

Repatha® (evolocumab)

When requesting Repatha® (evolocumab), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-Approved Indications

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:
 - o adults with hypercholesterolemia.
 - o adults and pediatric patients aged 10 years and older with heterozygous familial hypercholesterolemia (HeFH).
 - o adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH).

Coverage Guidelines

To Reduce Major Adverse Cardiovascular Events (*Note: This includes only patients with established cardiovascular disease*)

The individual must meet all of the following criteria for initial authorization:

- Is 18 years of age or older;
- Has had one of the following conditions or diagnoses:
 - o A previous myocardial infarction or a history of an acute coronary syndrome; OR
 - o Angina (stable or unstable); OR
 - o A past history of stroke or transient ischemic attack; OR
 - o Coronary artery disease; OR
 - o Peripheral arterial disease; OR
 - o Has undergone a coronary or other arterial revascularization procedure in the past (e.g., coronary artery bypass graft surgery, angioplasty, percutaneous coronary intervention, or coronary stent procedures);
- Meets one of the following:
 - o Has tried one high-intensity statin therapy (i.e., atorvastatin $\geq$ 40 mg daily; rosuvastatin $\geq$ 20 mg daily [as a single-entity or as a combination product]) for $\geq$ 8 continuous weeks AND LDL-C level still remains $\geq$ 55 mg/dL; OR

- o Has experienced statin-related rhabdomyolysis (*Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR*
- o Has experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) while receiving separate trials of both atorvastatin and rosuvastatin (as single entity or combination products) and skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin).

Heterozygous Familial Hypercholesterolemia (HeFH)

The individual must meet all of the following criteria for initial authorization:

- Is 10 years of age or older;
- Meets one of the following:
 - o Has an untreated low-density lipoprotein cholesterol (LDL-C) ≥ 190 mg/dL (i.e., prior to treatment with any antihyperlipidemic agents); OR
 - o If the patient is between 10 and 17 years of age with an untreated LDL-C ≥ 160 mg/dL but <190 mg/dL, must have a family history of early atherosclerotic cardiovascular disease (ASCVD) or elevated LDL-C or total cholesterol in a parent; OR
 - o The diagnosis has been confirmed by genetic testing (e.g., pathogenic variants at the low-density lipoprotein receptor [LDLR], apolipoprotein B [APOB], proprotein convertase subtilisin kexin type 9 [PCSK9], or low-density lipoprotein receptor adaptor protein 1 [LDLRAP1] gene); OR
 - o Has been diagnosed with HeFH by meeting one of the following diagnostic criteria thresholds:
 - Dutch Lipid Network criteria score greater than 5; OR
 - Simon Broome criteria met the threshold for 'definite' or 'possible (or probable)' familial hypercholesterolemia;
- Meets one of the following:
 - o Has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single-entity or as a combination product]) for ≥ 8 continuous weeks AND LDL-C level still remains ≥ 70 mg/dL; OR
 - o Has experienced statin-related rhabdomyolysis (*Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR*

- o Has experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) while receiving separate trials of both atorvastatin and rosuvastatin (as single entity or combination products) and skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin).

Homozygous Familial Hypercholesterolemia (HoFH)

The individual must meet all of the following criteria for initial authorization:

- Is 10 years of age or older;
- Meets one of the following:
 - o The diagnosis has been confirmed by genetic testing (e.g., pathogenic variants at the low-density lipoprotein receptor [LDLR], apolipoprotein B [APOB], proprotein convertase subtilisin kexin type 9 [PCSK9], or low-density lipoprotein receptor adaptor protein 1 [LDLRAP1] gene); OR
 - o Has an untreated low-density lipoprotein cholesterol (LDL-C) > 400 mg/dL (i.e., prior to treatment with any antihyperlipidemic agent) OR has a treated LDL-C level ≥ 300 mg/dL (i.e., after therapy with at least one antihyperlipidemic agent) AND meets one of the following:
 - Had clinical manifestation of HoFH before 10 years of age (e.g., cutaneous xanthomas, tendon xanthomas, arcus cornea, tuberous xanthomas, or xanthelasma); OR
 - At least one parent of the patient had untreated LDL-C levels or total cholesterol levels consistent with familial hypercholesterolemia (*Note: an example of familial hypercholesterolemia is an untreated LDL-C ≥ 190 mg/dL and/or an untreated total cholesterol >250 mg/dL;*
- Meets one of the following:
 - o Has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single-entity or as a combination product]) for ≥ 8 continuous weeks AND LDL-C level still remains ≥ 70 mg/dL; OR
 - o Has experienced statin-related rhabdomyolysis (Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR
 - o Has experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) while receiving separate trials of both atorvastatin and rosuvastatin (as single entity or combination products) and skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin).

Hypercholesterolemia

The individual must meet all of the following criteria for initial authorization:

- Is 18 years of age or older;
- Meets one of the following:
 - o Is at risk for atherosclerotic cardiovascular disease (ASCVD), an ASCVD event, or a major adverse cardiovascular event; OR
 - o Has diabetes;
- Meets one of the following:
 - o Has tried one high-intensity statin therapy (i.e., atorvastatin $\geq$ 40 mg daily; rosuvastatin $\geq$ 20 mg daily [as a single-entity or as a combination product] AND LDL-C level still remains $\geq$ 70 mg/dL; OR
 - o Has experienced statin-related rhabdomyolysis (*Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a $\geq$ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]); OR*
 - o Has experienced skeletal-related muscle symptoms (e.g., myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness]) while receiving separate trials of both atorvastatin and rosuvastatin (as single entity or combination products) and skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin).

The individual must meet the following criterion for re-authorization (for all indications):

- Has experienced a response to Repatha therapy (e.g., decreasing LDL-C, total cholesterol, non-high-density lipoprotein cholesterol, or apolipoprotein B levels).
Note: An individual who is currently on therapy but has not been previously approved via EviCore coverage determination or is restarting therapy is reviewed under criteria for initial therapy.

Approval duration (initial and renewal): 12 months

Dosing Recommendations

In adults at increased risk for CV events or with hypercholesterolemia:

The recommended dosage is either 140 mg every 2 weeks or 420 mg once monthly administered subcutaneously.

In adults and pediatric patients aged 10 years and older with HeFH:

The recommended dosage is either 140 mg every 2 weeks or 420 mg once monthly administered subcutaneously.

In adults and pediatric patients aged 10 years and older with HoFH:

The initial recommended dosage is 420 mg once monthly administered subcutaneously. The 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 every 2 weeks to correspond with their apheresis schedule. Administer Repatha after the apheresis session is complete.

References

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6. Rao SV, O'Donoghue ML, Ruel M, et al. 2025 ACC/AHA/ACEP/NAEMSP/SCAI guideline for the management of patients with acute coronary syndromes. *J Am Coll Cardiol*. 2025 Feb 27. [Online ahead of print].
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8. Gidding SS, Champagne MA, de Ferranti SD, et al. The agenda for familial hypercholesterolemia. A scientific statement from the American Heart Association. *Circulation*. 2015;132(22):2167-2192.
9. Haase A, Goldberg AC. Identification of people with heterozygous familial hypercholesterolemia. *Curr Opin Lipidol*. 2012;23:282-289.