Washington State Health Care Authority

Antihyperlipidemics –
Proprotein Convertase Subtilisin Kexin Type 9 (PCSK-9) Inhibitors

Medical policy no. 39.35.00-2 Effective Date: July 1, 2018

Related medical policies:

- **Antihyperlipidemics – Apolipoprotein B Synthesis Inhibitors: lomitapide mesylate (JUXTAPID®)**

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Background:

PCSK-9 is an enzyme that acts as part of the cholesterol homeostasis process in humans. PCSK-9 binds to the epidermal growth factor-like domain of the low-density lipoprotein (LDL) receptor on human hepatocytes. This binding forces LDL receptors to remain in the "open" confirmation, which facilitates their destruction, limiting the ability of the liver to remove LDL cholesterol from circulation. Humans with loss of function mutations in PCSK-9 have notable lower LDL cholesterol concentrations, and somewhat lower risk of cardiovascular disease.

Medical necessity

Drug	Medical Necessity
Evolocumab (**REPATHA®**)	Evolocumab may be considered medically necessary when: • Used for the treatment of adults with primary hypercholesterolemia (including heterozygous familial hypercholesterolemia) • Used for the treatment of homozygous familial hypercholesterolemia (HoFH) • Used as secondary prophylaxis for adults with established cardiovascular disease (CVD)
Alirocumab (**PRALUENT®**)	Alirocumab may be considered medically necessary when: • Used for the treatment of adults with primary hypercholesterolemia (including heterozygous familial hypercholesterolemia) • Used as secondary prophylaxis for adults with established cardiovascular disease (CVD)

Clinical policy:

Clinical Criteria	
	1. Diagnosis of Primary Hypercholesterolemia **OR** Heterozygous Familial Hypercholesterolemia defined by **ONE** of the following:

Primary Hypercholesterolemia/ Heterozygous Familial Hypercholesterolemia (HeFH)	a. Clinical diagnosis using diagnostic tools such as US MedPed, Simon Broome Register Group, or Dutch Lipid Panel; **OR** b. Age ≥20 and LDL ≥190mg/dL on maximally tolerated statin therapy prior to adding a PCSK-9 Inhibitor; **OR** c. Age <20 and LDL ≥160mg/dL on maximally tolerated statin therapy prior to adding a PCSK-9 Inhibitor; **OR** d. Genetic typing confirming presence of familial hypercholesterolemia genes 2. Concomitant therapy with the highest-tolerated statin dose (see definitions below) and ezetimibe for at least 6 consecutive weeks **AND ONE** of the following: a. LDL has not achieved at least 50% reduction from baseline; **OR** b. Inability to achieve LDL cholesterol level <100mg/dL 3. Greater than or equal to (≥) 18 years of age 4. Prescribed by or in consultation with a provider specializing in lipid management (e.g. cardiologist, lipid specialist, or endocrinologist) 5. **Not** used in combination with PCSK-9 inhibitor 6. For non-preferred products, trial and failure of greater than or equal to (≥) 1 preferred products **Approve for 6 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration. **Criteria (Reauthorization)** 1. Continues to receive the maximum tolerated dose of statin unless contraindicated or intolerant to statin therapy 2. Documentation of continued clinical benefit, (e.g. at least a 30% reduction in LDL from initiation of PCSK-9 Inhibitor or achievement of patient-specific goal) **Approve for 12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the reauthorization duration.
Secondary Prophylaxis in Adults with Established Cardiovascular Disease (CVD)	1. History of clinical atherosclerotic cardiovascular diseases (ASCVD), including at least **ONE** of the following: a. Myocardial infarction (MI) b. Acute coronary syndrome (ACS) c. Angina d. Transient ischemic attack (TIA)

	e. Coronary revascularization procedures f. Peripheral arterial disease (PAD) 2. Concomitant therapy with the highest-tolerated statin dose (see definitions below) and ezetimibe for at least 6 consecutive weeks **AND ONE** of the following: a. LDL has not achieved at least 50% reduction from baseline; **OR** b. Inability to achieve LDL cholesterol level <100mg/dL; **OR** c. Inability to achieve LDL cholesterol level <70mg/dL for patients at very high risk. Very high risk is defined as **ONE** the following: i. History of multiple major ASCVD events; **OR** ii. One major ASCVD event and multiple high-risk conditions iii. See definitions below for "major ASCVD event" and "high-risk conditions" 3. Greater than or equal to (≥) 18 years of age 4. Prescribed by or in consultation with a provider specializing in lipid management (e.g. cardiologist, lipid specialist, or endocrinologist) 5. **Not** used in combination with another PCSK-9 inhibitor 6. For non-preferred products, trial and failure of greater than or equal to (≥) 1 preferred products **Approve for 6 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration. **Criteria (Reauthorization)** 1. Continues to receive the maximum tolerated dose of statin unless contraindicated or intolerant to statin therapy 2. Documentation of continued clinical benefit, (e.g. at least a 30% reduction in LDL from initiation of PCSK-9 Inhibitor or achievement of patient-specific goal) **Approve for 12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the reauthorization duration.
Homozygous Familial Hypercholesterolemia (HoFH)	1. Clinical diagnosis of homozygous familial hypercholesterolemia defined by **ONE** of the following: a. History of untreated LDL ≥500mg/dL with **ONE** of the following: i. A xanthoma before 10 years of age

	ii. Evidence of heterozygous familial hypercholesterolemia in both parents b. Genetic typing confirming presence of familial hypercholesterolemia genes 2. Concomitant therapy with the highest-tolerated statin dose (see definitions below) and ezetimibe for at least 6 consecutive weeks **AND ONE** of the following: a. LDL has not achieved at least 50% reduction from baseline; **OR** b. Inability to achieve LDL cholesterol level <100mg/dL 3. Greater than or equal to (≥) 13 years of age 4. Prescribed by or in consultation with a cardiologist, endocrinologist or lipid specialist 5. **NONE** of the following: a. Used in combination with another PCSK-9 inhibitor b. Used in combination with Juxtapid (lomitapide) **Approve for 6 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial authorization duration.
	Criteria (Reauthorization) 1. Continues to receive the maximum tolerated dose of statin unless contraindicated or intolerant to statin therapy 2. Documentation of continued clinical benefit, (e.g. at least a 30% reduction in LDL from initiation of PCSK-9 Inhibitor or achievement of patient-specific goal) **Approve for 12 months** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the reauthorization duration.

Dosage and quantity limits

Drug Name	Dose and Quantity Limits
Evolocumab (**REPATHA**®) 140mg	#2 syringes/pens per 28-days
Evolocumab (**REPATHA** ®) 420mg	#1 pens per 28-days
Alirocumab (**PRALUENT**®) 75mg	#2 syringes/pens per 28-days

Definitions

Term	Description
High-Intensity Statin Therapy	rosuvastatin 20mg or 40mg atorvastatin 80mg atorvastatin 40mg if down-titrating from atorvastatin 80mg due to intolerance symptoms
High Risk Conditions	This definition is used to define "very high risk" for Secondary Prophylaxis in Adults with Established Cardiovascular Disease (CVD), criteria 2c. • Age ≥65 • Heterozygous familial hypercholesterolemia • History of prior coronary artery bypass surgery or percutaneous intervention (PCI) outside of the "major ASCVD event(s)," defined below • Diabetes Mellitus • Hypertension • Chronic kidney disease (eGFR 15-59ml/min/1.73m^2) • Current smoking • Persistently elevated LDL-C (LDL-C ≥100mg/dL (≥2.6 mmol/L)) despite maximally tolerated statin therapy and ezetimibe • History of congestive heart failure
Highest-tolerated statin dose	1. Highest-tolerated statin dose is defined as **ONE** of the following: a. FDA labeled maximum dose for high-intensity statin therapy (e.g. atorvastatin 40 to 80mg and rosuvastatin 20 to 40mg) b. Treatment with statin therapy has been ineffective, contraindicated, or not tolerated. i. Statin therapy is considered ineffective if patients are not able to tolerate high-intensity or have not met criteria 2a or 2b while on a maximally tolerated dose of statin with ezetimibe for at least 6 weeks. ii. Statin intolerance is defined as the inability to tolerate at least two different statin medications, with or without ezetimibe, at the lowest FDA-approved starting dose when other potential causes of muscle symptoms have been maximally managed or ruled out
Lowest Starting Daily Doses (Statins)	rosuvastatin (Crestor®) 5mg atorvastatin 10mg simvastatin 10mg lovastatin 20mg pravastatin 40mg fluvastatin 40mg pitavastatin (Livalo®) 2mg

Major Atherosclerotic Cardiovascular (ASCVD) Event	This definition is used to define "very high risk" for Secondary Prophylaxis in Adults with Established Cardiovascular Disease (CVD), criteria 2c. • Recent acute coronary syndrome (within past 12 months) • History of myocardial infarction (other than recent acute coronary syndrome event listed above) • History of ischemic stroke • Symptomatic peripheral arterial disease (history of claudication with ankle brachial index <0.85, or previous revascularization or amputation)
Statin Intolerance	Documented trial and failure of at least two statins after ruling out hypothyroidism, changes in physical activity and exercise, and potential drug-drug interactions, due to pre-specified intolerance symptoms [see below] that began or increased during statin therapy and stopped when statin therapy was discontinued. Qualification of at least two statins is: one statin must be at lowest starting daily dose [see above] and a different statin may be at any dose. If patient is on combination therapy, such as a fibrate or niacin, discontinuing fibrate or niacin while maintaining statin therapy is required to establish statin intolerance. Rhabdomyolysis determined to be caused by any statin at any dose, after ruling out all other potential causes including drug-drug interactions, will be considered as a contraindication to statins as a class. Patients with history of rhabdomyolysis caused by statins must be managed by lipid specialists, and may be considered eligible for PCSK-9 Inhibitors on a case-by-case basis. Patients who have failed to meet criterion 2 in medical policy may be managed on non-daily (i.e. Every other day) statin therapy if able to demonstrate that they are on maximally-tolerated therapy and can maintain dose while on PCSK-9 Inhibitor.
Pre-Specified Intolerance Symptoms	Myopathy or myalgia (muscle pain, ache, or weakness without CK elevation) Myositis (muscle symptoms with increased CK levels)
Clinical Atherosclerotic Cardiovascular Disease (ASCVD)	Clinical ASCVD, for the purposes of this policy, include myocardial infarction (MI), acute coronary syndrome (ACS), angina, transient ischemic attack (TIA), coronary revascularization procedures, peripheral arterial disease (PAD)

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History

Date	Action and Summary of Changes
01/26/2021	Revised policy finalized

10/30/2020	Added clinical criteria to Secondary Prophylaxis in Adults with Established Cardiovascular Disease (CVD) for very high risk patients. Updated definitions to include specific information used to define very high risk patients.
10/21/2020	Approved by DUR Board
09/28/2020	Added information detailing which products are preferred/non-preferred.
07/23/2020	Revised "Note" at top to reflect new language for preferred/non-preferred products. Revised medical necessity to reflect new indication for alirocumab; condensed indications and revised wording to be more consistent between the two available PCSK-9 inhibitors. Revised clinical criteria, adding requirement for trial of ezetimibe for heterozygous familial hypercholesterolemia and secondary prophylaxis of cardiovascular disease; revised LDL requirement to reflect updated clinical practice guidelines in secondary prophylaxis section; condensed "prevention of CVD and ASCVD" sections into one section as same criteria, renamed to "secondary prophylaxis of CVD." Updated references.
10/02/2019	Edit Note
12/06/2018	Remove Kynamro related Policy
04/18/2018	Re-review
12.16.2015	New Policy