Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
02-01-2024	05-01-2017

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Praluent® (alirocumab) Injection	To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease As an adjunct to diet alone or in combination with other low density lipoprotein cholesterol (LDL-C)- lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C As an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C		1
Repatha® (evolocumab) Injection	In adults with established cardiovascular disease to reduce the risk of myocardial infarction, stroke, and coronary revascularization As an adjunct to diet, alone or in combination with other LDL-C-lowering therapies in adults with primary hyperlipidemia, including HeFH, to reduce LDL-C As an adjunct to other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH, to reduce LDL-C As an adjunct to diet and other LDL-C-lowering therapies in adults and pediatric patients aged 10 years and older with HoFH, to reduce LDL-C		2

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Heterozygous familial hypercholesterolemia (HeFH)	Criteria have been developed to aid in diagnosing HeFH. These include the Simon Broome Register criteria and Dutch Lipid clinic Network criteria. (5) Definitive diagnosis of HeFH according to Simon Broome diagnostic criteria requires the patient has one of the following:(3,5) • Total cholesterol greater than 6.7 mmol/L or low-density lipoprotein cholesterol (LDL-C) greater than 4.0 mmol/L in a child aged younger than 16 years, or greater than 7.5 mmol/L or LDL-C greater than 4.9 mmol/L in an adult (levels either pre-treatment or highest on treatment) **plus** tendon xanthomas in the

patient, or in first-degree relative (parent, sibling or child), or in second-degree relative (e.g., grandparent, uncle or aunt) **OR**

- DNA-based evidence of an LDL receptor mutation, familial defective Apo B-100, or a PCSK9 mutation

Possible diagnosis of HeFH according to Simon Broome diagnostic criteria requires the patient has:(3)

- Total cholesterol greater than 6.7 mmol/L or low-density lipoprotein cholesterol (LDL-C) greater than 4.0 mmol/L in a child aged younger than 16 years, or greater than 7.5 mmol/L or LDL-C greater than 4.9 mmol/L in an adult (levels either pre-treatment or highest on treatment)
  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 **OR**
- 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

The Dutch Lipid Clinic Network criteria assign points based on cholesterol levels, family history of hyperlipidemia or cardiovascular disease, clinical presentation, and/or presence of identified genetic mutation affecting plasma LDL-C. (5-7) A definitive diagnosis of HeFH can be made in patients with greater than 8 points. A probable diagnosis can be made in patients with 6-8 points.

Dutch Lipid Clinic Network criteria for diagnosis of heterozygous familial hypercholesterolemia(8)

Group 1: Family history
• First-degree relative with known premature (less than 55 years, men; less than 60 years, women) coronary heart disease (CHD) • First-degree relative with known LDL cholesterol greater than 95th percentile by age and gender for country • First-degree relative with tendon xanthoma and/or corneal arcus • Children less than 18 years with LDL cholesterol greater than 95th percentile by age and gender for country
Group 2: Clinical history
• Subject has premature (less than 55 years, men; less than 60 years, women) CHD • Subject has premature (less than 55 years, men; less than 60 years, women) cerebral or peripheral vascular disease
Group 3: Physical examination
• Tendon xanthoma • Corneal arcus in a person less than 45 years
Group 4: Biochemical results (LDL-C)
• greater than 8.5 mmol/L (greater than 325 mg/dL) • 6.5–8.4 mmol/L (251–325 mg/dL) • 5.0–6.4 mmol/L (191–250 mg/dL) • 4.0–4.9 mmol/L (155–190 mg/dL)
Group 5: Molecular genetic testing (DNA analysis)

	• Causative mutation shown in the LDLR, APOB, or PCSK9 genes 8 **Use and Interpretation** Assign only one score, the highest applicable, per group then add the points from each grou achieve the total score Definitive FH diagnosis: greater than 8 points Probable FH diagnosis: 6 to 8 points Possible FH diagnosis: 3 to 5 points Unlikely FH diagnosis: 0 to 2 points
Homozygous familial hypercholesterolemia (HoFH)	Guidelines advise that diagnosis of HoFH can be made based on genetic or clinical criteria. Genetic confirmation of the HoFH includes confirmation of two mutant alleles at the LDL-R, APOB, PCSK9, or LDLRAP1 genes.(4,6) While genetic testing may provide a definitive diagnosis of HoFH, it is recognized that in some patients, genetic confirmation remains elusive, despite exhaustive investigation; indeed, the existence of additional FH genes cannot be excluded. Historically, HoFH has been most commonly diagnosed based on either an untreated LDL-C plasma concentration greater than 13 mmol/L (greater than 500 mg/dL), or a treated LDL-C concentration of greater than or equal to 8 mmol/L (greater than or equal to 300 mg/dL), accompanied by the presence of cutaneous or tendon xanthomas before the age of 10 years, or the presence of untreated elevated LDL-C levels consistent with HeFH in both parents.(4,6) According the American Heart Association (AHA), initial treatment for FH should include high intensity statin.(9) If the LDL-C is not at goal after 3 months of therapy with the high intensity statin and the patient has been adherent, AHA recommends the addition ezetimibe. For patients who do not respond to this two drug regimen within 3 months, AHA recommends addition of a PCKS9, a bile acid sequestrant, or niacin. Patients with HoFH who require additional therapy despite treatment with the three drug regimen, AHA recommends addition of Juxtapid and LDL apheresis.(9)
Atherosclerotic Cardiovascular Disease (ASCVD) – Secondary Prevention	The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline lists the following as clinical ASCVD: • Acute coronary syndrome (ACS) • Myocardial infarction (MI) • Stable or unstable angina or coronary or other arterial revascularization • Stroke • Transient ischemic attack (TIA) or peripheral artery disease (PAD) including aortic aneurysm

Management	The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol states the following regarding PCSK9 therapy(9)
	
	• Severe hypercholesterolemia (LDL-C greater than or equal to 190 mg/dL [greater than or equal to 4.9 mmol/L])
	  ○ In patients 30-75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL (greater than or equal to 2.6 mmol/L) 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 (greater than or equal to 5.7 mmol/L) or higher while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered

The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol states the following regarding PCSK9 therapy:(9)

- Secondary atherosclerotic cardiovascular disease (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 (greater than or equal to 1.8 mmol/L) or higher or a non-HDL-C level of 100 mg/dL (greater than or equal to 2.6 mmol/L) or higher, it is reasonable to add PCSK9 inhibitor following a clinical-patient discussion about the net benefit, safety, and cost

The AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline categorizes the following statin intensities:(9)

	High Intensity	**Moderate Intensity**	**Low Intensity**
LDL-C Lowering	greater than or equal to 50%	30%-49%	less than 30%
Statins	Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg (a) Pravastatin 40-80 mg Lovastatin 40-80 mg Fluvastatin XL 80 mg Fluvastatin 40 mg twice daily Pitavastatin 1-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

a - Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA because of the risk of myopathy, including rhabdomyolysis

The National Lipid Association (NLA) 2019 consensus statement identifies the following patients, who are already on maximally tolerated statin therapy, as most likely to benefit from PCSK9 therapy.(10)

- Extreme high-risk (greater than or equal to 40% 10-year ASCVD risk on maximally tolerated statin therapy) with LDL-C greater than or equal to 70 mg/dL and either of the following:
    - Extensive or active burden of ASCVD (i.e., polyvascular ASCVD, which affects all 3 vascular beds—coronary, cerebrovascular, and peripheral arterial; clinical peripheral arterial disease in addition to coronary and/or cerebrovascular disease; a clinical ASCVD event with multivessel coronary artery disease defined as greater than or equal to 40% stenosis in greater than or equal to 2 large vessels; or recurrent myocardial infarction within 2 years of the initial event) in the presence of adverse or poorly controlled cardiometabolic risk factors
    - Extremely high-risk elevations in cardiometabolic factors with less-extensive ASCVD (i.e., HeFH, diabetes, LDL-C greater than or equal to 100 mg/dL, less than high–intensity statin therapy, chronic kidney disease, poorly controlled hypertension, high-sensitivity C-reactive protein greater than 3 mg/L, or metabolic syndrome, usually occurring with other extremely high–risk or very-high-risk characteristics), usually with other adverse or poorly controlled cardiometabolic risk factors present. Patients with ASCVD and HeFH or severe hyperlipidemia (SH) LDL-C greater than or equal to 220 mg/dL are an additional group of extremely high–risk patients, with greater than or equal to 45% 10- year ASCVD risk despite statin therapy. Statin-treated HeFH patients with coronary artery calcium (CAC) score greater than 100 Agatston units also have about a 45% 10-year ASCVD risk despite statin therapy
- Very high-risk (30-39% 10-year ASCVD risk on maximally tolerated statin therapy) with LDL-C greater than or equal to 100 mg/dL and the following:
    - Less-extensive clinical ASCVD (i.e., no polyvascular ASCVD, no clinical peripheral arterial disease, a prior ASCVD event greater than or equal to 2 years prior, and no coronary artery bypass grafting)
    - Adverse or poorly controlled cardiometabolic risk factor(s) including age greater than or equal to 65 years, current smoking, chronic kidney disease, lipoprotein(a) greater than or equal to 37 nmol/L, high-sensitivity C-reactive protein 1–3 mg/L, metabolic syndrome with a history of myocardial infarction, ischemic stroke, or symptomatic peripheral arterial disease, usually in the presence of other adverse or poorly controlled cardiometabolic risk factors
- High-risk (20-29% 10-year ASCVD risk on maximally tolerated statin therapy) with LDL-C greater than or equal to 130 mg/dL and either of the following:
    - High-risk patients with ASCVD who have the following:
        - Less-extensive ASCVD
        - Well-controlled cardiometabolic risk factors (i.e., no diabetes, nonsmoker, on high-intensity statin with LDL-C less than 100 mg/dL, blood pressure less than 140/90 mm Hg, and C-reactive protein less than 1 mg/dL)
    - Primary prevention patients with HeFH or SH LDL-C greater than or equal to 220 mg/dL and have the following:
        - No clinical ASCVD or CAC less than 100 Agatston units
        - Poorly controlled cardiometabolic risk factor

	CAC Agatston score in non-contrast CT can be used for patient risk classification for coronary heart disease:(11,12) • 0 CAC = no CAC, very low risk, • 1-99 CAC = mild CAC, mildly increased risk • 100 - 299 CAC = moderate CAC, moderately increased risk • greater than or equal to 300 CAC = moderate to severely increased risk In their 2022 Expert Consensus Decision, the American College of Cardiology stated that in view of the favorable net clinical benefit of the addition of nonstatin therapies is patients with clinical ASCVD at very high risk on high-intensity statin therapy and lifestyle management and the very low levels of LDL-C achieved in RCTs (randomized clinical trials) of nonstatin therapies, a lower LDL-C threshold of LDL-C less than or equal to 55 mg/dL is recommended. Patients in this group have a history of multiple major ASCVD events (e.g., recent [within the past 12 months] acute coronary syndrome, history of MI other than the recent ACS event listed previously, history of ischemic stroke, and symptomatic peripheral artery disease) or 1 major ASCVD event and multiple high-risk conditions (e.g., age greater than or equal to 65 years, HeFH, history of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event, diabetes, hypertension, chronic kidney disease, current smoking, persistently elevated LDL-C despite maximally tolerated statin therapy and ezetimibe, and history of congestive heart failure. (13)

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13	2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk. Journal of the American College of Cardiology, 80 (14) 2022, 1366-1418. https://www.sciencedirect.com/science/article/pii/S0735109722055942?ref=pdf_download&fr=RR-2&rr=7edef3f3691926bb

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Praluent	alirocumab subcutaneous solution auto-injector	150 MG/ML ; 75 MG/ML	M ; N ; O ; Y	N		
Repatha sureclick	evolocumab subcutaneous soln auto-injector	140 MG/ML	M ; N ; O ; Y	N		
Repatha pushtronex system	evolocumab subcutaneous soln cartridge/infusor	420 MG/3.5ML	M ; N ; O ; Y	N		
Repatha	evolocumab subcutaneous soln prefilled syringe	140 MG/ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Repatha	evolocumab subcutaneous soln prefilled syringe	140 MG/ML	2	Syringes	28	DAYS			
Repatha pushtronex system	evolocumab subcutaneous soln cartridge/infusor	420 MG/3.5 ML	2	Cartridges	28	DAYS			
Repatha sureclick	evolocumab subcutaneous soln auto-injector	140 MG/ML	2	Pens	28	DAYS			
Praluent	alirocumab subcutaneous solution auto-injector	150 MG/ML ; 75 MG/ML	2	Syringes	28	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Praluent	alirocumab subcutaneous solution auto-injector	150 MG/ML ; 75 MG/ML	Medicaid
Repatha	evolocumab subcutaneous soln prefilled syringe	140 MG/ML	Medicaid
Repatha pushtronex system	evolocumab subcutaneous soln cartridge/infusor	420 MG/3.5ML	Medicaid
Repatha sureclick	evolocumab subcutaneous soln auto-injector	140 MG/ML	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Repatha	evolocumab subcutaneous soln prefilled syringe	140 MG/ML	Medicaid
Repatha pushtronex system	evolocumab subcutaneous soln cartridge/infusor	420 MG/3.5ML	Medicaid
Repatha sureclick	evolocumab subcutaneous soln auto-injector	140 MG/ML	Medicaid
Praluent	alirocumab subcutaneous solution auto-injector	150 MG/ML ; 75 MG/ML	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. BOTH of the following: 1. ONE of the following: A. The patient has a diagnosis of heterozygous familial hypercholesterolemia (HeFH) AND ONE of the following: 1. Genetic confirmation of one mutant allele at the *LDLR, Apo-B, PCSK9*, or *1/LDLRAP1* gene **OR** 2. History of LDL-C greater than 190 mg/dL (greater than 4.9 mmol/L) (pretreatment) **OR** 3. The patient has clinical manifestations of HeFH (e.g., cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthoma, or xanthelasma) **OR** 4. The patient has "definite" or "possible" familial hypercholesterolemia as defined by the Simon Broome criteria **OR** 5. The Patient has a Dutch Lipid Clinic Network Criteria score of greater than 5 **OR** 6. The patient has a treated low-density lipoprotein cholesterol (LDL-C) level greater than or equal to 100 mg/dL after treatment with antihyperlipidemic agents but prior to PCSK9 inhibitor therapy **OR** B. The patient has a diagnosis of homozygous familial hypercholesterolemia (HoFH) AND ONE of the following: 1. Genetic confirmation of TWO mutant alleles at the *LDLR, Apo-B, PCSK9*, or *LDLRAP1* gene **OR** 2. History of untreated LDL-C greater than 500 mg/dL (greater than 13 mmol/L) or treated LDL-C greater than or equal to 300 mg/dL (greater than or equal to 7.76 mmol/L) **OR** 3. The patient has clinical manifestations of HoFH (e.g., cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas, or xanthelasma) **OR** C. The patient has a diagnosis of clinical atherosclerotic cardiovascular disease (ASCVD) AND has ONE of the following: 1. Acute coronary syndrome 2. History of myocardial infarction 3. Stable or unstable angina 4. Coronary or other arterial revascularization 5. History of stroke 6. History of transient ischemic attack 7. Peripheral arterial disease, including aortic aneurysm, presumed to be of atherosclerotic origin **OR**

Module	Clinical Criteria for Approval
	D. The patient has a diagnosis of primary hyperlipidemia AND ONE of the following: 1. The patient has a coronary artery calcium or calcification (CAC) score greater than or equal to 300 Agatston units **OR** 2. The patient has an LDL-C level greater than or equal to 220 mg/dL (greater than or equal to 5.7 mmol/L) while receiving maximally tolerated statin and ezetimibe therapy **OR** E. The patient has greater than or equal to 20% 10-year ASCVD risk AND ONE of the following: 1. The patient has greater than or equal to 40% 10-year ASCVD risk AND BOTH of the following: A. LDL-C greater than or equal to 70 mg/dL while on maximally tolerated statin therapy **AND** B. ONE of the following: 1. The patient has extensive or active burden of ASCVD (i.e., polyvascular ASCVD, which affects all 3 vascular beds—coronary, cerebrovascular, and peripheral arterial; clinical peripheral arterial disease in addition to coronary and/or cerebrovascular disease; a clinical ASCVD event with multivessel coronary artery disease defined as greater than or equal to 40% stenosis in greater than or equal to 2 large vessels; or recurrent myocardial infarction within 2 years of the initial event) in the presence of adverse or poorly controlled cardiometabolic risk factors **OR** 2. Extremely high-risk elevations in cardiometabolic factors with less-extensive ASCVD (i.e., diabetes, LDL-C greater than or equal to 100 mg/dL, less than high–intensity statin therapy, chronic kidney disease, poorly controlled hypertension, high-sensitivity C-reactive protein greater than 3 mg/L, or metabolic syndrome, usually occurring with other extremely high–risk or very-high-risk characteristics), usually with other adverse or poorly controlled cardiometabolic risk factors present. **OR** 3. Patients with ASCVD and LDL-C greater than or equal to 220 mg/dL with greater than or equal to 45% 10- year ASCVD risk despite statin therapy **OR** 2. The patient has 30-39% 10-year ASCVD risk AND ALL of the following: A. LDL-C greater than or equal to 100 mg/dL while on maximally tolerated statin therapy **AND** B. Less-extensive clinical ASCVD (i.e., no polyvascular ASCVD, no clinical peripheral arterial disease, a prior ASCVD event greater than or equal to 2 years prior, and no coronary artery bypass grafting) **AND** C. Adverse or poorly controlled cardiometabolic risk factor(s) including age 65 years or older, current smoking, chronic kidney disease, lipoprotein(a) greater than or equal to 37 nmol/L, high-

Module	Clinical Criteria for Approval
	sensitivity C-reactive protein 1–3 mg/L, metabolic syndrome with a history of myocardial infarction, ischemic stroke, or symptomatic peripheral arterial disease, usually in the presence of other adverse or poorly controlled cardiometabolic risk factors **OR** 3. The patient has 20-29% 10-year ASCVD risk AND BOTH of the following: A. LDL-C greater than or equal to 130 mg/dL while on maximally tolerated statins **AND** B. ONE of the following: 1. The patient has less extensive ASCVD and well-controlled cardiometabolic risk factors (i.e., no diabetes, nonsmoker, on high-intensity statin with LDL-C less than 100 mg/dL, blood pressure less than 140/90 mm Hg, and C-reactive protein less than 1 mg/dL) **OR** 2. The use is for primary prevention with LDL-C greater than or equal to 220 mg/dL AND BOTH of the following: A. No clinical ASCVD or CAC less than 100 Agatston units **AND** B. Poorly controlled cardiometabolic risk factor **AND** 2. ONE of the following: A. The patient has been adherent to high-intensity statin therapy (i.e., rosuvastatin greater than or equal to 20 mg daily, atorvastatin greater than or equal to 40 mg daily) for greater than or equal to 8 continuous weeks AND ONE of the following: 1. The patient's LDL-C level after this treatment regimen remains greater than or equal to 70 mg/dL **OR** 2. The patient has not achieved a 50% reduction in LDL-C from baseline after this treatment regimen **OR** 3. If the patient has ASCVD, and ONE of the following: 1. The patient's non HDL-C level after this treatment regimen remains greater than or equal to 100 mg/dL **OR** 2. The patient is at very high risk and the patient's LDL-C level after this treatment regimen remains great than or equal to 55 mg/dL **OR** B. The patient has been determined to be statin intolerant by meeting ONE of the following criteria: 1. The patient experienced statin-related rhabdomyolysis **OR** 2. The patient experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) and BOTH of the following: A. The skeletal-related muscle symptoms (e.g., myopathy or myalgia) occurred while receiving separate trials of both atorvastatin AND rosuvastatin (as single-entity or as combination products) **AND** B. When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms (e.g., myopathy, myalgia) resolved upon discontinuation of each respective statin therapy (atorvastatin AND rosuvastatin) **OR** 3. The patient experienced elevations in hepatic transaminase while receiving separate trials of both

Module	Clinical Criteria for Approval
	atorvastatin and rosuvastatin (as single-entity or as combination products) **OR** C. The patient has a hypersensitivity to atorvastatin AND rosuvastatin **OR** D. The patient has an FDA labeled contraindication to atorvastatin AND rosuvastatin **OR** E. The patient's medication history includes use of high intensity atorvastatin or rosuvastatin therapy, or a drug in the same pharmacological class with the same mechanism of action, AND ONE of the following: 1. High intensity atorvastatin or rosuvastatin or a drug in the same pharmacological class with the same mechanism of action was discontinued due to lack of effectiveness or an adverse event **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over high-intensity rosuvastatin or atorvastatin therapy **OR** F. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** G. The prescriber has provided documentation that atorvastatin AND rosuvastatin cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** B. The patient has another FDA approved indication for the requested agent and route of administration **OR** C. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The agent was prescribed by, or in consultation with, a cardiologist, an endocrinologist, and/or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders **AND** 4. The patient will NOT be using the requested agent in combination with another PCSK9 agent for the requested indication **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation**

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. The patient has been previously approved for therapy for PCSK9 inhibitors through the plan's prior authorization process **AND** 2. ONE of the following: A. The request is for a preferred agent **OR** B. The patient's medication history includes a preferred agent AND ONE of the following: 1. The patient has had an inadequate response a preferred agent **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over ALL preferred agents **OR** C. The patient has an intolerance or hypersensitivity to the preferred agent **OR** D. The patient has an FDA labeled contraindication to ALL preferred agents **OR** E. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** F. The prescriber has provided documentation that ALL preferred agents cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 3. The patient has shown clinical benefit with a PCSK9 inhibitor **AND** 4. The patient is currently adherent to therapy with a PCSK9 inhibitor **AND** 5. If the patient has cardiovascular disease OR hyperlipidemia, then ONE of the following: A. The patient is currently adherent to high-intensity statin therapy (i.e., rosuvastatin greater than or equal to 20 mg daily, atorvastatin greater than or equal to 40 mg daily) **OR** B. The patient has been determined to be statin intolerant by meeting ONE of the following criteria: 1. The patient experienced statin-related rhabdomyolysis **OR** 2. The patient experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) and BOTH of the following: A. The skeletal-related muscle symptoms (e.g., myopathy or myalgia) occurred while receiving separate trials of both atorvastatin AND rosuvastatin (as single-entity or as combination products) **AND** B. When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms (e.g., myopathy, myalgia) resolved upon discontinuation of each respective statin therapy (atorvastatin AND rosuvastatin) **OR** 3. The patient experienced elevations in hepatic transaminase while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) **OR** C. The patient has a hypersensitivity to atorvastatin AND rosuvastatin **OR** D. The patient has an FDA labeled contraindication to atorvastatin AND rosuvastatin **OR** E. The patient's medication history includes use of high-intensity rosuvastatin or atorvastatin therapy or a drug in the same pharmacological class with the same mechanism of action AND ONE of the following: 1. High-intensity rosuvastatin or atorvastatin, or a drug in the same pharmacological class with the same mechanism of action, was discontinued due to lack of effectiveness or an adverse event **OR**

Module	Clinical Criteria for Approval
	2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over high-intensity rosuvastatin or atorvastatin therapy **OR** F. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** G. The prescriber has provided documentation that atorvastatin and rosuvastatin cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 6. The agent was prescribed by, or in consultation with, a cardiologist, an endocrinologist, and/or a physician who focuses in the treatment of cardiovascular (CV) risk management and/or lipid disorders **AND** 7. The patient will NOT be using the requested agent in combination with another PCSK9 agent for the requested indication **AND** 8. The patient does NOT have any FDA labeled contraindications to the requested agent Length of approval: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of approval:** 12 months

