. Praluent is also approved as an adjunct to other LDL-C-lowering therapies in patients with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C. Praluent (alirocumab) is non-covered for Tufts Health RITogether.

COVERAGE GUIDELINES

Tufts Health Plan may authorize coverage of **Repatha (evolocumab)** for Members when all of the following criteria are met:

Initial

Clinical atherosclerotic cardiovascular disease

1. Documentation the Member has a history of clinical atherosclerotic cardiovascular disease or has experienced a cardiovascular event

AND

2. Documentation the Member has a current LDL-C level ≥70 mg/dL

AND

3. Documentation the Member has previously failed at least two lipid lowering therapies

AND

4. Documentation of at least one of the following:
   a. Member is receiving maximally tolerated statin therapy
   b. Member is statin intolerant
   c. Member has a contraindication to statin therapy

Primary or familial hyperlipidemia

1. The Member had an untreated (i.e., before any lipid lowering therapy was initiated) LDL-C level ≥190 mg/dL

OR

The Member is 10-17 years of age and had an untreated LDL-C level ≥ 160 mg/dL

AND

2. Documentation the Member has a current LDL-C level ≥100 mg/dL

AND

3. Documentation the Member has previously failed at least two generic lipid lowering therapies

AND

4. Documentation of at least one of the following:
   a. Member is receiving maximally tolerated statin therapy
   b. Member is statin intolerant
   c. Member has a contraindication to statin therapy

Reauthorization

1. Documentation of a positive response to therapy confirmed by consistent pharmacy claims and reduction in LDL-C since beginning therapy with the requested agent

LIMITATIONS

1. Initial authorization will be limited to 12 months. Subsequent authorization requests may be given in 12-month intervals for Members who are continuing PCSK9 inhibitor therapy.
2. Coverage of Repatha (evolocumab) will be limited to 28-day supplies as follows:
   - 140 mg dose every 14 days
   - 420 mg every 28 days
3. Adult and pediatric patients 10 years of age and older with HoFH may be approved for 420 mg every 2 weeks if a clinically meaningful response is not achieved after at least 12 weeks of therapy with 420 mg every 28 days.

CODES

Medical billing codes may not be used for these medications. These medications must be obtained via the member's pharmacy benefit.

REFERENCES

1. Ahmad Z. Statin intolerance. *Am J Cardiol*. 2014;113(10):1765-1771.
2. Ahmed CD. New treatment on the horizon—what is a PCSK9 inhibitor? FH Foundation website. thefhfoundation.org/new-treatment-horizon-pcsk9-inhibitor. Accessed 2015 June 22.
3. Akram ON, Bernier A, Petrides F, Wong G, Lambert G. Beyond LDL cholesterol, a new role for PCSK9. *Arterioscler Thromb Vasc Biol.* 2010;30:1279-1281.
4. Amgen announces positive top-line results from phase 3 TESLA trial of evolocumab (AMG 145) in patients with homozygous familial hypercholesterolemia. Press release. Amgen website. amgen.com/media/media_pr_detail.jsp?releaseID=1909327. March 17, 2014. Accessed 2014 July 22.
5. Boekholdt SM, Hovingh GK, Mora S, et al. Very low levels of atherogenic lipoproteins and the risk for cardiovascular events: a meta-analysis of statin trials. *J Am Coll Cardiol*. 2014;64(5)(PMC4443441):485-494.
6. Burton, Thomas M. "FDA Panel Backs Cholesterol Drug, but Raises Concerns." *The Wall Street Journal.* June 9, 2015.
7. Carroll MD, Kit BK, Lacher DA, Yoon SS. Total and High-density Lipoprotein Cholesterol in Adults: National Health and Nutrition Examination Survey, 2011–2012. NCHS Data Brief, No. 132. Hyattsville, MD, National Center for Health Statistics; 2013.
8. Choudhry NK, Fischer MA, Avorn J, et al. The implications of therapeutic complexity on adherence to cardiovascular medications. *Arch Intern Med*. 2011;171(9):814-822.
9. Cohen JC, Boerwinkle E, Mosley TH Jr, Hobbs HH. Sequence variations in *PCSK9*, low LDL, and protection against coronary heart disease. *N Engl J Med*. 2006;354:1264-1272.
10. Fischer MA, Stedman MR, Lii J, et al. Primary medication non-adherence: analysis of 195,930 electronic prescriptions. *J Gen Intern Med*. 2010;25(4)(PMC2842539):284-290.
11. Goldberg AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients. Clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. *J Clin Lipidol*. 2011;5:S1-S8.
12. Gryn SE, Hegele RA. Pharmacogenomics, lipid disorders, and treatment options. *Clin Pharmacol Ther*. 2014;96(1):36-47.
13. Guyton JR, Bays HE, Grundy SM, Jacobson TA. An assessment by the Statin Intolerance Panel: 2014 update. *J Clin Lipidol*. 2014;8(3 Suppl):S72-S81.
14. Fitchett D, Hegele R, Subodh V. Statin intolerance. *Circulation*. 2015;131:e389-e391.
15. High cholesterol facts. Centers for Disease Control and Prevention website. cdc.gov/cholesterol/facts.htm. Accessed 2015 July 22.

16. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. *Circulation*. 2009;119(23):3028-3035.
17. Jacobson TA. NLA Task Force on Statin Safety—2014 update. *J Clin Lipidol*. 2014;8(3 Suppl):S1-S4.
18. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2017 focused update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: A report of the American College of Cardiology task force on expert consensus decision pathways. J Am Coll Cardiol. 2017 Oct 3;70(14): 1785-1822.
19. Maningat P, Gordon BR, Breslow JL. How do we improve patient compliance and adherence to long-term statin therapy? *Curr Atheroscler Rep*. 2013;15(1)(PMC3534845):291.
20. Maxwell KN, Breslow JL. Antibodies to PCSK9: a superior way to lower LDL cholesterol? *Circ Res.* 2012;111:274-277.
21. McGowan MP, Hosseini SH, Moriarty PM, Duell PB. Diagnosis and treatment of heterozygous familial hypercholesterolemia. *JAHA.* 2019;8:e013225.
22. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart Disease and Stroke Statistics—2015 Update: A Report from the American Heart Association. *Circulation*. 2014 Dec 17.
23. National Institutes of Health. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. September 2002. NIH Publication No. 02-5215.
24. ODYSSEY outcomes: evaluation of cardiovascular outcomes after an acute coronary syndrome during treatment with alirocumab. Available on the Internet. URL: https://clinicaltrials.gov/ct2/show/NCT01663402. Accessed 2018 October 1.
25. O'Riordan M. IMPROVE-IT: 'modest' benefit with ezetimibe in post-ACS patients. Medscape website. medscape.com/viewarticle/835030. Accessed 2015 July 23.
26. O'Riordan M. Knowns and unknowns: *Lancet* reviews role of lipids in CVD. Medscape website. medscape.com/viewarticle/830178?nlid=63748_1984&src=wnl_edit_medn_card&uac=3773BK&spon=2. August 20, 2014. Accessed 2015 July 22.
27. Palmieri A, Stavnitser A, Patel NV, Miller AR, Matlin OS, Kymes SM. Trends in statin treatment costs and potential impact of novel therapies. *Am J Pharm Benefits*. 2013;5(2):74-78.
28. PCSK9. National Library of Medicine website. ghr.nlm.nih.gov/gene/PCSK9. Reviewed March 2007. Accessed 2015 June 22.
29. Praluent (alirocumab) [package insert]. Bridgewater, NJ: 3anofi-aventis U.S. LLC, and Tarrytown, NY: Regeneron Pharmaceuticals, Inc; April 2021.
30. Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. *JAMA*. 2007;297(2):177-186.
31. Repatha (evolocumab) [package insert]. Thousand Oaks, CA: Amgen Inc.; September 2021.
32. Ridker PM, Revkin J, Amarenco P, et al. Cardiovascular efficacy and safety of bococizumab in high-risk patients. N Engl J Med. 2017;376:1527-39.
33. Robinson JG. Management of familial hypercholesterolemia; a review of the recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. *J Manag Care Pharm.* 2013;10(2);139-149.
34. Robinson JG, Farnier M, Krempf M et al. Efficacy and safety of alirocumab in reducing lipids and cardiovascular events. *N Engl J Med.* Epub ahead of print. March 15, 2015.
35. Robinson JG, Nedergaard BS, Rogers WJ, et al. Effect of evolocumab or ezetimibe added to moderate- or high-intensity statin therapy on LDL-C lowering in patients with hypercholesterolemiathe LAPLACE-2 randomized clinical trial. *JAMA.* 2014;311(18):1870-1882. jama.jamanetwork.com/article.aspx?articleid=1869210. Accessed 2015 July 22.
36. Sabatine MS, Giugliano RP, Wiviott SD, et al. Efficacy and safety of evolocumab in reducing lipids and cardiovascular events. *N Engl J Med.* Epub ahead of print. March 15, 2015.
37. Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. N Engl J Med. 2017;376:1713-22.
38. Shrank WH, Lotvin A, Singh S, Brrennan T. In the debate about cost and efficacy, PCSK9 inhibitors may be the biggest challenge yet. Health Affairs Blog website. healthaffairs.org/blog/2015/02/17/in-the-debate-about-cost-and-efficacy-pcsk9-inhibitors-may-be-the-biggest-challenge-yet. Accessed 2015 July 22.
39. Stock J. ACC 2014 RUTHERFORD-2: evolocumab in heterozygous FH. PCSK9 Forum website. pcsk9forum.org/acc-2014-rutherford-2-evolocumab-in-heterozygous-fh/. Accessed 2015 July 22.
40. 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;129:S1-S45.
41. Stroes ES, Thompson PD, Corsini A, et al. Statin-associated muscle symptoms: impact on statin therapy—European Atherosclerosis Society Consensus Panel Statement on Assessment, Aetiology and Management. *Eur Heart J*. 2015;36(17)(PMC4416140):1012-1022.
42. The Physician's Guide to Homozygous Familial Hypercholesterolemia (HoFH). Danbury, CT: National Organization for Rare Disorders; 2014. Nordphysicianguides.org/homozygous-familial-hypercholesterolemia. Accessed 2015 July 22.
43. Vogel RA. PCSK9 inhibition: the next statin? *J Am Col Cardiol*. 2012;59(25):2354-2355.
44. Writing Committee, Lloyd-Jones DM, Morris PB, et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: A report of the American College of Cardiology task force on clinical expert consensus documents. J Am Coll Cardiol. 2016 Jul 5;68(1):92-125.

APPROVAL HISTORY

September 13, 2022: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:
1. November 14, 2023: Effective February 1, 2024, added reauthorization criteria to require consistent pharmacy claims and reduced LDL. Updated initial approval criteria to include contraindication to statin therapy in step therapy language. Updated fax number for Pharmacy UM.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.

Provider Services