

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

Medical policy no. 39.35.00-2

Effective Date: TBD

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.

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 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-C concentrations, and somewhat lower risk of cardiovascular disease.

Medical necessity

Drug	Medical Necessity
<p>Preferred Evolocumab (REPATHA®) – Multisource generic products</p> <p>Non-Preferred Evolocumab (REPATHA®) – Single source products</p> <p>See Apple Health Preferred Drug List publication for specific NDCs.</p>	<p>Evolocumab may be considered medically necessary when:</p> <ul style="list-style-type: none"> • 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)
<p>Non-Preferred Alirocumab (PRALUENT®)</p>	<p>Alirocumab may be considered medically necessary when:</p> <ul style="list-style-type: none"> • 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

<p>Primary Hypercholesterolemia/ Heterozygous Familial Hypercholesterolemia (HeFH)</p>	<ol style="list-style-type: none"> 1. Diagnosis of Primary Hypercholesterolemia OR Heterozygous Familial Hypercholesterolemia defined by ONE of the following: <ol style="list-style-type: none"> a. Clinical diagnosis using diagnostic tools such as US MedPed, Simon Broome Register Group, or Dutch Lipid Panel b. Age ≥ 20 and LDL ≥ 190mg/dL on maximally tolerated statin therapy prior to adding a PCSK9 Inhibitor c. Age < 20 and LDL ≥ 160mg/dL on maximally tolerated statin therapy prior to adding a PCSK9 Inhibitor d. Genetic typing confirming presence of familial hypercholesterolemia genes 2. Concomitant therapy with the highest-tolerated statin regimen and ezetimibe for at least 6 consecutive weeks AND ONE of the following: <ol style="list-style-type: none"> a. LDL has not achieved at least 50% reduction from baseline; OR b. Inability to achieve LDL cholesterol level < 100mg/dL c. Highest-tolerated dose is defined as ONE of the following: <ol style="list-style-type: none"> i. FDA labeled maximum dose for high-intensity statin therapy (e.g. atorvastatin 40 to 80mg and rosuvastatin 20 to 40mg) ii. Treatment with maximally tolerated statin therapy has been ineffective, contraindicated, or not tolerated. <ol style="list-style-type: none"> 1. 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. 2. Statin intolerance is defined as the inability to tolerate at least two different statin medications at the lowest FDA-approved starting dose when other potential causes of muscle symptoms have been maximally managed or ruled out 3. Greater than or equal to (\geq) 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. NONE of the following: <ol style="list-style-type: none"> a. Used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor 6. For non-preferred products, trial and failure of greater than or equal to (\geq) 1 preferred products <p>Approve for 6 months</p>
	<p>Criteria (Reauthorization)</p> <ol style="list-style-type: none"> 1. Continues to receive the maximum tolerated dose of statin unless contraindicated or intolerant to statin therapy

	<p>2. Documentation of continued clinical benefit, (e.g. at least a 30% reduction in LDL from initiation of PCSK9 Inhibitor or achievement of patient-specific goal)</p> <p>Approve for 12 months</p>
<p>Secondary Prophylaxis in Adults with Established Cardiovascular Disease (CVD)</p>	<ol style="list-style-type: none"> 1. History of clinical atherosclerotic cardiovascular diseases (ASCVD), including at least ONE of the following: <ol style="list-style-type: none"> a. myocardial infarction (MI) b. acute coronary syndrome (ACS) c. angina d. transient ischemic attack (TIA) e. coronary revascularization procedures f. peripheral arterial disease 2. Concomitant therapy with the highest-tolerated statin regimen and ezetimibe for at least 6 consecutive weeks AND ONE of the following: <ol style="list-style-type: none"> a. LDL has not achieved at least 50% reduction from baseline; OR b. Inability to achieve LDL cholesterol level <100mg/dL c. Highest-tolerated dose is defined as ONE of the following: <ol style="list-style-type: none"> i. FDA labeled maximum dose for high-intensity statin therapy (e.g. atorvastatin 40 to 80mg and rosuvastatin 20 to 40mg) ii. Treatment with maximally tolerated statin therapy has been ineffective, contraindicated, or not tolerated. <ol style="list-style-type: none"> 1. 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. 2. Statin intolerance is defined as the inability to tolerate at least two different statin medications at the lowest FDA-approved starting dose when other potential causes of muscle symptoms have been maximally managed or ruled out 3. Greater than or equal to (\geq) 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. NONE of the following: <ol style="list-style-type: none"> a. Used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor 6. For non-preferred products, trial and failure of greater than or equal to (\geq) 1 preferred products <p>Approve for 6 months</p>

	<p>Criteria (Reauthorization)</p>
<p>Homozygous Familial Hypercholesterolemia (HoFH)</p>	<ol style="list-style-type: none"> 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 PCSK9 Inhibitor or achievement of patient-specific goal) <p>Approve for 12 months</p> <hr/> <ol style="list-style-type: none"> 1. Clinical diagnosis of Homozygous Familial Hypercholesterolemia defined by ONE of the following: <ol style="list-style-type: none"> a. history of untreated LDL \geq500mg/dL with ONE of the following: <ol style="list-style-type: none"> 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 regimen and ezetimibe for at least 6 consecutive weeks AND ONE of the following: <ol style="list-style-type: none"> a. LDL has not achieved at least 50% reduction from baseline; OR b. Inability to achieve LDL cholesterol level $<$100mg/dL c. Highest-tolerated dose is defined as ONE of the following: <ol style="list-style-type: none"> i. FDA labeled maximum dose for high-intensity statin therapy (e.g. atorvastatin 40 to 80mg and rosuvastatin 20 to 40mg) ii. Treatment with maximally tolerated statin therapy has been ineffective, contraindicated, or not tolerated. <ol style="list-style-type: none"> 1. 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. 2. Statin intolerance is defined as the inability to tolerate at least two different statin medications at the lowest FDA-approved starting dose when other potential causes of muscle symptoms have been maximally managed or ruled out 3. Greater than or equal to (\geq) 13 years of age 4. Prescribed by or in consultation with a cardiologist, endocrinologist or lipid specialist 5. NONE of the following: <ol style="list-style-type: none"> a. Used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor b. Used in combination with Juxtapid (Iomitapide) <p>Approve for 6 months</p>

	Criteria (Reauthorization)
	<ol style="list-style-type: none"> 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 PCSK9 Inhibitor or achievement of patient-specific goal) <p>Approve for 12 months</p>

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 (Crestor®) 20mg or 40mg atorvastatin 80mg atorvastatin 40mg if down-titrating from atorvastatin 80mg due to intolerance symptoms
Lowest Starting Daily Doses (Statins)	rosuvastatin (Crestor®) 5mg atorvastatin 10mg simvastatin 10mg lovastatin 20mg pravastatin 40mg fluvastatin 40mg pitavastatin (Livalo®) 2mg
Statin Intolerance	<p>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 below] and a different statin may be at any dose.</p> <p>If patient is on combination therapy, such as a fibrate or niacin, tapering of fibrate or niacin while maintaining statin therapy is required to establish statin intolerance.</p>

	<p>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 PCSK9 Inhibitors on a case-by-case basis.</p> <p>Patients who have failed to meet criterion 2 in medical policy may be managed on non-daily statin therapy if able to demonstrate that they are on maximally-tolerated therapy and can maintain dose while on PCSK9 Inhibitor.</p>
Pre-Specified Intolerance Symptoms	<p>Myopathy or myalgia (muscle pain, ache, or weakness without CK elevation)</p> <p>Myositis (muscle symptoms with increased CK levels)</p>
Diagnosis of ASCVD	<p>Acute coronary syndrome, or a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin</p>

References

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History

Date	Action and Summary of Changes
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 PCSK9 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

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.**

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:
 - Heterozygous Familial Hypercholesterolemia (HeFH)
 - Secondary Prophylaxis in Adults with Established Cardiovascular Disease (CVD)
 - Homozygous Familial Hypercholesterolemia (HoFH)
 - Other. Specify: _____

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

3. What is the current LDL? _____

4. What is the patient specific LDL goal? _____

5. Please indicate which applies to your patient and answer the corresponding questions:
 - Patient completed at least 6 weeks of:
 - A high-intensity statin The highest tolerated statin
 - What is the current statin regimen (name and strength): _____
 - What was the patients LDL after at least 8 weeks? _____
 - Did patient achieve at least a 50% 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 PCSK9 Inhibitor? Yes No

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

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

- 9. What is the current LDL? _____
- 10. What is the patient-specific LDL goal? _____
- 11. 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
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