

UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2021 P 2063-15
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
Effective Date	9/1/2021; Oxford only: 9/1/2021

1. Background:

Repatha® (evolocumab) is a PCSK9 (Proprotein Convertase Subtilisin Kexin Type 9) inhibitor antibody 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 lipid-lowering therapies (e.g., statins, ezetimibe), for treatment of adults with primary hyperlipidemia (including heterozygous familial hypercholesterolemia) to reduce low-density lipoprotein cholesterol (LDL-C).[‡]
- As an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.¹

2. Coverage Criteria^a:

A. Hyperlipidemia

1. Initial Authorization

Repatha will be approved based on **one** of the following criteria:

- a. Member is currently on Praluent (as evidenced by paid claims in the past 120 days) and converting to Repatha, **ALL** of the following:

(1) Patient continues to receive statin at maximally tolerated dose (unless patient has an inability to take statins)

-AND-

(2) Patient is continuing a low-fat diet and exercise regimen

-AND-

(3) Documentation of a positive clinical response to PCSK9 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) Prescriber attests to the following: the information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided

-OR-

b. **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 190 mg/dL (greater than 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 190 mg/dL (greater than 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

-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 CK elevations)
 2. Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

-AND-

ii. **One** of the following:

1. Patient has been receiving at least 12 consecutive weeks of **moderate-intensity** [i.e. atorvastatin 10-20 mg, rosuvastatin 5-10 mg, simvastatin \geq 20 mg, pravastatin \geq 40 mg, lovastatin 40 mg, Lescol XL (fluvastatin XL) 80 mg, fluvastatin 40 mg twice daily or Livalo (pitavastatin) \geq 2 mg] and will continue to receive a moderate-intensity statin at maximally tolerated dose

-OR-

2. Patient has been receiving at least 12 consecutive weeks of **low-intensity** [i.e. simvastatin 10 mg, pravastatin 10-20 mg, lovastatin 20 mg, fluvastatin 20-40 mg, or Livalo (pitavastatin) 1 mg] statin therapy and will continue to receive a low-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 70 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) Used as an adjunct to a low-fat diet and exercise

-AND-

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

-AND-

(6) Prescriber attests to the following: the information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided

*Results of prior genetic testing can be submitted as confirmation of diagnosis of HeFH, however please note that UnitedHealthcare does not currently cover genetic testing for evidence of an LDL-receptor mutation, familial defective apo B-100 or a PCSK9 mutation.

‡ No coverage of Repatha will be provided for the primary prevention of cardiovascular events and/or for the lowering of low-density lipoprotein cholesterol in patients with primary hyperlipidemia who do not have heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease (ASCVD) as the use of PCSK9 inhibitors in this population is not supported by the 2018 American College of Cardiology/ American Heart Association Cholesterol Clinical Practice Guidelines.

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 is continuing a low-fat diet and exercise regimen

-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) Prescriber attests to the following: the information provided is true and accurate to the best of their knowledge and they understand that

UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided

Authorization will be issued for 12 months

B. Homozygous Familial Hypercholesterolemia

1. Initial Authorization

Repatha will be approved based on **ONE** of the following criteria:

a. Member is currently on Praluent (as evidenced by paid claims in the past 120 days) and converting to Repatha, **ALL** of the following:

(1) Patient is continuing a low-fat diet and exercise regimen

-AND-

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

-AND-

(3) Documentation of a positive clinical response to PCSK9 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)

-AND-

(6) Prescriber attests to the following: the information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided

-OR-

b. **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 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) Used as an adjunct to a low-fat diet and exercise
- 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)
- AND-
- (6) Prescriber attests to the following: the information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided

*Results of prior genetic testing can be submitted as confirmation of diagnosis of HoFH, however please note that UnitedHealthcare does not currently cover genetic testing for evidence of an LDL-receptor mutation, familial defective apo B-100 or a PCSK9 mutation.

Authorization will be issued for 12 months.

2. Reauthorization

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

(1) Patient is continuing a low-fat diet and exercise regimen

-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)

-AND-

(6) Prescriber attests to the following: the information provided is true and accurate to the best of their knowledge and they understand that UnitedHealthcare may perform a routine audit and request the medical information necessary to verify the accuracy of the information provided

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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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
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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.

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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.