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 with established cardiovascular disease
- As an adjunct to diet, alone or combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C
- As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older with HeFH, to reduce LDL-C
- As an adjunct to other LDL-C-lowering therapies in adults and pediatric patients aged 10 years and older with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C

Coverage Guidelines

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:
    - A previous myocardial infarction or a history of an acute coronary syndrome; OR
    - Angina (stable or unstable); OR
    - A past history of stroke or transient ischemic attack; OR
    - Coronary artery disease; OR
    - Peripheral arterial disease; OR
    - 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:
    - 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 ≥ 55 mg/dL; OR

- 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
- 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:
  - Has an untreated low-density lipoprotein cholesterol (LDL-C) ≥ 190 mg/dL (i.e., prior to treatment with any antihyperlipidemic agents); OR
  - 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
  - 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:
  - 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
  - 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
  - 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:
    - 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
    - Has an untreated low-density lipoprotein cholesterol (LDL-C) > 400 mg/dL (i.e., prior to treatment with any antihyperlipidemic agents) 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;
- Meets one of the following:
    - 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
    - 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
    - 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).

Primary Hyperlipidemia

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

- Is 18 years of age or older;
- Meets one of the following:
  - Has a coronary artery calcium or calcification score ≥ 300 Agatston units; OR
  - Has diabetes;
- Meets one of the following:
  - 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]) along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks AND LDL-C level still remains ≥ 70 mg/dL; OR
  - 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
  - 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 criteria for re-authorization – for all indications
(NOTE: Patients who are currently receiving Repatha but has not previously received approval of Repatha or those who are restarting therapy with Repatha should be considered under initial criteria)

- Has experienced a response to therapy (e.g., decreasing low-density lipoprotein cholesterol (LDL-C), total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels).

Approval duration: 12 months

Dosing Recommendations

In adults with established cardiovascular disease or with primary hyperlipidemia:
The recommended dosage is either 140 mg every 2 weeks or 420 mg once monthly administered subcutaneously.

In 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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3. Leqvio® subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis; June 2024.
4. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 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.* 2022;80(14):1366-1418.
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16. 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].
17. Patel SB, Wyne KL, Afreen S, et al. American Association of Clinical Endocrinology clinical practice guideline on pharmacologic management of adults with dyslipidemia. *Endocrine Pract*. 2025;31:236-262.

