Washington State Health Care Authority

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

Medical policy no. 39.35.00-3 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®**) Alirocumab (**PRALUENT®**)	• PCSK-9 inhibitors may be considered medically necessary in patients who meet the criteria described in the clinical policy below. • 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. • Clients new to Apple Health or new to an MCO, who are requesting regimens for continuation of therapy should be reviewed following the reauthorization criteria listed below.

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. Genetic typing confirming presence of familial hypercholesterolemia genes; **AND** 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. For adults with known coronary heart disease or diabetes, inability to achieve LDL cholesterol level <70mg/dL; **AND** 3. Greater than or equal to (≥) 18 years of age; **AND** 4. **Not** used in combination with another PCSK-9 inhibitor; **AND** 5. 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; **AND** 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); **OR** b. Acute coronary syndrome (ACS); **OR** c. Angina; **OR** d. Transient ischemic attack (TIA); **OR** e. Coronary revascularization procedures; **OR** f. Peripheral arterial disease (PAD); **AND**

	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 <70mg/dL; **AND** 3. Greater than or equal to (≥) 18 years of age; **AND** 4. **Not** used in combination with another PCSK-9 inhibitor; **AND** 5. 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; **AND** 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 for adults, untreated LDL ≥400mg/dL for children, or treated LDL ≥300mg/dL for adults and children with **ONE** of the following: i. A xanthoma before 10 years of age; **OR** ii. Evidence of heterozygous familial hypercholesterolemia in both parents; **OR** b. Genetic typing confirming presence of familial hypercholesterolemia genes; **AND** 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 for adults or <135mg/dL for children; **AND**

	3. For evolocumab, greater than or equal to (≥) 13 years of age; **AND** 4. For alirocumab, greater than or equal to (≥) 18 years of age; **AND** 5. **NONE** of the following: a. Used in combination with another PCSK-9 inhibitor; **AND** b. Used in combination with Juxtapid (lomitapide); **AND** 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; **AND** 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	Homozygous Familial Hypercholesteorlemia: #2 cartridges per 28-days Primary hypercholesterolemia, heterozygous familial hypercholesterolemia, & secondary prophylaxis in adults with established CVD: #1 cartridge per 28-days
Alirocumab (**PRALUENT**®) 75mg	#2 pens per 28-days
Alirocumab (**PRALUENT**®) 150mg	#2 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
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. Client is adherent to a statin with documentation supporting intolerance to at least two other statins c. Treatment with statin therapy is contraindicated or not tolerated. i. Statin intolerance is defined below
Lowest Starting Daily Doses (Statins)	rosuvastatin (Crestor®) 5mg atorvastatin 10mg simvastatin 10mg lovastatin 20mg pravastatin 40mg fluvastatin 40mg pitavastatin (Livalo®) 2mg
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, or in consultation with, a specialist, and may be considered eligible for PCSK-9 Inhibitors on a case-by-case basis.
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

10/01/2021	Updated highest-tolerated statin dose in definitions section to allow statin regimens that do not meet high-intensity statin therapy. Removed specialists as a requirement.
09/21/2021	Updated clinical criteria to include Praluent for HoFH. "Medical Necessity" language, and "dosage and quantity limits" section. Updated LDL requirements for secondary prophylaxis.
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

Washington State Health Care Authority

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

Please provide the information below, please print your answer, attach supporting documentation, sign, date, and return to our office as soon as possible to expedite this request. **Without this information, we may deny the request in seven (7) working days.**

Apple Health Preferred Drug list: *https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx*

Date of request:	Reference #:	MAS:	
Patient	Date of birth	ProviderOne ID	
Pharmacy name	Pharmacy NPI	Telephone number	Fax number
Prescriber	Prescriber NPI	Telephone number	Fax number
Medication and strength	Directions for use	Qty/Days supply	

1. Indicate patient's diagnosis:
   - ☐ Primary Hypercholesterolemia
   - ☐ Heterozygous Familial Hypercholesterolemia (HeFH)
   - ☐ Secondary Prophylaxis in Adults with Established Cardiovascular Disease (CVD)
     Does the patient have a history of any of the following clinical atherosclerotic cardiovascular diseases (ASCVD)? (Check all that apply)
     - ☐ Acute coronary syndrome (ACS)
     - ☐ Angina
     - ☐ Coronary revascularization procedures
     - ☐ Myocardial infarction (MI)
     - ☐ Transient ischemic attack (TIA)
     - ☐ Peripheral arterial disease (PAD)
   - ☐ Homozygous Familial Hypercholesterolemia (HoFH)
   - ☐ Other. Specify:

2. What was the baseline LDL prior to any treatment? _____ mg/dL

3. What is the current LDL? _____ mg/dL

4. What is the patient specific LDL goal? _____ mg/dL

5. Please indicate which applies to your patient and answer the corresponding questions:

   ☐ Patient completed at least 6 consecutive weeks of the highest tolerated statin regimen with ezetimibe
   What is the current statin regimen (name and strength): _____
   What was the patients LDL after at least 6 weeks? _____ mg/dL
   Did patient achieve at least a 50% LDL reduction from baseline? ☐ Yes ☐ No
   What other statin regimens (name and strength) were attempted? _____

   ☐ Patient is statin intolerant
   What statin regimens (name and strength) were attempted? _____
   What were the reasons leading to discontinuation? _____

6. Will patient be continuing on the statin listed on question #5 while on a PCSK9 Inhibitor? ☐ Yes ☐ No

7. Will this be used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor? ☐ Yes ☐ No

8. Indicate all PCSK9 inhibitors patient has tried and failed with reason for discontinuation:

9. Is this prescribed by a provider specializing in lipid management (e.g. cardiologist, endocrinologist or lipid specialist)? ☐ Yes ☐ No

   If no, has there been a consultation with a provider specializing in lipid management (e.g. cardiologist, endocrinologist or lipid specialist)? ☐ Yes ☐ No
   If yes, please provide consultation note

For diagnosis of homozygous familial hypercholesterolemia (HoFH):

10. Please indicate which of the following applies to your patient and answer the corresponding questions:

    ☐ The patient has a history of untreated LDL ≥500mg/dL for adults, untreated LDL ≥400mg/dL for children, or treated LDL ≥300mg/dL for adults and children.
    - ☐ A xanthoma before 10 years of age
    - ☐ Evidence of heterozygous familial hypercholesterolemia in both parents

    ☐ Genetic typing confirming presence of familial hypercholesterolemia genes
    ☐ Other. Specify: _____

11. Will this be used in combination with Juxtapid (lomitapide)? ☐ Yes ☐ No

For diagnosis primary Hypercholesterolemia / heterozygous familial hypercholesterolemia (HeFH):

12. Indicate what diagnostic tool (e.g., US MedPod, Simon Broome, etc.) or genetic typing was used to confirm diagnosis:

13. For adults: Does patient have any of the following (check all that apply):
    ☐ Coronary heart disease
    ☐ Diabetes

For re-authorization requests only: Chart notes and labs documenting clinical benefit in continuing a PCSK9 Inhibitor is required for re-authorization.

14. Will the patient continue to receive the maximum tolerated dose of statin, unless contraindicated or intolerant to statin therapy? ☐ Yes ☐ No
15. What is the current LDL? _____
16. What is the patient-specific LDL goal? _____
17. Has patient had at least a 30% reduction in LDL or an achievement of a patient specific goal since initiation of a PCSK9 Inhibitor? ☐ Yes ☐ No

CHART NOTES ARE REQUIRED WITH THIS REQUEST

Prescriber signature	Prescriber specialty	Date