Pharmacy Medical Necessity Guidelines: PCSK9 Inhibitor Therapy

Effective: May 12, 2020

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:

Commercial Products

☐ Tufts Health Plan Commercial products – large group plans
☐ Tufts Health Plan Commercial products – small group and individual plans
☐ Tufts Health Freedom Plan products – large group plans
☐ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☐ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☐ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:

RXUM: 617.673.0988

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 to reduce low-density lipoprotein cholesterol
- **Homozygous familial hypercholesterolemia**
  As an adjunct to diet and other low density lipoprotein (LDL)-lowering therapies for the treatment of patients with homozygous familial hypercholesterolemia who require additional lowering of LDL cholesterol

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 (alirocumab) is currently non-covered.

COVERAGE GUIDELINES

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

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 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

Primary or familial hyperlipidemia

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

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. The plan does not cover the following medications on all Commercial and Medicaid formularies: Praluent. Refer to the Pharmacy Medical Necessity Guidelines for Noncovered Drugs with Suggested Alternatives or Drugs Without Drug- or Drug Class-Specific Criteria.
3. Coverage of Repatha (evolocumab) will be limited to 28-day supplies as follows:
   - 140 mg dose every 14 days
   - 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. 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.
22. 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.
23. 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.
24. O'Riordan M. IMPROVE-IT: 'modest' benefit with ezetimibe in post-ACS patients. Medscape website. medscape.com/viewarticle/835030. Accessed 2015 July 23.
25. 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.
26. 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.
27. PCSK9. National Library of Medicine website. ghr.nlm.nih.gov/gene/PCSK9. Reviewed March 2007. Accessed 2015 June 22.
28. Praluent (alirocumab) [package insert]. Bridgewater, NJ: sanofi-aventis U.S. LLC, and Tarrytown, NY: Regeneron Pharmaceuticals, Inc; March 2020.
29. 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.
30. Repatha (evolocumab) [package insert]. Thousand Oaks, CA: Amgen Inc.; February 2019.
31. 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.
32. 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.
33. 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.
34. 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.
35. 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.
36. 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.
37. 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.
38. 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.
39. 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.

40. 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.
41. 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.
42. Vogel RA. PCSK9 inhibition: the next statin? *J Am Col Cardiol*. 2012;59(25):2354-2355.
43. 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

January 12, 2016: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:
1. February 14, 2016: No changes.
2. April 11, 2017: Administrative update. Effective 6/1/2017, Medical Necessity Guideline applies to Tufts Health RITogether.
3. October 17, 2017: Based on the results of the FOURIER trial and current treatment guidelines, the criteria was updated to remove the requirement of ezetimibe monotherapy for patients with a statin intolerance, allow coverage of PCSK9 inhibitor therapy for patients with ASCVD on moderate intensity statins who are not meeting LDL goal and who are unable to receive high intensity statins, and to remove requirement for triglyceride levels to be less than 400 mg/dL.
4. November 14, 2017: Removed the requirement of provider attestation the patient is not experiencing any significant adverse events related to therapy from reauthorization criteria.
5. October 16, 2018: Effective January 1, 2019, updated coverage criteria to require documentation of previous failure of at least two generic lipid lowering therapies, the Member is receiving maximally tolerated statin therapy or is statin intolerant, a current LDL-C level ≥70 mg.dL (for clinical atherosclerotic cardiovascular disease) or ≥100 mg/dL (for primary or familial hyperlipidemia), and documentation the Member has a history of clinical atherosclerotic cardiovascular disease or has experienced a cardiovascular event or an untreated LDL-C level ≥190 mg/dL. Updated the duration of approval to 12 month interval and updated continuation of therapy requirements. Added the following Limitation: The plan does not cover the following medications on all Commercial and Medicaid formularies: Praluent. Refer to the Pharmacy Medical Necessity Guidelines for Noncovered Drugs with Suggested Alternatives or Drugs Without Drug- or Drug Class-Specific Criteria. Removed the following limitations: a) The plan will not cover other PCSK9 inhibitors (including Praluent [alirocumab]) unless the Member has either failed an adequate trial of or has a contraindication to Repatha (evolocumab). Coverage Guidelines for PCSK9 inhibitors as outlined for Repatha (evolocumab) above apply; b) Members new to the Plan and currently taking a PCSK9 inhibitor must meet initial authorization criteria if on PCSK9 inhibitor therapy for less than 6 months and must meet reauthorization criteria if on PCSK9 inhibitor therapy for at least 6 months; c) For Praluent (alirocumab), the Plan requires documentation of a therapeutic failure on Praluent 75 mg every 2 weeks before the 150 mg dose may be approved. Therapeutic failure to Praluent 75 mg every 2 weeks is defined as an inability to reach target LDL goals despite an adherent ≥4 to 8 week trial (adherence calculation must be supported by claims data or, if not available, by physician attestation); and d) Coverage of Praluent (alirocumab) will be limited to 28-day supplies as follows: Praluent 75 mg/mL or 150 mg/mL – two single-dose prefilled pens or syringes every 28 days.
6. June 11, 2019: Added supplemental indication to Praluent. No changes to criteria itself.
7. May 12, 2020: No changes.

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.