

Clinical Policy: Evolocumab (Repatha)

Reference Number: HIM.PA.156

Effective Date: 06.01.21

Last Review Date: 08.26

Line of Business: HIM*

[Coding Implications](#)[Revision Log](#)

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

Description

Evolocumab (Repatha®) is a proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor antibody.

**These criteria do NOT apply to New York Exchange Plans.*

FDA Approved Indication(s)

Repatha 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 at increased risk for these events
- As an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in:
 - Adults with hypercholesterolemia
 - Adults and pediatric patients aged 10 years and older with heterozygous familial hypercholesterolemia (HeFH)
 - Adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH)

Policy/Criteria

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

I. Initial Approval Criteria**A. Primary Hypercholesterolemia (including HeFH) and Cardiovascular Event Risk Reduction (must meet all):**

1. Diagnosis of one of the following (a, b, or c):
 - a. **HeFH**, and provider's attestation of both of the following (i and ii):
 - i. Baseline LDL-C $\geq$ 160 mg/dL (prior to any lipid-lowering pharmacologic therapy);
 - ii. HeFH diagnosis is confirmed by one of the following (1 or 2):
 - 1) World Health Organization (WHO)/Dutch Lipid Network familial hypercholesterolemia diagnostic criteria score of > 8 as determined by requesting provider (*see Appendix D*);
 - 2) Definite diagnosis per Simon Broome criteria (*see Appendix D*);
 - b. **Primary hypercholesterolemia that is not HeFH**, and both of the following (i and ii):

- i. Provider's attestation that baseline LDL-C $\geq$ 190 mg/dL (prior to any lipid-lowering pharmacologic therapy);
 - ii. Provider's attestation of one of the following (1 or 2):
 - 1) Presence of a genetically mediated form of primary hypercholesterolemia as evidenced by confirmatory genetic testing results;
 - 2) A diagnosis of secondary hypercholesterolemia has been ruled out with absence of all of the following potential causes of elevated cholesterol (a - f):
 - a) Poor diet;
 - b) Hypothyroidism;
 - c) Obstructive liver disease;
 - d) Renal disease;
 - e) Nephrosis;
 - f) Medications that have had a clinically relevant contributory effect on the current degree of the member's elevated lipid levels including, but not limited to: glucocorticoids, sex hormones, antipsychotics, antiretrovirals, immunosuppressive agents, retinoic acid derivatives;
 - c. **Increased risk for CV events** as evidenced by provider's attestation of one of the following (i, ii, iii, or iv):
 - i. Diabetes;
 - ii. 10-year estimated risk for atherosclerotic cardiovascular disease (ASCVD) $\geq$ 10%;
 - iii. Coronary artery calcium (CAC) score $\geq$ 100 Agatston units (AU);
 - iv. History of ASCVD including any one of the following conditions (1-8):
 - 1) Acute coronary syndromes;
 - 2) 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);
 - 3) CAC score $\geq$ 300 AU;
 - 4) Coronary or other arterial revascularization;
 - 5) Myocardial infarction;
 - 6) Peripheral arterial disease presumed to be of atherosclerotic origin;
 - 7) Stable or unstable angina;
 - 8) Stroke or transient ischemic attack (TIA);
2. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
 3. Age is one of the following (a or b):
 - a. If diagnosis is primary hypercholesterolemia (not including HeFH) or increased risk for CV events: $\geq$ 18 years;
 - b. If diagnosis is HeFH: $\geq$ 10 years;
 4. For members $\geq$ 18 years old and on statin therapy, provider's attestation of both of the following (a and b):*

**For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*

 - a. Repatha is prescribed in conjunction with a statin at the maximally tolerated dose;
 - b. Member has been adherent for at least the last 8 weeks to maximally tolerated doses of one of the following statin regimens (i or ii):

- i. A high intensity statin (*see Appendix E*);
- ii. A moderate or low intensity statin (*see Appendix E*), and member has one of the following (1 or 2):
 - 1) Previous use of one high-intensity statin (i.e., atorvastatin $\geq$ 40 mg daily; rosuvastatin $\geq$ 20 mg daily [as a single-entity or as a combination product]) for a minimum of 8 weeks continuously and LDL-C goal was not achieved;
 - 2) Member has tried both rosuvastatin and atorvastatin and has experienced skeletal-muscle related symptoms on both agents which also resolved upon discontinuation;
5. For members $\geq$ 18 years old and not on statin therapy, provider's attestation that member meets one of the following (a or b):*

**For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*

 - a. Statin therapy is contraindicated per Appendix F;
 - b. For members who are statin intolerant, both of the following (i and ii):
 - i. Member has tried at least two statins, one of which must be hydrophilic (pravastatin, fluvastatin, or rosuvastatin);
 - ii. Member meets one of the following (1 or 2):
 - 1) Member has statin risk factors (*see Appendix G*);
 - 2) Member is statin intolerant due to statin-associated muscle symptoms (SAMS) and meets both of the following (a and b):
 - a) Member had intolerable SAMS persisting at least two weeks, which disappeared with discontinuing the statin therapy and recurred with a statin re-challenge;
 - b) Previous re-challenge with titration from lowest possible dose and/or intermittent dosing frequency (e.g., 1 to 3 times weekly);
6. Provider's attestation of recent (within the last 60 days) LDL-C of one of the following (a, b, or c):
 - a. If member has history of ASCVD: $\geq$ 55 mg/dL;
 - b. If member has HeFH, severe primary hypercholesterolemia with ASCVD risk factors (*see Appendix H*), or increased risk for CV events (not including history of ASCVD): $\geq$ 70 mg/dL;
 - c. If member has severe primary hypercholesterolemia without ASCVD risk factors: $\geq$ 100 mg/dL;
7. Treatment plan does not include coadministration with Leqvio[®], Juxtapid[®], Praluent[®], or Lerochol[™];
8. Dose does not exceed one of the following (a or b):
 - a. 140 mg every 2 weeks;
 - b. 420 mg per month.

Approval duration: 12 months

B. Homozygous Familial Hypercholesterolemia (must meet all):

1. Diagnosis of HoFH;
2. Provider's attestation that diagnosis is defined by one of the following (a, b, or c):

- a. Genetic mutation indicating HoFH (e.g., mutations in low density lipoprotein receptor [LDLR] gene, PCSK9 gene, apo B gene, low density lipoprotein receptor adaptor protein 1 [LDLRAP1] gene);
 - b. Treated LDL-C $\geq$ 300 mg/dL or non-HDL-C $\geq$ 330 mg/dL;
 - c. Untreated LDL-C $\geq$ 400 mg/dL, and one of the following (i or ii):
 - i. Tendinous or cutaneous xanthoma prior to age 10 years;
 - ii. Evidence of familial hypercholesterolemia (HeFH or HoFH) in at least one parent (e.g., history of elevated LDL-C $\geq$ 190 mg/dL prior to lipid-lowering therapy);
3. Prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist;
 4. Provider's attestation that member meets one of the following (a or b):
 - a. Both of the following (i and ii):
 - i. Age $\geq$ 10 years and $<$ 18 years;
 - ii. LDL-C $\geq$ 100 mg/dL within the last 60 days despite statin therapy, unless member has a contraindication (*see Appendix F*) or history of intolerance to each such therapy;
 - b. Age $\geq$ 18 years, and recent (within the last 60 days) LDL-C of one of the following (i or ii):
 - i. $\geq$ 70 mg/dL;
 - ii. $\geq$ 55 mg/dL if member has ASCVD;
 5. For members $\geq$ 18 years old and on statin therapy, provider's attestation of both of the following (a and b):*

**For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*

 - a. Repatha is prescribed in conjunction with a statin at the maximally tolerated dose;
 - b. Member has been adherent for at least the last 8 weeks to maximally tolerated doses of one of the following statin regimens (i or ii):
 - i. A high intensity statin (*see Appendix E*);
 - ii. A moderate or low intensity statin (*see Appendix E*) and member has one of the following (1 or 2):
 - 1) Previous use of one high-intensity statin (i.e., atorvastatin $\geq$ 40 mg daily; rosuvastatin $\geq$ 20 mg daily [as a single-entity or as a combination product]) for a minimum of 8 weeks continuously and LDL-C goal was not achieved;
 - 2) Member has tried both rosuvastatin and atorvastatin and has experienced skeletal-muscle related symptoms on both agents which also resolved upon discontinuation;
 6. For members $\geq$ 18 years old and not on statin therapy, provider's attestation that member meets one of the following (a or b):*

**For Illinois HIM requests, the step therapy requirements below do not apply per IL HB 5395*

 - a. Statin therapy is contraindicated per Appendix F;
 - b. For members who are statin intolerant, both of the following (i and ii):
 - i. Member has tried at least two statins, one of which must be hydrophilic (pravastatin, fluvastatin, or rosuvastatin);
 - ii. Member meets one of the following (1 or 2):
 - 1) Member has statin risk factors (*see Appendix G*);

- 2) Member is statin intolerant due to statin-associated muscle symptoms (SAMS) and meets both of the following (a and b):
 - a) Member had intolerable SAMS persisting at least two weeks, which disappeared with discontinuing the statin therapy and recurred with a statin re-challenge;
 - b) Previous re-challenge with titration from lowest possible dose and/or intermittent dosing frequency (e.g., 1 to 3 times weekly);
7. Treatment plan does not include coadministration with Leqvio, Juxtapid, Praluent, or Lerchol;
8. Dose does not exceed one of the following (a or b):
 - a. 420 mg per month;
 - b. 420 mg every 2 weeks, and provider's attestation that member is currently receiving lipid apheresis.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
 2. If statin tolerant, provider's attestation of adherence to a statin at the maximally tolerated dose;*
- *For Illinois HIM requests, the step therapy requirements above do not apply per IL HB 5395*
3. Member is responding positively to therapy as evidenced by provider's attestation of lab results within the last 3 months showing an LDL-C reduction since initiation of Repatha therapy;
 4. Treatment plan does not include coadministration with Leqvio, Juxtapid, Praluent, or Lerchol;

5. If request is for a dose increase, new dose does not exceed either of the following (a or b):
 - a. Primary hypercholesterolemia (including HeFH) or CV event risk reduction: one of the following (i or ii):
 - i. 140 mg every 2 weeks;
 - ii. 420 mg per month;
 - b. HoFH: one of the following (i or ii):
 - i. 420 mg per month;
 - ii. 420 mg every 2 weeks, and provider's attestation of one of the following (1 or 2):
 - 1) Member is currently receiving lipid apheresis;
 - 2) Member did not achieve a clinically meaningful response, defined as not having achieved $\geq 30\%$ reduction in LDL from baseline, with initial dosing.

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace.

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 – HIM.PA.154 for health insurance marketplace 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

AU: Agatston units

CAC: coronary artery calcium

CHD: coronary heart disease

CV: cardiovascular

FDA: Food and Drug Administration

FH: familial hypercholesterolemia

HeFH: heterozygous familial hypercholesterolemia

HoFH: homozygous familial hypercholesterolemia

LDL-C: low density lipoprotein cholesterol

LDLR: low density lipoprotein receptor
LDLRAP1: low density lipoprotein
receptor adaptor protein 1
PCSK9: proprotein convertase subtilisin
kexin 9

SAMS: statin-associated muscle
symptoms
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 Name	Dosing Regimen	Dose Limit/ Maximum Dose
atorvastatin (Lipitor®)	40 mg PO QD	80 mg/day
rosuvastatin (Crestor®)	5 - 40 mg PO QD	40 mg/day
pravastatin	10 - 80 mg PO QD	80 mg/day
fluvastatin (Lescol®)	20 - 80 mg PO QD	80 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/Boxed Warnings

- Contraindication(s): hypersensitivity
- Boxed warning(s): none reported

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
LDL-C 250 – 329 mg/dL (6.5 – 8.4)	5	

FH Criteria	Points	Member's Score†
LDL-C 190 – 249 mg/dL (5.0 – 6.4)	3	(0, 1, 3, 5 or 8)
LDL-C 155 – 189 mg/dL (4.0 – 4.9)	1	
DNA Analysis		
Functional mutation in the <i>LDLR</i> , <i>apo B</i> or <i>PCSK9</i> gene	8	Place score here (0 or 8)
TOTAL SCORE	Definite FH: > 8	Place total score 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;

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 ≥ 50%</i>
• 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>
• Atorvastatin 10-20 mg • Fluvastatin XL 80 mg • Fluvastatin 40 mg BID • Lovastatin 40-80 mg • Pitavastatin 1-4 mg • Pravastatin 40-80 mg • Rosuvastatin 5-10 mg • Simvastatin 20-40 mg
Low Intensity Statin Therapy <i>Daily dose shown to lower LDL-C, on average, by < 30%</i>
• Fluvastatin 20-40 mg • Lovastatin 20 mg

Moderate Intensity Statin Therapy

Daily dose shown to lower LDL-C, on average, by approximately 30% to 50%

- Pravastatin 10-20 mg
- Simvastatin 10 mg

Appendix F: Statin Contraindications

Statins

- 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

**In July 2021, the FDA requested removal of the contraindication against use of statins in pregnant women. Because the benefits of statins may include prevention of serious or potentially fatal events in a small group of very high-risk pregnant patients, contraindicating these drugs in all pregnant women is not appropriate. <https://www.fda.gov/safety/medical-product-safety-information/statins-drug-safety-communication-fda-requests-removal-strongest-warning-against-using-cholesterol>*

Appendix G: Statin Risk Factors

Statin Risk Factors

- 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: ASCVD Risk Factors

ASCVD Risk Factors

- History of premature ASCVD in a parent or sibling (onset age < 55 years for men, < 65 years for women)
- Higher risk ancestry (e.g. South Asian, Filipino)
- High polygenic risk (if measured)
- Chronic inflammatory diseases (e.g. systemic lupus, rheumatoid arthritis, advanced psoriasis, inflammatory arthritis)
- Lp(a) ≥ 125 nmol/L or ≥ 50 mg/dL
- hsCRP ≥ 2 mg/L on > 1 occasion (if measured)
- TG persistently ≥ 175 mg/dL (2 mmol/L) (if nonfasting) and ≥ 150 mg/dL (1.7 mmol/L) (if fasting)
- Cardiovascular-kidney-metabolic (CKM) syndrome
- LDL-C persistently ≥ 160-189 mg/dL (4.1-4.9 mmol/L), non-HDL-C ≥ 190-219 mg/dL or apoB ≥ 120 mg/dL

ASCVD Risk Factors

- Reproductive risk markers (premature menopause, preeclampsia, gestational diabetes, gestational hypertension, preterm delivery)

Appendix I: General Information

- FDA Endocrinologic and Metabolic Drugs Advisory Committee briefing documents for another PCSK-9 inhibitor, 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.
- Examples of genetically mediated primary hypercholesterolemia include but are not limited to the following:
 - Familial hypercholesterolemia
 - Familial combined hyperlipidemia (FCHL)
 - Polygenic hypercholesterolemia
 - Familial dysbetalipoproteinemia
- The diagnosis of SAMS is often on the basis of clinical criteria. Typical SAMS include muscle pain and aching (myalgia), cramps, and weakness. Symptoms are usually bilateral and involve large muscle groups, including the thigh, buttock, back, and shoulder girdle musculature. In contrast, cramping is usually unilateral and may involve small muscles of the hands and feet. Symptoms may be more frequent in physically active patients. Symptoms often appear early after starting statin therapy or after an increase in dose and usually resolve or start to dissipate within weeks after cessation of therapy, although it may take several months for symptoms to totally resolve. Persistence of symptoms for more than 2 months after drug cessation should prompt a search for other causes or for underlying muscle disease possibly provoked by statin therapy. The reappearance of symptoms with statin rechallenge and their disappearance with drug cessation offers the best evidence that the symptoms are truly SAMS.
- Pravastatin, fluvastatin, and rosuvastatin are hydrophilic statins which have been reported to confer fewer adverse drug reactions than lipophilic statins.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Primary hypercholesterolemia (including HeFH) or hypercholesterolemia with increased risk for CV events	140 mg SC Q2 weeks or 420 mg SC once monthly	420 mg/month
HoFH	420 mg SC once monthly; Dosage can be increased to 420 mg every 2 weeks if a clinically meaningful response is not achieved in 12 weeks. Patients on lipid apheresis may initiate treatment with 420 mg	420 mg/2 weeks

Indication	Dosing Regimen	Maximum Dose
	every 2 weeks to correspond with their apheresis schedule	

VI. Product Availability

- Prefilled syringe, prefilled pen, and SureClick® autoinjector (not made with latex): 140 mg/mL
- Prefilled syringe and SureClick autoinjector (contains dry natural rubber): 140 mg/mL

VII. References

1. Repatha Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; July 2026. Available at: www.repatha.com. Accessed July 21, 2026.
- Guidelines
2. Blumenthal RS, Morris PB, Gaudino M, et al. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *J Am Coll Cardiol*. 2026 Mar 13;S0735-1097(25)10254-4. doi: 10.1016/j.jacc.2025.11.016.
3. Lloyd-Jones DM, Morris PB, Minissian MB, et al. 2017 Focused update of the 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* 2017; 70(14):1785-1822. <http://dx.doi.org/10.1016/j.jacc.2017.07.745>
4. Lloyd-Jones DM, Morris PB, Ballntyne CM, et al. 2022 ACC expert consensus decision pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: A report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2022; 80 (14): 1366-1418.
5. 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>.
6. Goldberg 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.
7. 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>.
8. Mach F, Baigent C, Catapano AL, et al; ESC Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2020 Jan 1;41(1):111-188. doi: 10.1093/eurheartj/ehz455. Erratum in: *Eur Heart J*. 2020 Nov 21;41(44):4255. doi: 10.1093/eurheartj/ehz826.
9. Cuchel M, Raal FJ, Hegele RA, et al. 2023 Update on European Atherosclerosis Society consensus statement on homozygous familial hypercholesterolaemia: new treatments and clinical guidance. *Eur Heart J*. 2023 Jul 1;44(25):2277-2291. doi: 10.1093/eurheartj/ehad197.

10. Jackson EJ, Willard KE, Ballantyne CM. LDL cholesterol management simplified in adults—Lower for longer is better: Guidance from the National Lipid Association. *J Clin Lipidol*. 2025 Jun 18;S1933-2874(25)00317-4. doi: 10.1016/j.jacl.2025.06.002.
11. Clinical Lipidology Resource Center, sponsored by the National Lipid Association and the Journal of Clinical Lipidology. Genetic classification of dyslipidemia. Available at: <http://nlaresourcecenter.lipidjournal.com/Content/PDFs/Tables/1.pdf>. Accessed October 22, 2025.
12. Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline from the American Heart Association/American Stroke Association. *Stroke*. 2021; 52: e354-e467.
13. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2023 Aug 29;148(9):e9-e119.
Statin Tolerance
14. Fitchett DH, Hegele RA, Verma S. Statin intolerance. *Circulation* 2015;131:e389-391. <https://doi.org/10.1161/CIRCULATIONAHA.114.013189>.
15. 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 October 22, 2025.
16. Manpuya WM, Cho L, Frid D, et al. Treatment strategies in patients with statin intolerance: the Cleveland Clinic experience. *American Heart Journal* 2013; 166(3):597-603.
17. Zhang H, Plutzky J, Skentzos S, et al. Discontinuation of statins in routine care settings. *Ann of Intern Med* 2013; 158(7):526-534.
18. Backes JM, Ruisinger JF, Gibson CA, et al. Statin-associated muscle symptoms—managing the highly intolerant. *J Clin Lipidol*. 2017;11:24-33. Jan-Feb;11(1):24-33. doi: 10.1016/j.jacl.2017.01.006
19. Thompson PD, Panza G, Zaleski A, et al. Statin-associated side effects. *J Am Coll Cardio* 2016 May 24;67(20):2395-2410. doi: 10.1016/j.jacc.2016.02.071.
20. Warden BA, Guyton JR, Kovacs AC, et al. Assessment and management of statin-associated muscle symptoms (SAMS): A clinical perspective from the National Lipid Association. *J Clin Lipidol*. 2023 Jan-Feb;17(1):19-39. doi: 10.1016/j.jacl.2022.09.001.
21. Cheeley MK, Saseen JJ, Agarwala A, et al. NLA scientific statement on statin intolerance: a new definition and key considerations for ASCVD risk reduction in the statin intolerant patient. *J Clin Lipidol*. 2022 Jul-Aug;16(4):361-375. doi: 10.1016/j.jacl.2022.05.068.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals

HCPCS Codes	Description
J3590	Unclassified biologics

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created (removed HIM line of business from CP.PHAR.123) per March SDC to revise criteria requirements to require provider attestation rather than documentation.	03.26.21	05.21
RT4: Updated HoFH continuation criteria based on FDA label update to allow a maximum dose of 420 mg every 2 wks if clinically meaningful response not achieved after 12 wks of 420 mg monthly.	07.13.21	
1Q 2022 annual review: RT4: updated criteria per pediatric age expansion for HeFH and HoFH; for HoFH, added option for 420 mg every 2 weeks if member is currently receiving lipid apheresis per FDA label update; removed references to Kynamro since it has been withdrawn from market; references reviewed and updated.	09.29.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.11.22	
1Q 2023 annual review: per 2022 ACC expert consensus decision pathway and as supported by specialist feedback – added bypass of ezetimibe trial if member requires > 25% additional lowering of LDL, and lowered minimum LDL requirement to 55 mg/dL for members with ASCVD at very high risk with corresponding Appendix I; references reviewed and updated.	10.18.22	02.23
Per guidelines: for primary hypercholesterolemia, modified baseline, and recent LDL requirements for non-genetically mediated disease to be the same as genetically mediated disease, and for HeFH, added pathway for baseline LDL of at least 160 mg/dL for age < 20 years.	05.17.23	08.23
Per November SDC, for all indications, reduced statin adherence duration from 4 months to 8 weeks, simplified statin trial and failure criteria for moderate- and low-intensity statin regimens to require insufficient therapeutic response to one high intensity statin for 8 weeks or reversible muscle-related symptoms associated with both rosuvastatin and atorvastatin, removed ezetimibe trial criteria.	11.08.23	12.23
1Q 2024 annual review: added Leqvio to list of drugs where coadministration is not allowed; added the following requirement from initial approval criteria to also require for continuation of therapy “Treatment plan does not include coadministration with Leqvio, Juxtapid or Praluent”; divided criteria with multiple elements into separate bullets for added clarity; Appendix I clarified smoking is specific to tobacco; references reviewed and updated. Reorganized diagnostic criteria in section I.A for improved clarity (no changes to clinical content).	02.09.24	02.24
Per SDC, for pediatric HoFH, removed ezetimibe trial criteria.	04.24.24	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2025 annual review: RT4: revised FDA approved indication wording to align CV disease wording with PI; for HeFH, lowered untreated LDL requirement to 400 mg/dL and revised evidence of HeFH in both parents to evidence of familial hypercholesterolemia in at least one parent per 2022 ACC expert consensus decision pathway; in Appendix B, added pravastatin and fluvastatin as therapeutic alternatives; in Section VI, clarified non-latex and latex formulations; references reviewed and updated.	12.03.24	02.25
In Appendix D, removed ASCVD risk information for HeFH diagnosis.	04.08.25	
RT4: per PI, updated indication to reflect revised the following revised uses: as an adjunct to exercise (rather than LDL-lowering therapy) for HeFH and HoFH and to reduce major adverse CV events in adults at increased risk for these events (rather than adults with established CV disease); revised “hyperlipidemia” to “hypercholesterolemia” throughout the criteria.	09.04.25	
1Q 2026 annual review: for all indications, added step therapy bypass for IL HIM per IL HB 5395; extended initial approval duration from 3 months to 12 months for this maintenance medication for a chronic condition; references reviewed and updated.	10.22.25	02.26
Per 2026 guideline updates: for all indications, modified moderate or low intensity statin requirement therapy from requiring previous use of one high intensity statin and LDL remained ≥ 70 mg/dL to LDL <i>goal was not achieved</i> to reflect differing LDL goals based on specific indication; modified recent LDL requirements to ≥ 55 mg/dL for history of ASCVD regardless of very high risk status; for increased risk for CV events, added diabetes, 10-year estimated risk for ASCVD $\geq 10\%$, and CAC score ≥ 100 to 299 AU as examples of increased risk for CV events, added CAC score ≥ 300 AU as example of history of ASCVD, added recent LDL requirement ≥ 70 mg/dL separate from history of ASCVD; for HeFH, simplified baseline LDL to at least 160 mg/dL for all ages, revised recent LDL requirement to ≥ 70 mg/dL; for primary hypercholesterolemia, added recent LDL requirement of ≥ 70 mg/dL for severe primary hypercholesterolemia <i>with ASCVD risk factors</i> with corresponding Appendix H, clarified recent LDL requirement of ≥ 100 mg/dL is for without ASCVD risk factors, added requirement that treatment plan does not include coadministration with Lerochol to prevent duplicate therapy; for HoFH, revised LDL requirements to ≥ 100 mg/dL for pediatric population; removed ‘very high risk’ qualifier from adult LDL requirement. RT4: added non-latex pen dosage form and removed discontinued 420 mg cartridge.	07.21.26	08.26

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.

©2021 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.