

Clinical Policy: Alirocumab (Praluent)

Reference Number: CP.PHAR.124

Effective Date: 10.15

Last Review Date: 08.18

Line of Business: Commercial, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Alirocumab (Praluent[®]) is a PCSK9 (proprotein convertase subtilisin kexin type 9) inhibitor antibody.

FDA Approved Indication(s)

Praluent is indicated as adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein (LDL)-cholesterol (LDL-C).

Limitation(s) of use: The effect of Praluent on cardiovascular morbidity and mortality has not been determined.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Praluent is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria**A. Heterozygous Familial Hypercholesterolemia and Atherosclerotic Cardiovascular Disease (must meet all):**

1. Diagnosis of one of the following (a or b):
 - a. HeFH as defined by one of the following (i or ii):
 - i. World Health Organization (WHO)/Dutch Lipid Network familial hypercholesterolemia diagnostic criteria score of > 8 as determined by requesting provider (*see Appendix D*);
 - ii. Definite diagnosis per Simon Broome criteria (*see Appendix D*);
 - b. ASCVD as evidenced by a history of any one of the following conditions (i-vii):
 - i. Acute coronary syndromes;
 - ii. Clinically significant coronary heart disease (CHD) diagnosed by invasive or noninvasive testing (such as coronary angiography, stress test using treadmill, stress echocardiography, or nuclear imaging);
 - iii. Coronary or other arterial revascularization;
 - iv. Myocardial infarction;
 - v. Peripheral arterial disease presumed to be of atherosclerotic origin;
 - vi. Stable or unstable angina;

- vii. Stroke or transient ischemic attack (TIA);
2. Prescribed by or in consultation with a cardiologist, endocrinologist or lipid specialist;
3. Age is ≥ 18 years;
4. Documentation of recent (within the last 30 days) LDL-C ≥ 70 mg/dL;
5. Member has been adherent to a high intensity statin (*see Appendix D*) regimen for at least the last 4 months, unless one of the following applies (a, b, or c):
 - a. Statin therapy is contraindicated per Appendix F;
 - b. Member has been adherent to a moderate intensity statin (*see Appendix D*) regimen for at least the last 4 months due to one of the following (i or ii):
 - i. Intolerance to two high intensity statins;
 - ii. A statin risk factor (*see Appendix G*);
 - c. Member is unable to take a high or moderate intensity statin due to one of the following (i or ii):
 - i. Intolerance to two high and two moderate intensity statins;
 - ii. A statin risk factor (*see Appendix G*) and history of intolerance to two moderate intensity statins;
6. Member meets one of the following (a or b):
 - a. Use is in conjunction with a statin at the maximally tolerated dose;
 - b. For members not on statin therapy (statin intolerant), member has tried at least two of the hydrophilic statins (i.e., pravastatin, fluvastatin, rosuvastatin) titrated from lowest possible dose at intermittent dosing frequency (e.g., 1 to 3 times weekly);
7. Member has been adherent to ezetimibe therapy concomitantly with a statin at the maximally tolerated dose for at least the last 4 months, unless contraindicated per Appendix F or a history of ezetimibe intolerance (e.g., associated diarrhea or upper respiratory tract infection);
8. Treatment plan does not include coadministration with Juxtapid[®], Kynamro[®], Repatha[®];
9. Dose does not exceed 75 mg every 2 weeks or 300 mg every month.

Approval duration:

Medicaid – 3 months

Commercial – 6 months or to the member’s renewal date, whichever is longer

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Heterozygous Familial Hypercholesterolemia and Atherosclerotic Cardiovascular Disease Primary Hyperlipidemia (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. If statin tolerant, documentation of adherence to a statin at the maximally tolerated dose;

3. Member meets one of the following (a or b):
 - a. Request is for 75 mg every 2 weeks and documentation of LDL-C reduction since initiation of Praluent therapy;
 - b. Request is for 150 mg every 2 weeks and one of the following (i or ii):
 - i. If request represents a new dose increase, member has demonstrated adherence to Praluent and, if applicable, Zetia and/or statin therapies and lab results within the last 3 months are submitted showing an LDL-C > 70 mg/dL after a minimum of 8 weeks of Praluent therapy at 75 mg;
 - ii. If request represents a continuation of Praluent 150 mg, lab results within the last 3 months are submitted showing an LDL-C reduction since initiation of the Praluent dose increase.

**Lab results must be within the last 3 months*

Approval duration:

Medicaid – 12 months (*3 months if request is for dose increase*)

Commercial – 6 months or to the member’s renewal date, whichever is longer

B. Other diagnoses/indications (1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALT: Alanine transaminase

apo B: apolipoprotein B

ASCVD: atherosclerotic cardiovascular disease

CHD: coronary heart disease

FDA: Food and Drug Administration

FH: familial hypercholesterolemia

HeFH: heterozygous familial hypercholesterolemia

LDL-C: low density lipoprotein cholesterol

LDLR: low density lipoprotein receptor

PCSK9: proprotein convertase subtilisin kexin 9

TIA: transient ischemic attack

WHO: World Health Organization

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
ezetimibe/ simvastatin (Vytorin [®])	10/40 mg PO QD	10 mg-40 mg/day (Use of the 10/80 mg dose is restricted to patients who have been taking simvastatin 80 mg for 12 months or more without evidence of muscle toxicity)
ezetimibe (Zetia [®])	10 mg PO QD	10 mg/day
atorvastatin (Lipitor [®])	40 mg PO QD	80 mg/day
rosuvastatin (Crestor [®])	5 - 40 mg PO QD	40 mg/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications
Not applicable

Appendix D: Criteria for Diagnosis of HeFH

- Dutch Lipid Clinic Network criteria for Familial Hypercholesterolemia (FH)

FH Criteria	Points	Member's Score†
Family History		
First-degree relative with known premature* coronary and vascular disease	1	Place highest score here (0, 1 or 2)
First-degree relative with known LDL-C level above the 95 th percentile	1	
First-degree relative with tendinous xanthomata and/or arcus cornealis	2	
Children aged < 18 years with LDL-C level above the 95 th percentile	2	
Clinical History		
Patient with premature* coronary artery disease	2	Place highest score here (0, 1 or 2)
Patient with premature* cerebral or peripheral vascular disease	1	
Physical Examination		
Tendinous xanthomata	6	Place highest score here (0, 4 or 6)
Arcus cornealis prior to age 45 years	4	
Cholesterol Levels - mg/dL (mmol/liter)		
LDL-C ≥330 mg/dL (≥8.5)	8	Place highest score here (0, 1, 3, 5 or 8)
LDL-C 250 – 329 mg/dL (6.5 – 8.4)	5	
LDL-C 190 – 249 mg/dL (5.0 – 6.4)	3	
LDL-C 155 – 189 mg/dL (4.0 – 4.9)	1	
DNA Analysis		
Functional mutation in the low density lipoprotein receptor (LDLR), apo B or PCSK9 gene	8	Place highest score here (0 or 8)

FH Criteria	Points	Member's Score [†]
TOTAL SCORE	Definite FH: >8	Place score total here ___

*Premature – men < 55 years or women < 60 years

[†]Choose the highest score from each of the five categories and then add together for a total score. The five categories are 1) Family History, 2) Clinical History, 3) Physical Examination, 4) Cholesterol Levels, and 5) DNA Analysis.

- Simon Broome Register Group Definition of Definite FH (meets 1 and 2):
 1. One of the following (a or b):
 - a. Total cholesterol level above 7.5 mmol/l (290 mg/dl) in adults or a total cholesterol level above 6.7 mmol/l (260 mg/dl) for children under 16
 - b. LDL levels above 4.9 mmol/l (190 mg/dl) in adults (4.0 mmol/l in children) (either pre-treatment or highest on treatment)
 2. One of the following (a or b):
 - a. Tendinous xanthomas in patient or relative (parent, child, sibling, grandparent, aunt, uncle)
 - b. DNA-based evidence of an LDL receptor mutation or familial defective apo B-100
- High and Moderate Risk of ASCVD:
 - Patients with high risk of ASCVD include the following:
 - History of clinical atherosclerotic cardiovascular disease (as defined in section II)
 - Diabetes with an estimated 10-year ASCVD risk $\geq 7.5\%$ for adults 40-75 years of age
 - Untreated LDL ≥ 190 mg/dL
 - Patients with moderate risk of ASCVD include the following:
 - Diabetes with an estimated 10-year ASCVD risk $< 7.5\%$ for adults 40-75 years of age
 - Estimated 10-year ASCVD risk $\geq 5\%$ for adults 40-75 years of age
 - The calculator for the 10-year ASCVD risk estimator can be found here: <http://tools.cardiosource.org/ASCVD-Risk-Estimator/>. Information needed to complete the ASCVD Risk Estimator include: gender, race (white, African American, other), systolic blood pressure, diabetes, age, total cholesterol, HDL-Cholesterol, treatment for hypertension, current smoker.

Appendix E: High and Moderate Intensity Daily Statin Therapy for Adults

High Intensity Statin Therapy
<i>Daily dose shown to lower LDL-C, on average, by approximately $\geq 50\%$</i>
<ul style="list-style-type: none"> • Atorvastatin 40-80 mg • Rosuvastatin 20-40 mg
Moderate Intensity Statin Therapy
<i>Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%</i>
<ul style="list-style-type: none"> • Atorvastatin 10-20mg • Fluvastatin XL 80 mg • Fluvastatin 40 mg 2x/day

<ul style="list-style-type: none"> • Lovastatin 40 mg • Pitavastatin 2-4 mg • Pravastatin 40-80 mg • Rosuvastatin 5-10 mg • Simvastatin 20-40 mg
<p>Low Intensity Statin Therapy <i>Daily dose shown to lower LDL-C, on average, by <30%</i></p>
<ul style="list-style-type: none"> • Simvastatin 10 mg • Pravastatin 10–20 mg • Lovastatin 20 mg • Fluvastatin 20–40 mg • Pitavastatin 1 mg

Appendix F: Statin and Ezetimibe Contraindications

<p>Statins</p> <ul style="list-style-type: none"> • Decompensated liver disease (development of jaundice, ascites, variceal bleeding, encephalopathy) • Laboratory-confirmed acute liver injury or rhabdomyolysis resulting from statin treatment • Pregnancy, actively trying to become pregnant, or nursing • Immune-mediated hypersensitivity to the HMG-CoA reductase inhibitor drug class (statins) as evidenced by an allergic reaction occurring with at least TWO different statins
<p>Ezetimibe</p> <ul style="list-style-type: none"> • Moderate or severe hepatic impairment [Child-Pugh classes B and C] • Hypersensitivity to ezetimibe (e.g., anaphylaxis, angioedema, rash, urticaria)

Appendix G: Statin Risk Factors

<p>Statin Risk Factors</p> <ul style="list-style-type: none"> • Multiple or serious comorbidities, including impaired renal or hepatic function • Unexplained alanine transaminase (ALT) elevations > 3 times upper limit of normal, or active liver disease • Concomitant use of drugs adversely affecting statin metabolism • Age > 75 years, or history of hemorrhagic stroke • Asian ancestry

Appendix H: General Information

- FDA Endocrinologic and Metabolic Drugs Advisory Committee briefing documents for Praluent discuss the questionable determination of statin intolerance, stating: “many patients who are not able to take statins are not truly intolerant of the pharmacological class.”
- Patients should remain on concomitant therapy with a statin if tolerated due to the established long term cardiovascular benefits.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hypercholesterolemia with ASCVD	75 mg SC once every 2 weeks or 300 mg SC once every 4 weeks If response to 75 mg every 2 weeks or 300 mg every 4 weeks is inadequate, dose may be increased to 150 mg once every 2 weeks.	300 mg/month

VI. Product Availability

Single-use pre-filled pen, syringe: 75 mg/mL, 150 mg/mL

VII. References

1. Praluent Prescribing Information. Bridgewater, NJ: Sanofi-Eventis U.S. LLC; January 2018. Available at <http://products.sanofi.us/praluent/praluent.pdf>. Accessed on May 22, 2018.
2. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk. J Am Coll Cardiol. 2016; 68(1): 92-125.
3. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014 June 24; 129[suppl 2]: S1-S45.
4. Jacobson TA, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 – full report. Journal of Clinical Lipidology. March-April 2015; 9(2): 129-169. <http://dx.doi.org/10.1016/j.jacl.2015.02.003>
5. Goldber AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. Journal of Clinical Lipidology. June 2011; 5(3S): 1-15.
6. Al-Rasadi K, Al-Waili K, Al-Sabti HA, et al. Criteria for diagnosis of familial hypercholesterolemia: A comprehensive analysis of the different guidelines, appraising their suitability in the Omani Arab population. Oman Medical Journal. 2014; 29(2): 85–91. <http://doi.org/10.5001/omj.2014.22>
7. Fitchett DH, Hegele RA, Verma S. Statin intolerance. Circulation 2015;131:e389-391. <https://doi.org/10.1161/CIRCULATIONAHA.114.013189>
8. Food and Drug Administration Center for Drug Evaluation and Research: The Endocrinology and Metabolic Drugs Advisory Committee Meeting Briefing Document BLA 125559 – Praluent (alirocumab) injection. June 9, 2015. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/125559Orig1s000ODMemo.pdf. Accessed: May 22, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.15	10.15

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted policy to new template. Added examples of Zetia intolerance. Incorporated ASCVD and therapeutic lifestyle changes appendices into the criteria. Combined Zetia and statin contraindications (App D) and added nursing as a contraindication. Statin risk factors are listed at App E. Added scoring instructions to the Dutch criteria appendix. Modified renewal duration to 12 months. Added requirement for the use of statin and Zetia therapy for the last 4 months.	10.16	10.16
Modified the definition of ASCVD to include history of nonhemorrhagic stroke or transient ischemic attack. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs.	09.17	10.17
3Q 2018 annual review: combined policies for Medicaid and Commercial lines of business; added a separate requirement to check for continued statin use and adherence at reauthorization; Medicaid: aligned definition of ASCVD with commercial by addition of acute coronary syndrome and clinically significant CHD; aligned trial of Zetia language with commercial by requiring concomitant statin; added hydrophilic statin with intermittent dosing requirement; Commercial: aligned definition of ASCVD with Medicaid with removal of carotid artery occlusion and renal artery stenosis/stent; lowered minimum LDL value required for initial approval from 100 mg/dL to 70 mg/dL; references reviewed and updated.	05.22.18	08.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene[®] and Centene Corporation[®] are registered trademarks exclusively owned by Centene Corporation.