Original Effective Date: 06/01/2017
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Last P&T Approval/Version: 01/29/2025
Next Review Due By: 01/2026
Policy Number: C10800-A

PCSK9 Inhibitors (alirocumab, evolocumab)

PRODUCTS AFFECTED

Praluent (alirocumab), Repatha (evolocumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Hyperlipidemia Associated with Clinical Atherosclerotic Cardiovascular Disease, Homozygous familial hypercholesterolemia (HoFH), Primary hyperlipidemia, Heterozygous familial hypercholesterolemia (HeFH)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PRIMARY HYPERLIPIDEMIA:
1. Documented diagnosis of PRIMARY HYPERLIPIDEMIA (including heterozygous familial

hypercholesterolemia [HeFH)]
AND
2. Documentation that other secondary causes of dyslipidemia have been excluded or maximally treated (e.g., high triglycerides, hypothyroidism, etc.)
AND
3. Prescriber attests or clinical reviewer has found the requested medication will not be used concurrently with another proprotein convertase subtilisin/kexin type 9 inhibitor, Juxtapid or other PCSK9 Inhibitors (e.g., Leqvio [inclisiran])
AND
4. Documentation member is taking a maximally tolerated intensity/dose of statin OR has an FDA labeled contraindication to statins OR had serious side effects and is unable to tolerate an alternative dosing schedule (i.e., every other day dosing)
AND
5. Documentation member is taking ezetimibe 10mg daily OR has an FDA labeled contraindication or serious side effects
AND
6. Documentation of current (prior to PCSK9 therapy) LDL-C (within the last 3 months)
AND
7. Documentation in treatment plan member will be adherent to PCSK9 Inhibitor therapy AND continue adherence to maximally tolerated dose/intensity statin therapy (unless contraindicated as documented above) AND ezetimibe 10mg/day
Molina Reviewer Note: Verify member's medication fill history for compliance on statin therapy AND ezetimibe
AND
8. Documentation of trial, failure or contraindication to preferred formulary PCSK9 agent (Repatha)

B. HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA:
1. Documented diagnosis of homozygous familial hypercholesterolemia (HoFH)
AND
2. Prescriber attests or clinical reviewer has found the requested medication will not be used concurrently with another proprotein convertase subtilisin/kexin type 9 inhibitor or other PCSK9 Inhibitors (e.g., Leqvio [inclisiran])
AND
3. Documentation member is taking a maximally tolerated intensity/dose of statin OR has an FDA labeled contraindication to statins OR has serious side effects and is unable to tolerate an alternative dosing schedule (i.e., every other day dosing)
AND
4. Documentation member is taking ezetimibe 10mg daily OR has an FDA labeled contraindication or serious side effects
AND
5. Documentation of current (prior to PCSK9 therapy) LDL-C (within the last 3 months)
AND
6. Documentation in treatment plan member will be adherent to PCSK9 Inhibitor therapy AND continue adherence to maximally tolerated dose/intensity statin therapy (unless contraindicated as documented above) AND ezetimibe 10mg/day
Molina Reviewer Note: Verify member's medication fill history for compliance on statin therapy AND ezetimibe
AND
7. Documentation of trial, failure or contraindication to preferred formulary PCSK9 agent (Repatha)

C. HYPERLIPIDEMIA ASSOCIATED WITH CLINICAL ATHEROSCLEROTIC CARDIOVASCULAR DISEASE:
1. (a) Documentation of major atherosclerotic cardiovascular disease (ASCVD) defined as ONE of the following:
    (i) Recent acute coronary syndrome (ACS) (within the past 12 months)
    (ii) Myocardial infarction (MI)

(iii) Ischemic stroke
(iv) Symptomatic PAD

OR

(b) Documentation member has as least ONE of the following high risk factors for future ASCVD event:

(i) Age greater than 65 years
(ii) Current daily cigarette smoking
(iii) Heterozygous familial hypercholesterolemia
(iv) History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD events
(v) Diabetes
(vi) Hypertension
(vii) CKD (eGFR 15-59 mL/min/1.73m2)
(viii) Persistently elevated LDL-C (> 100 mg/dL) despite maximally tolerated statin therapy and ezetimibe
(ix) History of congestive heart failure

AND

2. Appropriate lifestyle modifications have been implemented, including adherence to a heart-healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight that will continue during treatment, supported by documentation of counseling in chart notes
AND
3. Documentation that other secondary causes of dyslipidemia have been excluded or maximally treated (e.g., high triglycerides, hypothyroidism, etc.)
AND
4. Documentation in treatment plan member will be adherent to PCSK9 Inhibitor therapy AND continue adherence to maximally tolerated dose/intensity statin therapy (unless contraindicated to statin therapy) AND ezetimibe 10mg/day
Molina Reviewer Note: Verify member's medication fill history for compliance on statin therapy AND ezetimibe
AND
5. Documentation of ONE of the following: baseline LDL-C between 70-189 mg/dL OR patient requires greater than 25 percent additional lowering of LDL-C OR patient has had a recent acute coronary syndrome (less than 3 months)
AND
6. Documentation of a therapeutic failure, serious side effects, or contraindication to high-intensity statin therapy shown by ONE of the following:

(i) Adherent* to maximally tolerated high-intensity statin therapy (daily dose of atorvastatin 40 to 80mg or rosuvastatin 20 to 40mg) and ezetimibe 10mg/day along with lifestyle modifications AND Inability to achieve and maintain an LDL cholesterol level at or below goal (< 100 mg/dL or < 70 mg/dL based on patient risk) by documentation of ONE of the following:

(a) LDL-C greater than goal (≥ 70 mg/dL for ASCVD or ≥100 mg/dL for HeFH) OR
(b) Has not achieved a 50% reduction in LDL-C from baseline without meeting treatment goal

*NOTE: Adherence to therapy is defined as at least 85% of the time as confirmed by claims history for at least 180 days OR attestation from the Prescriber.

OR

(ii) Member has ANY of the following contraindication(s) to statin therapy [ONE]: Hypersensitivity to statins or any component of the product, Active liver disease or CK levels (defined as >10 times the Upper Limit of Normal [ULN]), Unexplained persistent elevation of hepatic transaminases [greater than 3 times the upper limit of normal (ULN) occurring on 2 or more occasions], Women who are pregnant or may become pregnant or breastfeeding NOTE: Laboratory tests showing evidence of muscle inflammation, alterations of liver function tests from baseline and/or liver damage required.

OR

(iii) Documented therapeutic failure or intolerance to switching to a low- or moderate-intensity statin (e.g., simvastatin, pravastatin) OR alternative dosing schedule (i.e., every other day dosing)

AND

7. Prescriber attests or clinical reviewer has found the requested medication will not be used concurrently with another proprotein convertase subtilisin/kexin type 9 inhibitor, Juxtapid, or other PCSK9 inhibitor (e.g., Leqvio [inclisiran])
   AND
8. Documentation of trial, failure or contraindication to preferred formulary PCSK9 agent (Repatha)

CONTINUATION OF THERAPY:

A. FOR ALL INDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Documented positive response to therapy as indicated by decrease in LDL-C OR achievement of individual LDL-C patient goal
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
4. Documentation that the requested agent will continue to be used in combination with a maximally tolerated statin and ezetimibe or member has an FDA labeled contraindication or serious side effects to statins and ezetimibe

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

No requirements

AGE RESTRICTIONS:

Heterozygous familial hypercholesterolemia (HeFH): Praluent: 8 years of age and older; Repatha: 10 years of age and older
Homozygous familial hypercholesterolemia (HoFH): Praluent: 18 years of age and older; Repatha: 10 years of age and older
Atherosclerotic cardiovascular disease (ASCVD): 18 years of age and older
Primary hyperlipidemia: 18 years of age and older

QUANTITY:

Repatha 140mg/ml Prefilled Syringe: 3ml per month (3 syringes per 28 days)
Repatha SureClick 140mg/ml Autoinjector: 3ml per month (3 syringes per 28 days)
Repatha 420mg/3.5ml Pushtronex System: 3.5ml per month (1 syringe per 28 days)
Praluent 75 mg/mL (2 mL per 28 days)
Praluent 150 mg/mL (2 mL per 28 days)

PLACE OF ADMINISTRATION:

The recommendation is that subcutaneous injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

DRUG CLASS:
PCSK9 Inhibitors

FDA-APPROVED USES:
Repatha (evolocumab) is indicated:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, myocardial infarction, stroke, unstable angina requiring hospitalization, or coronary revascularization) 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 diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH, to reduce LDL-C
- as an adjunct to other LDL-C-lowering therapies in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C

Praluent (alirocumab) is indicated:

- To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease
- As 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.
- 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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:

Familial Hypercholesterolemia (FH) Diagnostic Categories		
ICD-10 Category	Clinical Criteria	Genetic Testing Performed
Heterozygous FH	LDL-C ≥160 mg/dL (4 mmol/L) for children and ≥190 mg/dL (5 mmol/L) for adults and with 1 first-degree relative similarly affected or with premature CAD or with positive genetic testing for an LDL-C–raising gene defect (LDL receptor, apoB, or PCSK9)	Presence of 1 abnormal LDL-C–raising gene defect (LDL receptor, apoB, or PCSK9) Diagnosed as heterozygous FH if LDL-C–raising defect positive and LDL-C <160 mg/dL (4 mmol/L) Occasionally, heterozygotes will have LDL-C >400 mg/dL (10 mmol/L); they should be treated similarly to homozygotes Presence of both abnormal LDL-C–raising gene defects (LDL receptor, apoB, or PCSK9) and LDL-C–lowering gene variant(s) with LDL-C <160 mg/dL (4 mmol/L)

Homozygous FH	LDL-C ≥400 mg/dL (10 mmol/L) and 1 or both parents having clinically diagnosed FH, positive genetic testing for an LDL-C–raising gene defect (LDL receptor, apoB, or PCSK9) or autosomal-recessive FH If LDL-C >560 mg/dL (14 mmol/L) or LDL-C >400 mg/dL (10 mmol/L) with aortic valve disease or xanthomata at <20 years of age, homozygous FH highly likely	Presence of 2 identical (true homozygous FH) or nonidentical (compound heterozygous FH) abnormal LDL–raising gene defects (LDL receptor, apoB, or PCSK9); includes the rare autosomal-recessive type Occasionally, homozygotes will have LDL-C <400 mg/dL (10 mmol/L)

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

High-intensity statin therapy: Atorvastatin (Lipitor) 40 - 80 mg a day, Rosuvastatin (Crestor) 20-40mg a day, Simvastatin (Zocor) 80 mg a day

Moderate-intensity statin therapy: Atorvastatin (Lipitor) 10 - 20mg a day, Rosuvastatin, (Crestor) 5 - 10mg a day, Simvastatin (Zocor) 20 - 40mg a day, Pravastatin (Pravachol) 40 - 80mg a day, Lovastatin (Mevacor) 40mg a day, Fluvastatin XL (Lescol XL) 80mg a day, Fluvastatin (Lescol)40mg twice a day, Pitavastatin (Livalo) 2 - 4mg a day

Low-intensity statin therapy: Simvastatin (Zocor) 10mg a day, Pravastatin (Pravachol)10 - 20mg a day, Lovastatin (Mevacor) 20mg a day, Fluvastatin (Lescol) 20 -40mg a day, Pitavastatin (Livalo)1mg a day

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Praluent (alirocumab) and Repatha (evolocumab) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Praluent (alirocumab) include: history of a serious hypersensitivity reaction to alirocumab or any of the excipients in Praluent. Contraindications to Repatha (evolocumab) include: patients with a history of a serious hypersensitivity reaction to evolocumab or any of the excipients in Repatha.

OTHER SPECIAL CONSIDERATIONS:

The recommended starting dose of Praluent is 75 mg administered subcutaneously once every 2 weeks since the majority of patients achieve sufficient LDL-C reduction with this dosage. If the LDL-C response is inadequate, the dosage may be increased to the maximum dosage of 150 mg administered every 2 weeks. Measure LDL-C levels within 4 to 8 weeks of initiating or titrating Praluent to assess response and adjust the dose, if needed.

The recommended dosage of Praluent for pediatric patients with a body weight less than 50 kg is 150 mg once every 4 weeks administered subcutaneously. If the LDL-C lowering response is inadequate, the dosage may be adjusted to 75 mg subcutaneously once every 2 weeks. The recommended dosage of Praluent for patients with a body weight of 50 kg or more is 300 mg once every 4 weeks administered subcutaneously. If the LDL-C lowering response is inadequate, the dosage may be adjusted to 150 mg subcutaneously once every 2 weeks.

The recommended subcutaneous dosage of Repatha in patients with HeFH or patients with primary hyperlipidemia with established clinical atherosclerotic CVD is either 140 mg every 2 weeks OR 420 mg once monthly. When switching dosage regimens, administer the first dose of the new regimen on the next scheduled date of the prior regimen.

The recommended subcutaneous dosage of Repatha in patients with HoFH is 420 mg once monthly. In

patients with HoFH, measure LDL-C levels 4 to 8 weeks after starting Repatha, since response to therapy will depend on the degree of LDL-receptor function.
Note: To administer the 420 mg dose, give 3 Repatha injections consecutively within 30 minutes.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Repatha Pushtronex System SOCT 420MG/3.5ML
Repatha SOSY 140MG/ML
Repatha SureClick SOAJ 140MG/ML
Praluent Prefilled Pen 75 MG/ML
Praluent Prefilled Pen 150 MG/ML

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Age Restrictions FDA-Approved Uses References	Q1 2025
REVISION- Notable revisions: Age Restrictions FDA-Approved Uses Other Special Considerations	Q2 2024

REVISION- Notable revisions: Required Medical Information Continuation of Therapy Age Restrictions References	Q1 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval FDA-Approved Uses Appendix Contraindications/Exclusions/Discontinuation References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file