UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 2063-20
Program	Prior Authorization/Medical Necessity
Medication	Repatha® (evolocumab)
P&T Approval Date	5/2015, 9/2015, 11/2015, 1/2016, 8/2016, 12/2016, 11/2017, 12/2018, 1/2019, 12/2019, 2/2020, 2/2021, 6/2021, 8/2021, 6/2022, 1/2023, 6/2023, 10/2023, 2/2024
Effective Date	5/1/2024

1. Background:

Repatha® (evolocumab) is a PCSK9 (Proprotein Convertase Subtilisin Kexin Type 9) inhibitor indicated:

- To reduce the risk of myocardial infarction, stroke, and 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 (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce LDL-C.
- As an adjunct to other LDL-C-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.[1]
- As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with heterozygous familial hypercholesterolemia (HeFH) to reduce LDL-C.

2. Coverage Criteria[a]:

A. <u>Primary Hyperlipidemia (including heterozygous familial hypercholesterolemia) and ASCVD</u>

1. **<u>Initial Authorization</u>**

a. **Repatha** will be approved based on **<u>ALL</u>** of the following criteria:

(1) **<u>One</u>** of the following diagnoses:

(a) Heterozygous familial hypercholesterolemia (HeFH) as confirmed by **<u>one</u>** of the following:

i. **<u>Both</u>** of the following:[14-16]

1. Pre-treatment LDL-C greater than or equal to 190 mg/dL (greater than or equal to 155 mg/dL if less than 16 years of age)

-AND-

2. **<u>One</u>** of the following:

a. Family history of myocardial infarction in first-degree relative < 60 years of age

b. Family history of myocardial infarction in second-degree relative < 50 years of age
c. Family history of LDL-C greater than 190 mg/dL in first- or second-degree relative
d. Family history of heterozygous or homozygous familial hypercholesterolemia in first- or second-degree relative
e. Family history of tendinous xanthomata and/or arcus cornealis in first- or second degree relative

-OR-

ii. **Both** of the following:[14-16]

1. Pre-treatment LDL-C greater than or equal to 190 mg/dL (greater than or equal to 155 mg/dL if less than 16 years of age)

-AND-

2. **One** of the following:

a. Functional mutation in LDL, apoB, or PCSK9 gene
b. Tendinous xanthomata
c. Arcus cornealis before age 45

-OR-

(b) Atherosclerotic cardiovascular disease (ASCVD) as confirmed by **one** of the following:

i. Acute coronary syndromes
ii. History of myocardial infarction
iii. Stable or unstable angina
iv. Coronary or other arterial revascularization
v. Stroke
vi. Transient ischemic attack
vii. Peripheral arterial disease presumed to be of atherosclerotic origin

-OR-

(c) Primary hyperlipidemia with pre-treatment LDL-C greater than or equal to 190 mg/dL

-AND-

(2) **One** of the following:

(a) Patient has been receiving at least 12 consecutive weeks **of high-intensity statin therapy** [i.e., atorvastatin 40-80 mg, rosuvastatin 20-40 mg] and will continue to receive a high-intensity statin at maximally tolerated dose

-OR-

(b) **Both** of the following:

i. Patient is unable to tolerate high-intensity statin as evidenced by **one** of the following intolerable and persistent (i.e., more than 2 weeks) symptoms:

1. Myalgia [muscle symptoms without creatine kinase (CK) elevations]
2. Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

-AND-

ii. Patient has been receiving at least 12 consecutive weeks of low-intensity or moderate-intensity statin therapy [i.e. atorvastatin 10-20 mg, rosuvastatin 5-10 mg, simvastatin ≥ 10 mg, pravastatin ≥ 10 mg, lovastatin 20-40 mg, fluvastatin XL 80 mg, fluvastatin 20-40 mg up to 40mg twice daily or Livalo (pitavastatin) ≥ 1 mg] and will continue to receive a low-intensity or moderate-intensity statin at maximally tolerated dose

-OR-

(c) Patient is unable to tolerate **low or moderate, and high-intensity statins** as evidenced by **one** of the following:

i. **One** of the following intolerable and persistent (i.e. more than 2 weeks) symptoms for low or moderate-, and high-intensity statins:

1. Myalgia (muscle symptoms without CK elevations)
2. Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

-OR-

ii. Patient has a labeled contraindication to all statins

-OR-

iii. Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN

-AND-

(3) **One** of the following:

(a) **One** of the following LDL-C values while on maximally tolerated lipid lowering therapy for a minimum of at least 12 weeks within the last 120 days or 120 days prior to starting PCSK9 inhibitor therapy:

i. LDL-C ≥ 100 mg/dL with ASCVD

ii. LDL-C ≥ 130 mg/dL without ASCVD

-OR-

(b) **Both** of the following:

i. **One** of the following LDL-C values while on maximally tolerated lipid lowering therapy for a minimum of at least 12 weeks within the last 120 days or 120 days prior to starting PCSK9 inhibitor therapy:

1. LDL-C between 55 mg/dL and 99 mg/dL with ASCVD
2. LDL-C between 100 mg/dL and 129 mg/dL without ASCVD

-AND-

ii. **One** of the following:

1. Patient has been receiving at least 12 consecutive weeks of ezetimibe (Zetia®) therapy as adjunct to maximally tolerated statin therapy

-OR-

2. Patient has a history of contraindication, or intolerance to ezetimibe

-AND-

(4) Patient has received comprehensive counseling regarding appropriate diet

-AND-

(5) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor [e.g., Praluent (alirocumab)]

-AND-

(6) Not used in combination with Leqvio (inclisiran)

Authorization will be issued for 12 months

2. **Reauthorization**

a. **Repatha** will be approved based on **all** of the following criteria:

(1) Documentation of a positive clinical response to Repatha therapy

-AND-

(2) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor [e.g., Praluent (alirocumab)]

-AND-

(3) Not used in combination with Leqvio (inclisiran)

Authorization will be issued for 12 months

B. **Homozygous Familial Hypercholesterolemia**

1. **Initial Authorization**

a. **Repatha** will be approved based on **ALL** of the following criteria:

(1) Diagnosis of homozygous familial hypercholesterolemia (HoFH) as confirmed by **one** of the following:

(a) Submission of medical records (e.g., chart notes, laboratory values) confirming genetic confirmation of two mutant alleles at the *LDLR*, *APOB*, *PCSK9*, or *LDLRAP1* gene locus

-OR-

(b) **Both** of the following:

i. Pre-treatment LDL-C greater than 400 mg/dL

-AND-

ii. **One** of the following:

- Xanthoma before 10 years of age
- Evidence of heterozygous familial hypercholesterolemia (HeFH) in both parents

-AND-

(2) Patient has received comprehensive counseling regarding appropriate diet

-AND-

(3) Patient is receiving other lipid-lowering therapy (e.g., statin, ezetimibe, LDL apheresis)

-AND-

(4) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor [e.g., Praluent (alirocumab)]

-AND-

(5) Not used in combination with Juxtapid (lomitapide)

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Repatha** will be approved based on **all** of the following criteria:

(1) Documentation of a positive clinical response to Repatha therapy

--AND-

(2) Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor [e.g., Praluent (alirocumab)]

-AND-

(3) Not used in combination with Juxtapid (lomitapide)

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply Limits and Step Therapy may be in place.

4. References:

1. Repatha [package insert]. Thousand Oaks, CA : Amgen Inc.; September 2021.
2. WHO Familial Hypercholesterolemia Consultation Group. Familial Hypercholesterolemia (FH): report of a second WHO consultation. Geneva: World Health Organization; 1999.
3. Scientific Steering Committee on behalf of the Simon Broome Register Group. Risk of fatal coronary heart disease in familial hypercholesterolaemia. BMJ. 1991;303:893-6.
4. 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. J Am Coll Cardiol. 2014;63:2889-934.
5. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med. 2015a; DOI: 10.1056/NEJMoa1410489 [Epub ahead of print].

6. The Lipid Research Clinics Coronary Primary Prevention Trial results. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA. 1984;251:365-74.
7. ATP III Final Report PDF. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. Circulation. 2002;106:3143-3421.
8. Per clinical drug consult with cardiologist. August 3, 2015.
9. Blom DJ, Hala T, Bolognese M, et al. A 52-week placebo-controlled trial of evolocumab in hyperlipidemia. N Engl J Med. 2014;370:1809-19.
10. Raal FJ, Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis. 2012;223:262-8.
11. Raal FJ, Honarpour N, Blom DJ, et al. Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial. Lancet. 2015;385:341-50.
12. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercohlesterolaemia of the European Atherosclerosis Society. Eur Heart J. 2014;35:2146-57.
13. Lloyd-Jones D, Morris P, Ballantyne C, et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholersterol lowering in the management of atherosclerotic cardiovascular disease risk. J Am Coll Cardiol. 2016;68:92-125.
14. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. American journal of epidemiology. 2004;160:407-420
15. Haase A, Goldberg AC. Identification of people with heterozygous familial hypercholesterolemia. Current opinion in lipidology. 2012;23:282-289.
16. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: consensus statement of the European Atherosclerosis Society. European heart journal. 2013;34:3478-3490a.
17. Jellinger PS, Handelsman Y, Rosenblit PD, et al. American association of clinical endocrinologists and American college of endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease. Endocr Pract. 2017; Suppl 2;23:1-87.
18. Lloyd-Jones D, Morris P, Ballantyne C, et al. 2017 Focused update of the 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholersterol lowering in the management of atherosclerotic cardiovascular disease risk. J Am Coll Cardiol. 2017.
19. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2018; DOI: 10.1161/CIR.0000000000000625.
20. Writing Committee, Lloyd-Jones DM, Morris PB, 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. doi:10.1016/j.jacc.2022.07.006
21. 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;44(25):2277-2291. doi:10.1093/eurheartj/ehad197

Program	Prior Authorization/Medical Necessity – Repatha® (evolocumab)
Change Control	
5/2015	New program.
5/2015	Added examples of atherosclerotic cardiovascular disease.
9/2015	Revised clinical criteria to include combination use of high-intensity statin or documented intolerance to high-, moderate- and low intensity statin therapy to achieve the maximally tolerated statin therapy.
11/2015	Added step therapy requirement language for Primary Hyperlipidemia
1/2016	Removed continuation of therapy criterion.
8/2016	Add requirement of Praluent failure at maximum labeled dosing. Added MD, IN, and WV coverage information. Updated reference.
11/2016	Added California coverage information.
12/2016	Modified medical record criteria to include review of prescription claims history. Updated references.
11/2017	Updated medical record requirement, modified criteria for HeFH diagnosis, modified previous statin requirement requiring failure, intolerance to high intensity and either moderate or low intensity statin. Modified target LDL values and ezetimibe trial requirement. Extended timeline for lipid panel submission to 120 days. Added physician attestation criterion. Updated state mandate verbiage. Updated references.
12/2018	Updated criteria providing clarity on criteria for use in patients for the primary prevention of cardiovascular events. Removed Kynamro from homozygous familial hypercholesterolemia criteria as no longer on market. Updated references.
1/2019	Removed Praluent trial requirement for patients with HeFH, ASCVD.
12/2019	Annual review with no change to coverage criteria. Updated reference.
2/2020	Updated criteria providing clarity on laboratory monitoring requirements. Updated reference.
2/2021	Annual review with no change to coverage criteria.
6/2021	Aligned language to step therapy program. Removed prescriber specialist requirement. Removed submission of medical records requirement throughout criteria. Changed initial authorization duration to 12 months to align all PCSK9 programs. Updated reference.
8/2021	Updated LDL-C requirement to 120 days or 120 days prior to starting PCSK9 inhibitor therapy. Added pathway to Repatha approval for members converting from Praluent.
6/2022	Annual review. Updated background to include new indications for pediatric patients with heterozygous familial hypercholesterolemia and homozygous familial hypercholesterolemia. Condensed low intensity and moderate-intensity statin therapy sections. Updated references.
1/2023	Lowered LDL-C threshold requirement for initiation of Repatha therapy per American College of Cardiology guidance. Removed genetic testing coverage footnote. Updated references.
6/2023	Annual review. Updated background. Removed pathway to Repatha approval for members converting from Praluent with claims in past 120 days. Added criteria that Repatha is not to be used in combination with Leqvio and updated diet requirement.

10/2023	Removed “routine audit” language from criteria. Updated and clarified criteria for patients with primary hyperlipidemia with baseline LDL-C level ≥ 190 on statin therapy for primary prevention per American College of Cardiology guidance. Updated background.
2/2024	Updated diagnostic criteria per European Atherosclerosis Society guidance. Simplified reauthorization criteria. Updated references.