Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCCAR034O.0226	**CARDIOVASCULAR AGENTS** **PCSK9 INHIBITORS** See FDA Approved Indications for medications covered by policy
Effective Date: 4/1/2026	**Review/Revised Date**: 10/15, 01/16, 03/17, 9/17, 07/18, 09/19, 09/20, 05/21, 04/22, 05/22, 05/23, 05/24, 02/25, 10/25, 02/26 (snm)
Original Effective Date: 08/15	**P&T Committee Meeting Date**: 08/15, 09/15, 10/15, 01/16 (cv), 02/16, 10/16, 04/17, 10/17, 08/18, 08/19, 10/19, 10/20, 06/21, 04/22, 06/22, 06/23, 06/24, 02/25, 12/25, 02/26
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA) approved indications not otherwise excluded from the benefit.

REQUIRED MEDICAL INFORMATION:
1. One of the following:
    a. Current use of high-intensity statin therapy for at least three months, defined as atorvastatin 40 mg to 80 mg daily or rosuvastatin 20 mg to 40 mg daily, OR
    b. Documented statin intolerance to low dose atorvastatin or rosuvastatin (atorvastatin 10 mg daily or rosuvastatin 5 mg daily) and any other statin at any dose. Statin intolerance is defined as intolerable muscle side effects or biomarker changes (such as elevations of creatinine kinase) that decrease or resolve after discontinuation of therapy with statin.

AND

2. Current use of ezetimibe 10 mg daily for at least three months, or documented intolerance/contraindication to its use. If patient is more than 30% above the goal low-density lipoprotein (LDL) level outlined in the hyperlipidemia criteria below, this criterion for ezetimibe may be waived.

AND

3. Must meet listed criteria below for each specific diagnosis:
    a. For **familial hypercholesterolemia (FH)** (heterozygous or homozygous familial hypercholesterolemia), both of the following:
        i. Confirmed diagnosis by one of the following:

1) Genetic mutation in one of the following genes: low-density lipoprotein receptors (LDLR), apolipoprotein B gene (APOB), or proprotein convertase subtilisin kexin type 9 (PCSK9) OR
2) LDL-C greater than 190 mg/dL (pretreatment or highest level while on treatment) and secondary causes have been ruled out. Secondary causes may include hypothyroidism, nephrosis, or extreme dietary patterns
3) A "possible" or "definite" diagnosis of FH via Simon Broome criteria or a "probable" or "certain" diagnosis of FH via Dutch Lipid Clinic Network Criteria score of greater than or equal to 6 (see appendix)

ii. Documentation of current (within previous three months) LDL-C greater than 100 mg/dL, taken after at least three months of continuous therapy with statin and ezetimibe outlined in criterion 1 above

b. For **ASCVD**, both of the following:
   i. Documentation of current (within previous three months) LDL-C greater than or equal to 70 mg/dL, taken after at least three months of continuous therapy with statin and ezetimibe outlined in criterion 1 above
   ii. Documentation of very high-risk clinical ASCVD, defined as history of multiple ASCVD events [acute coronary syndrome (ACS) within previous 12 months, history of myocardial infarction, history of ischemic stroke, symptomatic peripheral artery disease] OR one ASCVD event and multiple of the following high-risk conditions:
      1) Age 65 years and older
      2) Heterozygous familial hypercholesterolemia
      3) History of coronary revascularization (CABG or PCI)
      4) Diabetes mellitus
      5) Hypertension
      6) Chronic kidney disease
      7) Current smoking
      8) Persistently elevated LDL-C above 100 despite maximally tolerated statin therapy and ezetimibe
      9) History of congestive heart failure
c. For **primary prevention of major cardiovascular events,** Repatha and Praluent may be covered in adults at increased risk for major cardiovascular events indicated by a 10-year ASCVD risk estimate of 20% or greater based on a clinical risk calculator (see appendix)

4. For Leqvio:

a. Documented trial and failure, intolerance, or contraindication to evolocumab (Repatha) or alirocumab (Praluent). Failure of these PCSK9 inhibitors includes adherence to the PCSK9 inhibitor for at least 12 weeks with an LDL-C that remains >70 mg/dL in patients with evidence of clinical ASCVD.

Initial Reauthorization:
Documentation of response to therapy, defined as a decrease in LDL-C levels compared to pre-treatment levels.

EXCLUSION CRITERIA:
- Non-familial hyperlipidemia/hypercholesterolemia
- Primary prevention of ASCVD **(Leqvio only)**

AGE RESTRICTIONS:
The patient's age must be within FDA labeling for the requested indication

PRESCRIBER RESTRICTIONS: N/A

COVERAGE DURATION:
Initial authorization for one year. Reauthorization will be approved until no longer eligible with the plan, subject to formulary and/or benefit changes.

QUANTITY LIMIT:
- Praluent: Two injections per 28 days
  - 75 mg/mL – two injections (2.0 mL) per 28 days
  - 150 mg/mL – two injections (2.0 mL) per 28 days
- Repatha: Two injections per 28 days
  - 420 mg/3.5 mL prefilled cartridge – one injection (3.5 mL) per 28 days
  - 140 mg/mL – two injections (2.0 mL) per 28 days

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCCAR034O.1225	CARDIOVASCULAR AGENTS PCSK9 INHIBITORS See FDA Approved Indications for medications covered by policy

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Alirocumab (Praluent) and evolocumab (Repatha) are human monoclonal antibody that binds to PCSK9. Inclisiran (Leqvio) is a double-stranded small interfering RNA (siRNA) that inhibits proprotein convertase subtilisin kexin type 9 (PCSK9) synthesis. The inhibition of PCSK9 results in increased numbers of LDLR on the surface of hepatocytes. LDLRs clear LDL-cholesterol from the blood; therefore, PCSK9 inhibitors reduce serum levels of LDL-C.

FDA APPROVED INDICATIONS:

Praluent:

- To reduce the risk of major adverse cardiovascular (CV) events (coronary heart disease death, myocardial infarction, stroke, or unstable angina requiring hospitalization) in adults at increased risk for these events**.**
- As an adjunct to diet and exercise to reduce low- density lipoprotein cholesterol (LDL-C) in:
    - Adults with hypercholesterolemia.
    - Adults and pediatric patients aged 8 years and older with heterozygous familial hypercholesterolemia (HeFH).
    - Adults with homozygous familial hypercholesterolemia (HoFH).

Repatha:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, myocardial infarction, stroke, unstable angina requiring hospitalization, or coronary revascularization) in adults at increased risk for these events.
- As an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in:
    - adults with hypercholesterolemia.
    - adults and pediatric patients aged 10 years and older with heterozygous familial hypercholesterolemia (HeFH).
    - adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH).

Leqvio:

- Adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C)

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POSITION STATEMENT:
Alirocumab (Praluent) and evolocumab (Repatha) have shown significant LDL-C lowering effects (40-75%) in clinical trials, in addition to maximally tolerated statin therapy. A trial evaluating hard cardiovascular outcomes for evolocumab was recently published (FOURIER). This trial evaluated 27,594 patients with clinically evident atherosclerotic disease and additional risk factors for recurrent. These patients were randomized in 1:1 fashion to evolocumab (either 140 mg every 2 weeks or 420 mg every month, according to patient preference) or matching placebo for a median follow-up of 26 months. There was a statistically significant benefit for the primary endpoint, which was a composite of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization (NNT = 67 over two years). However, when the individual components of the composite endpoints were studies, there was no clinical benefit for mortality. There was a statistically significant benefit for reducing the risk of myocardial infarction (NNT =83 over two years) and coronary revascularization (NNT = 67 over two years). Of note, there were no safety signals identified in the trial, even with a majority of patients achieving very low LDL levels (>20 mg/dL).

The initial clinical trials for these agents were designed prior to the guidelines for cholesterol management being published in 2013. Therefore, the inclusion criteria were based on LDL goals from NCEP/ATPIII guideline and the criteria for approval are also based on these LDL targets, despite current guideline recommendations veering away from specific LDL targets.

Inclisiran (Leqvio) showed significant LDL-C lowering effects in clinical trials (39.7-51.3%) in addition to maximally tolerated statin therapy. Inclisiran was studied in three clinical phase 3 trials demonstrating that inclisiran compared to placebo as adjunct to maximally tolerated statin therapy reduces LDL-C in adults with HeFH (ORION-9 study) and in adults with ASCVD (ORION-10 and ORION-11). The cardiovascular outcomes trial for inclisiran, ORION-4, is not expected to be completed until 2026.

Familial hypercholesterolemia (FH) is typically diagnosed by either genetic testing or clinical presentation. A definitive diagnosis can be made with genetic mutations in any of the following genes: LDLR, APOB, or PCSK9. Clinical presentation involves many different patient factors. However, in the clinical trials for alirocumab, patients were diagnosed with definite FH using the Simon Broome criteria (see Appendix) or the World Health Organization/Dutch Lipid Network criteria (See Appendix). Severely elevated LDL-C levels and the presences or tendon xanthomas are typically diagnostic of FH.

The AHA/ACC/AACVRP/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol states the following regarding PCSK9 inhibitors for:[12]

- Severe hypercholesterolemia (LDL-C greater than or equal to 190 mg/dL)
    - In patients 30-75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL or higher while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered
    - In patients 40-75 years of age with a baseline LDL-C level of 220 mg/dL or higher while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered
    - Regardless of whether a patient with LDL-C levels ≥190 mg/dL is found to have a genetic mutation associated with FH, those with very high LDL-C values are most likely to achieve the greatest benefit from evidence-based LDL-C–lowering therapy. Consequently, patients who have a baseline LDL-C level ≥220 mg/dL and an on-treatment LDL-C level ≥130 mg/dL despite maximally tolerated statin and ezetimibe therapy may be considered for treatment with a PCSK9 inhibitor
- Secondary ASCVD Prevention
    - In patients with clinical ASCVD who are judged to be very high risk and considered for PCSK9 inhibitor therapy, maximally tolerated LDL-C lowering therapy should include maximally tolerated statin therapy and ezetimibe
    - In patients with clinical ASCVD who are judged to be very high risk and who are on maximally tolerated LDL-C lowering therapy with LDL-C 70 mg/dL or higher or a non-HDL-C level of 100 mg/dL or higher, it is reasonable to add PCSK9 inhibitor following a clinical-patient discussion about the net benefit, safety, and cost
- Primary prevention of ASCVD in high-risk patients
    - In adults 40-75 years old with LDL levels 70-189 mg/dL without diabetes, ASCVD risk should be estimated using the race- and sex-specific pooled-cohort equation (PCE, ASCVD risk estimator plus), and should be categorized as being low risk (<5%), borderline risk (5% to <7.5%), intermediate risk (≥7.5% to <20%), and high-risk (≥20%).
    - In adults with diabetes mellitus and 10-year ASCVD risk of 20% or higher, it may be reasonable to add on non-statin therapy (e.g., ezetimibe) to maximally tolerated statin therapy to reduce LDL-C levels by 50% or more.

Clinical ASCVD is defined as acute coronary syndrome, history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack or peripheral arterial disease including aortic aneurysm[12]. In 2022, the ACC updated this definition to also include coronary heart disease with or without revascularization.[17] Coronary heart disease is defined as “a

type of heart disease that occurs when the arteries of the heart cannot deliver enough oxygen-rich blood to the heart muscle due to narrowing from the buildup of fatty deposits called plaque. It is also sometimes called coronary artery disease or ischemic heart disease."[18]

The FDA approved the updated evolocumab (Repatha) indication on September 2021 to include "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 (HeFH) to reduce low-density lipoprotein cholesterol (LDL-C)." In the FDA's statement on September 2021, the FDA specifically stated that they approved evolocumab (Repatha) as an add-on treatment to diet alone or together with certain other therapies for patients aged 10 years and older with heterozygous familial hypercholesterolemia (HeFH) and homozygous familial hypercholesterolemia (HoFH). Therefore, this policy is intended to limit coverage of evolocumab (Repatha) to patients with confirmed diagnosis of HoFH, HeFH, or clinical ASCVD. In July 2023, the FDA updated the indication for Leqvio to remove approval for patients with clinical ASCVD and expand the treatment eligible population with familial hypercholesterolemia by removing requirement to have used "maximally tolerated" statin therapy.[19] The FDA approved the updated alirocumab (Praluent) indication on March 2024 to include "As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 8 years and older with HeFH to reduce LDL-C." In August 2025, the FDA revised the labelled indications for evolocumab (Repatha) to include primary prevention of cardiovascular disease in adult patients at high risk of major adverse cardiovascular events such as CV death, myocardial infarction, stroke, unstable angina requiring hospitalization, and coronary revascularization.[20]

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11. Oregon Health Authority. Drug Class Update: Non-statins for Management of Blood Cholesterol (May 2019). Available at https://www.orpdl.org/durm/meetings/meetingdocs/2019_05_23/archives/2019_05_23_Non-Statin_ClassUpdate.pdf (Accessed September 16, 2020).
12. 2018 AHA/ACC/AACVRP/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. Journal of the American College of Cardiology. 2019 Jun, 73 (24) e285-e350. Available at: https://www.jacc.org/doi/abs/10.1016/j.jacc.2018.11.003?_ga=2.130559624.666084477.1543267586-144035656.1543267586.
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19. Leqvio package insert. East Hanover (NJ): Novartis Pharmaceuticals Corporation; 2024 Jun.
20. Repatha (evolocumab) package insert. Thousand Oaks (CA): Amgen Inc.; 2025 Aug.

APPENDIX: Diagnostic Scoring Tools for familial hypercholesterolemia

Simon Broome criteria for FH

1. Diagnose a person with definite familial hypercholesterolemia (FH) if they have:
   - Cholesterol concentrations as defined in table 1 and tendon xanthomas, or evidence of these signs in first- or second-degree relative

   OR
   - Deoxyribonucleic acid (DNA)-based evidence of an LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation.
2. Diagnose a person with possible FH if they have cholesterol concentrations as defined in table 1 and at least one of the following.
   - Family history of myocardial infarction: aged younger than 50 years in second-degree relative or aged younger than 60 years in first-degree relative.
   - Family history of raised total cholesterol: greater than 7.5 mmol/l in adult first- or second-degree relative or greater than 6.7 mmol/l in child, brother or sister aged younger than 16 years.

Table 1. Cholesterol levels to be used as diagnostic criteria for the index individual levels either pre-treatment or highest on treatment

	Total cholesterol	LDL-C
Child/young person	> 6.7 mmol/L (260 mg/dL)	> 4.0 mmol/L (154 mg/dL)
Adults	> 7.5 mmol/L (290 mg/dL)	> 4.9 mmol/L (190 mg/dL)

World Health Organization (WHO)/Dutch Lipid Network criteria

Family history			
a	First degree relative known with premature (men<55 yrs, women <60yrs) coronary and vascular disease.		1
b	First degree relative known with LDL-cholesterol >95th percentile.		
	and/or		
a	First degree relative with tendon xanthomata and/or arcus cornealis.		2
b	Children below 18 yrs. with LDL-cholesterol >95th percentile.		
Clinical history			
a	Patient has premature (men<55 yrs, women <60yrs) CAD		2
b	Patient has premature (men<55 yrs, women <60yrs) cerebral or peripheral vascular disease.		1
Physical examination			
a	Tendon xanthomata		6
b	Arcus cornealis below the age of 45 yrs.		4
Laboratory analysis			
		mmol/l	mg/dl
a	LDL-cholesterol >8.5	>330	8
b	LDL-cholesterol 6.5 - 8.4	250-329	5
c	LDL-cholesterol 5.0 - 6.4	190-249	3
d	LDL-cholesterol 4.0 - 4.9	155-189	1
	(HDL-cholesterol and triglycerides are normal)		
DNA-analysis			
a	Functional mutation low-density lipoprotein receptor gene present		8

Diagnosis of FH is:	
certain when	>8 points
probable when	6-8 points
possible when	3-5 points

ASCVD Risk Calculators:

ACC ASCVD Risk Estimator Plus: https://tools.acc.org/ascvd-risk-estimatorplus/#!/calculate/estimate/

Reynolds Risk Score: https://www.scymed.com/en/smnxph/phqgg440.htm and https://reference.medscape.com/calculator/192/reynolds-cad-risk