

UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2023 P 2063-19
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
Effective Date	1/1/2024

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. Primary Hyperlipidemia (including heterozygous familial hypercholesterolemia) and ASCVD

1. Initial Authorization

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

(1) **One** of the following diagnoses:

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

i. **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. 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 \geq 10 mg, pravastatin \geq 10 mg, lovastatin 20-40 mg, fluvastatin XL 80 mg, fluvastatin 20-40 mg up to 40mg twice daily or Livalo (pitavastatin) \geq 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 \geq 100 mg/dL with ASCVD
- ii. LDL-C \geq 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) Patient continues to receive statin at maximally tolerated dose (unless patient has an inability to take statins)

-AND-

- (2) Patient continues to receive comprehensive counseling regarding appropriate diet

-AND-

- (3) Documentation of a positive clinical response to therapy from pre-treatment baseline

-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 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 both of the following:

- (a) One of the following:

- i. Pre-treatment LDL-C greater than 500 mg/dL
- ii. Treated LDL-C greater than or equal to 300 mg/dL

-AND-

- (b) One of the following:

- i. Xanthoma before 10 years of age
- ii. 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) Patient continues to receive comprehensive counseling regarding appropriate diet

-AND-

- (2) Patient continues to receive other lipid-lowering therapy (e.g., statin, LDL apheresis)

-AND-

- (3) Documentation of a positive clinical response to therapy from pre-treatment baseline

--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.

^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:

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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-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk. *J Am Coll Cardiol.* 2017.
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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.