UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2021 P 2062-14
Program	Prior Authorization/Medical Necessity
Medication	Praluent® (alirocumab)*
P&T Approval Date	5/2015, 8/2015, 9/2015, 9/2016, 12/2016, 11/2017, 12/2018, 12/2019, 2/2020, 2/2021, 6/2021, 8/2021
Effective Date	9/1/2021; Oxford only: 9/1/2021

1. Background:

Praluent® (alirocumab) is a PCSK9 (Proprotein Convertase Subtilisin Kexin Type 9) inhibitor antibody indicated:

- To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease.
- As 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) to reduce low-density lipoprotein cholesterol (LDL-C). ¥
- As an adjunct to other lipid-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.[1]

2. Coverage Criteria[a]:

A. <u>Hyperlipidemia</u>

a. **Praluent** will be approved based on **<u>all</u>** of the following criteria:

(1) **<u>One</u>** of the following diagnoses:

(a) Heterozygous familial hypercholesterolemia (HeFH) as confirmed by **<u>one</u>** of the following*¥:

i. **<u>Both</u>** of the following:[14-16]

1. Pre-treatment LDL-C greater than 190 mg/dL (greater than 155 mg/dL if less than 16 years of age)

-AND-

2. **<u>One</u>** of the following:

a. Family history of myocardial infarction in first-degree relative < 60 years of age
b. Family history of myocardial infarction in second-degree relative <50 years of age

c. Family history of LDL-C greater than 190 mg/dL in first- or second-degree relative
d. Family history of heterozygous or homozygous familial hypercholesterolemia in first- or second-degree relative
e. Family history of tendinous xanthomata and/or arcus cornealis in first- or second degree relative

-OR-

ii. **Both** of the following:[14-16]

1. Pre-treatment LDL-C greater than 190 mg/dL (greater than 155 mg/dL if less than 16 years of age)

-AND-

2. **One** of the following:

a. Functional mutation in LDL, apoB, or PCSK9 gene*
b. Tendinous xanthomata
c. Arcus cornealis before age 45

-OR-

(b) Atherosclerotic cardiovascular disease (ASCVD) as confirmed by **one** of the following:

i. Acute coronary syndromes
ii. History of myocardial infarction
iii. Stable or unstable angina
iv. Coronary or other arterial revascularization
v. Stroke
vi. Transient ischemic attack
vii. Peripheral arterial disease presumed to be of atherosclerotic origin

-AND-

(2) **One** of the following:

(a) Patient has been receiving at least 12 consecutive weeks **of high intensity statin therapy** [i.e. atorvastatin 40-80 mg, rosuvastatin 20-40 mg] and will continue to receive a high intensity statin at maximally tolerated dose

-OR-

(b) **Both** of the following:

i. Patient is unable to tolerate high-intensity statin as evidenced by **one** of the following intolerable and persistent (i.e. more than 2 weeks) symptoms:

1. Myalgia (muscle symptoms without CK elevations)
2. Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

-AND-

ii. **One** of the following:

1. Patient has been receiving at least 12 consecutive weeks of **moderate-intensity** [i.e. atorvastatin 10-20 mg, rosuvastatin 5-10 mg, simvastatin ≥ 20 mg, pravastatin ≥ 40 mg, lovastatin 40 mg, Lescol XL (fluvastatin XL) 80 mg, fluvastatin 40 mg twice daily or Livalo (pitavastatin) ≥ 2 mg] and will continue to receive a moderate-intensity statin at maximally tolerated dose

-OR-

2. Patient has been receiving at least 12 consecutive weeks of **low-intensity** [i.e. simvastatin 10 mg, pravastatin 10-20 mg, lovastatin 20 mg, fluvastatin 20-40 mg, or Livalo (pitavastatin) 1 mg] statin therapy and will continue to receive a low-intensity statin at maximally tolerated dose

-OR-

(c) Patient is unable to tolerate **low or moderate-, and high-intensity statins** as evidenced by **one** of the following:

i. **One** of the following intolerable and persistent (i.e. more than 2 weeks) symptoms for low or moderate-, and high-intensity statins:

1. Myalgia (muscle symptoms without CK elevations)
2. Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

-OR-

ii. Patient has a labeled contraindication to all statins

-OR-

iii. Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN

-AND-

(3) **One** of the following:

(a) **One** of the following LDL-C values while on maximally tolerated lipid lowering therapy for a minimum of at least 12 weeks within the last 120 days or 120 days prior to starting PCSK9 inhibitor therapy:

i. LDL-C ≥ 100 mg/dL with ASCVD

ii. LDL-C ≥ 130 mg/dL without ASCVD

-OR-

(b) **Both** of the following:

i. **One** of the following LDL-C values while on maximally tolerated lipid lowering therapy for a minimum of at least 12 weeks within the last 120 days or 120 days prior to starting PCSK9 inhibitor therapy:

1. LDL-C between 70 mg/dL and 99 mg/dL with ASCVD

2. LDL-C between 100 mg/dL and 129 mg/dL without ASCVD

-AND-

ii. **One** of the following:

1. Patient has been receiving at least 12 consecutive weeks of ezetimibe (Zetia®) therapy as adjunct to maximally tolerated statin therapy

-OR-

2. Patient has a history of contraindication, or intolerance to ezetimibe

-AND-

(4) History of failure, contraindication, or intolerance to Repatha (evolocumab) (document date of trial and list reason for therapeutic failure, contraindication, or intolerance)

-AND-

(5) Used as an adjunct to a low-fat diet and exercise

-AND-

(6) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor [e.g., Repatha (evolocumab)]

-AND-

(7) Prescriber attests to the following: the information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided

*Results of prior genetic testing can be submitted as confirmation of diagnosis of HeFH, however please note that UnitedHealthcare does not currently cover genetic testing for evidence of an LDL-receptor mutation, familial defective apo B-100 or a PCSK9 mutation.

¥ No coverage of Praluent will be provided for the primary prevention of cardiovascular events and/or for the lowering of low-density lipoprotein cholesterol in patients with primary hyperlipidemia who do not have heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease (ASCVD) as the use of PCSK9 inhibitors in this population is not supported by the 2018 American College of Cardiology/ American Heart Association Cholesterol Clinical Practice Guidelines.

Authorization will be issued for 12 months

B. **Homozygous Familial Hypercholesterolemia**

a. **Praluent** will be approved based on **all** of the following criteria:

(1) Diagnosis of homozygous familial hypercholesterolemia (HoFH) as confirmed by **both** of the following:*

(a) **One** of the following:

i. Pre-Treatment LDL-C greater than 500 mg/dL
ii. Treated LDL-C greater than 300 mg/dL

-AND-

(b) **One** of the following:
i. Xanthoma before 10 years of age
ii. Evidence of heterozygous familial hypercholesterolemia (HeFH) in both parents

-AND-

(2) Used as an adjunct to a low-fat diet and exercise

-AND-

(3) Patient is receiving other lipid-lowering therapy (e.g., statin, ezetimibe, LDL apheresis)

-AND-

(4) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor [e.g., Repatha (evolocumab)]

-AND-

(5) Not used in combination with Juxtapid (lomitapide)

-AND-

(6) History of failure, contraindication, or intolerance to Repatha (evolocumab) (document date of trial and list reason for therapeutic failure, contraindication, or intolerance)

-AND-

(7) Prescriber attests to the following: the information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided

*Results of prior genetic testing can be submitted as confirmation of diagnosis of HoFH, however please note that UnitedHealthcare does not currently cover genetic testing for evidence of an LDL-receptor mutation, familial defective apo B-100 or a PCSK9 mutation.

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

*Praluent is excluded from coverage for the majority of our benefits

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class
- Supply limits may be in place and Step therapy may be in place

4. References:

1. Praluent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals; April2021.
2. WHO Familial Hypercholesterolemia Consultation Group. Familial Hypercholesterolemia (FH): report of a second WHO consultation. Geneva: World Health Organization; 1999.
3. Scientific Steering Committee on behalf of the Simon Broome Register Group. Risk of fatal coronary heart disease in familial hypercholesterolaemia. BMJ. 1991;303:893-6.
4. 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. J Am Coll Cardiol. 2014;63:2889-934.
5. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med. 2015a; DOI: 10.1056/NEJMoa1410489 [Epub ahead of print].
6. The Lipid Research Clinics Coronary Primary Prevention Trial results. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA. 1984;251:365-74.
7. ATP III Final Report PDF. 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. Circulation. 2002;106:3143-3421.
8. Per clinical drug consult with cardiologist. August 3, 2015.
9. Blom DJ, Hala T, Bolognese M, et al. A 52-week placebo-controlled trial of evolocumab in hyperlipidemia. N Engl J Med. 2014;370:1809-19.
10. Raal FJ, Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis. 2012;223:262-8.
11. Raal FJ, Honarpour N, Blom DJ, et al. Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial. Lancet. 2015;385:341-50.
12. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position

paper from the Consensus Panel on Familial Hypercohlesterolaemia of the European Atherosclerosis Society. Eur Heart J. 2014;35:2146-57.
13. Lloyd-Jones D, Morris P, Ballantyne C, et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholersterol lowering in the management of atherosclerotic cardiovascular disease risk. J Am Coll Cardiol. 2016;68:92-125.
14. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. American journal of epidemiology. 2004;160:407-420
15. Haase A, Goldberg AC. Identification of people with heterozygous familial hypercholesterolemia. Current opinion in lipidology. 2012;23:282-289.
16. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. European heart journal. 2013;34:3478-3490a.
17. Jellinger PS, Handelsman Y, Rosenblit PD, et al. American association of clinical endocrinologists and American college of endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocr Pract. 2017; Suppl 2;23:1-87.
18. Lloyd-Jones D, Morris P, Ballantyne C, 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. J Am Coll Cardiol. 2017.
19. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2018; DOI: 10.1161/CIR.0000000000000625.

Program	Prior Authorization/Medical Necessity - Praluent® (alirocumab)
Change Control	
5/2015	New program.
5/2015	Added examples of atherosclerotic cardiovascular disease.
8/2015	Revised clinical criteria
9/2015	Revised clinical criteria to include combination use of high-intensity statin or documented intolerance to high-, moderate- and low intensity statin therapy to achieve the maximally tolerated statin therapy.
7/2016	Added Indiana and West Virginia coverage information.
9/2016	Added Connecticut and Kentucky coverage information. Updated references.
11/2016	Added California coverage information.
12/2016	Modified medical record criteria to include review of prescription claims history. Updated references.
11/2017	Updated medical record requirement, modified criteria for HeFH diagnosis, modified previous statin requirement requiring failure, intolerance to high intensity and either moderate or low intensity statin. Modified target LDL values and ezetimibe trial requirement. Extended timeline for lipid panel submission to 120 days. Added physician attestation criterion. Updated state mandate verbiage. Updated references.

12/2018	Annual review. Updated formatting without changes to clinical intent. Updated references.
12/2019	Annual review. Updated background information without change to clinical coverage criteria. Updated references.
2/2020	Updated criteria providing clarity on laboratory monitoring requirements. Updated reference.
2/2021	Annual review with no change to coverage criteria. References updated.
6/2021	Added Praluent exclusion statement. Added history of failure, contraindication, or intolerance to Repatha to all criteria. Removed prescriber specialist requirement. Removed submission of medical records requirement throughout criteria. Changed initial authorization duration to 12 months to align all PCSK9 programs. Removed reauthorization criteria. Added HoFH criteria per new indication. Updated references.
8/2021	Updated LDL-C requirement to 120 days or 120 days prior to starting PCSK9 inhibitor therapy.