He looks to you to **FOCUS ON RISK REDUCTION for MI, stroke and coronary revascularization** in adult patients with ASCVD[1]

Prevention of cardiovascular events

Repatha® (evolocumab injection) is indicated as an adjunct to diet and standard of care therapy (including moderate- to high-intensity statin therapy alone or in combination with other lipid-lowering therapy) to reduce the risk of myocardial infarction, stroke and coronary revascularization in adult patients with atherosclerotic cardiovascular disease (ASCVD) by further lowering low-density lipoprotein cholesterol (LDL-C) levels.[1]

Primary hyperlipidemia (including HeFH and ASCVD)

Repatha® is indicated for the reduction of elevated LDL-C in adult patients with primary hyperlipidemia (including heterozygous familial hypercholesterolemia [HeFH] and ASCVD) as an adjunct to diet and statin therapy, with or without other lipid-lowering therapies, in patients who require additional lowering of LDL-C; or as an adjunct to diet, alone or in combination with non-statin lipid-lowering therapies, in patients for whom a statin is contraindicated.

Repatha®
evolocumab injection

ASCVD=atherosclerotic cardiovascular disease; MI=myocardial infarction
* Fictitious patient. May not be representative of all patients.

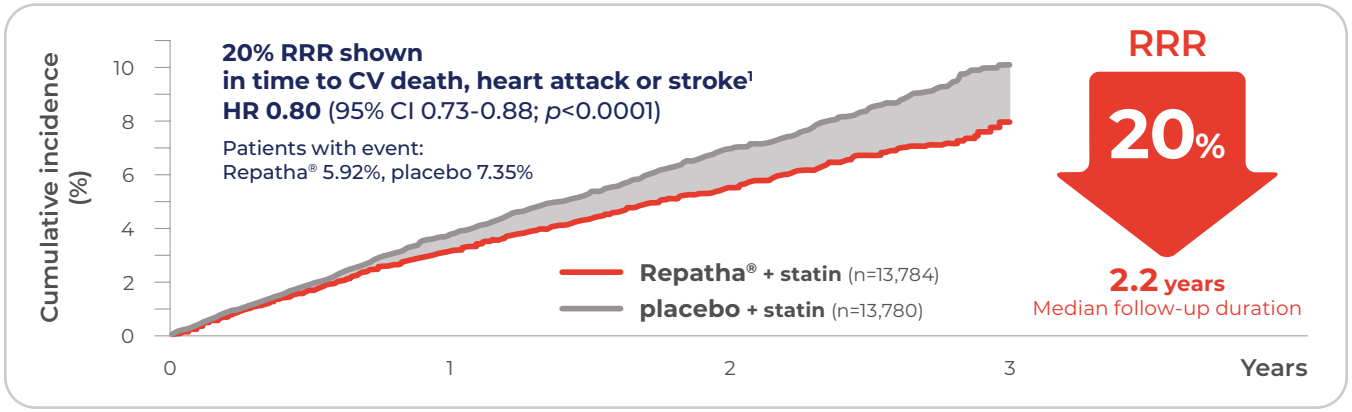


For these patients, consider Repatha® (fictitious patients represented).

Repatha® + statin

FOURIER study: Key secondary endpoint†

Cumulative incidence estimates over 3 years in patients with ASCVD



Time to CV death was not statistically significant vs. placebo (p=0.6188)[1]

Primary composite endpoint:
Demonstrated 15% reduced risk in time to CV death, heart attack, stroke, hospitalization for unstable angina or coronary revascularization, whichever occurred first vs. placebo; HR 0.85 (95% CI 0.79-0.92; p<0.0001). Patients with event: Repatha® 9.75%, placebo 11.34%.[1]

Exploratory analysis:
% change from baseline in LDL-C

Median baseline LDL-C: **2.4 mmol/L**

At week 12: LS (least squares) mean % change from baseline:
-63.11 Repatha® vs. **-2.42 placebo**

LAPLACE-2 study‡

Powerful LDL-C reduction shown in patients with primary hyperlipidemia[1,2]
Overall population included those with ASCVD†

Repatha® Q2W + statin provided an additional 73% LDL-C reduction overall (vs. placebo + statin)[1]

-73%
overall treatment difference[1]
(95% CI -77, -70)
p<0.0001

CV=cardiovascular; LDL-C=low-density lipoprotein cholesterol; Q2W=every 2 weeks; QM=monthly

† FOURIER cardiovascular outcomes study was a phase 3, double-blind, randomized, placebo-controlled, event-driven study to evaluate the effects of Repatha® in patients (N=27,564) with established CVD (history of MI, nonhemorrhagic stroke or symptomatic PAD). Patients had ≥1 additional major risk factors (e.g., diabetes mellitus, current daily cigarette smoking, age ≥65 years or recent MI [within 6 months]) or ≥2 minor risk factors (e.g., history of coronary revascularization, elevated non-HDL-C or metabolic syndrome). Patients were on stable, moderate- to high-intensity statin background therapy at randomization (at least atorvastatin 20 mg daily or equivalent) and, where locally approved, highly effective statin therapy (defined as at least atorvastatin 40 mg daily or equivalent) was recommended.[1]

‡ LAPLACE-2 study design: Phase 3, 12-week, randomized, double-blind, placebo- and ezetimibe-controlled trial (N=1,896) in patients with primary hyperlipidemia (including 526 who had ASCVD) on maximum dose statin therapy. Patients were initially randomized to an open-label specific statin regimen for a 4-week lipid-stabilization period followed by random assignment to Repatha® 140 mg Q2W, Repatha® 420 mg QM or placebo for 12 weeks as add-on to daily statin therapy. Baseline LDL-C 2.8 mmol/L, measured after the lipid stabilization period and before administration of first dose of Repatha®. Primary endpoint: Mean % change from baseline in LDL-C at week 12.[1,2]

Established safety profile – Over 30,000 patient-years of exposure[1]

The safety profile of Repatha® in the CV outcomes trial was consistent with the known safety profile in patients with primary hyperlipidemia[1]

FOURIER summary of adverse events: Repatha® 140 mg Q2W or 420 mg QM[3]

Outcome	Repatha® (n=13,769)	placebo (n=13,756)
Any adverse event	10,664 (77.4%)	10,644 (77.4%)
Serious	3,410 (24.8%)	3,404 (24.7%)
Thought to be related to study agent and leading to discontinuation	226 (1.6%)	201 (1.5%)

Please see the product monograph for complete safety profile information.

Common adverse reactions reported by ≥5% of patients in either treatment group[1] (Repatha® n=13,769, any placebo n=13,756), median duration 2.2 years

Diabetes mellitus: Repatha® 8.8%, placebo 8.2%; nasopharyngitis: Repatha® 7.8%, placebo 7.4%; upper respiratory tract infection: Repatha® 5.1%, placebo 4.8%

Adverse events reported by ≥1% of Repatha® patients with primary hyperlipidemia and HeFH and more frequently than placebo (12-week studies) (Repatha® n=2,052, placebo n=1,224): Nasopharyngitis 4.0%, 3.9%; back pain 2.3%, 2.2%; upper respiratory tract infection 2.1%, 2.0%; nausea 1.8%, 1.2%; arthralgia 1.8%, 1.6%; fatigue 1.6%, 1.0%; urinary tract infection 1.3%, 1.2%; muscle spasms 1.3%, 1.2%; influenza 1.2%, 1.1%; cough 1.2%, 0.7%; contusion 1.0%, 0.5%. (Includes studies LAPLACE-1, LAPLACE-2, RUTHERFORD-1, RUTHERFORD-2, MENDEL-1, MENDEL-2, YUKAWA.)[1]

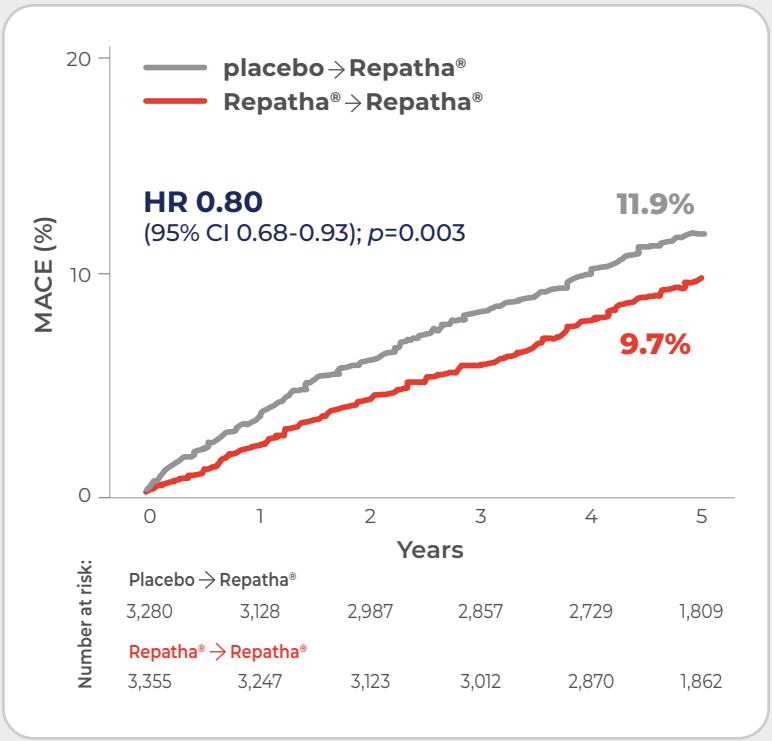
References: 1. Repatha® (evolocumab injection) Product Monograph. Amgen Canada Inc., September 27, 2023. **2.** Robinson JG, *et al.* Effect of evolocumab or ezetimibe added to moderate- or high-intensity statin therapy on LDL-C lowering in patients with hypercholesterolemia: The LAPLACE-2 randomized clinical trial. *JAMA* 2014;311(18):1870-82. **3.** Sabatine MS, *et al.* Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017;376:1713-22. **4.** O'Donoghue ML, *et al.* Long-term evolocumab in patients with established atherosclerotic cardiovascular disease. *Circulation* 2022;146(15):1109-19. **5.** Pearson GJ, *et al.* 2021 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult. *Can J Cardiol* 2021;37:1129-50. **6.** Amgen Data on File – RepathaREADY® copay coverage, July 11, 2023.

Repatha® evolocumab injection

The data in this grey box are sourced from pooled open-label extension studies for exploratory MACE endpoints and reflect a crossover design and change in comparator arm. Data should be interpreted with caution due to risk of bias.

FOURIER-OLE MACE (pre-specified exploratory endpoint)[4¶]

Kaplan-Meier curve for MACE[4§]



Adapted from O'Donoghue ML, *et al.* 2022

FOURIER-OLE: Two open-label extension studies (no concurrent placebo arm) evaluated the long-term safety and efficacy of Repatha® in patients who completed the FOURIER parent study. Primary analyses were pooled across the two studies. Primary endpoint was incidence of adverse events; MACE were prespecified exploratory endpoints. No adjustments were made for multiplicity, thereby increasing the risk for type 1 error.

CI=confidence interval; HR=hazard ratio; MACE=major adverse cardiovascular event; OLE=open-label extension
¶ The study parameters for these data can be found on the back of this flap.
§ Time 0 reflects entry into FOURIER-OLE.

Percent change from baseline in LDL-C

FOURIER study (exploratory endpoint):

At Week 12:

LS mean % change from baseline in LDL-C: -63.11 Repatha®, -2.42 placebo

Of Repatha®-treated patients: 9,518 (69.1%) achieved at least one LDL-C value <0.65 mmol/L

FOURIER-OLE post-baseline LDL-C levels

In the FOURIER-OLE studies, the observed mean percent reduction from baseline in LDL-C ranged from 53.4% to 67.2%. The subject incidences of achieving a post-baseline LDL-C level <1.03 mmol/L following treatment ranged from 54.6% to 76.1%.[1]

LDL-C=low-density lipoprotein cholesterol; LS=least squares; OLE=open-label extension; Q2W=every 2 weeks; QM=monthly

¶ FOURIER-OLE consisted of two OLE studies to evaluate the long-term safety and efficacy of Repatha® in patients who completed the FOURIER parent study. All patients received Repatha® 140 mg Q2W or 420 mg QM for approximately 5 years. A total of 6,630 patients received at least one dose of Repatha®.

Canadian Cardiovascular Society 2021

LDL-C treatment threshold for treatment intensification: ≥1.8 mmol/L (or non-HDL-C ≥2.4 mmol/L or ApoB ≥0.7 g/L)[5]

CCS recommends a PCSK9i (+/- ezetimibe) in secondary CV prevention patients on a maximally tolerated statin dose

See CCS Guidelines for full recommendations.
ApoB=apolipoprotein B; CCS=Canadian Cardiovascular Society; CV=cardiovascular; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; PCSK9i=proprotein convertase subtilisin-kexin type 9 inhibitor

A Canadian development

Repatha® evolocumab injection

Repatha® + statin

-73% **LDL-C reduction**[1]
Patients with primary hyperlipidemia (LAPLACE-2 study primary endpoint)

20% **Provided significant risk reduction in time to MI, stroke or CV death,** whichever occurred first vs. placebo + statin (secondary endpoint)[1]

Established safety profile[1]
Common adverse reactions reported (≥5% of patients in Repatha® and placebo treatment groups): diabetes mellitus (8.8%, 8.2%), nasopharyngitis (7.8%, 7.4%), upper respiratory tract infection (5.1%, 4.8%)

FIXED DOSE
FOR YOUR REPATHA® PATIENTS
140 mg Q2W OR
420 mg QM

RepathaREADY® PATIENT SUPPORT PROGRAM

by AMGEN Entrust® Patient Support Services#

Personalized support for you and your patients – to help get started and stay with Repatha®

- One-step enrolment
- Access to Repatha® navigation
- Getting started and patient reminders

Up to 100% of the drug cost is covered for all eligible Repatha® patients with private insurance deductibles.**

With RepathaREADY® copay support, the majority of private insurance patients have $0 out-of-pocket costs.[6]

Contraindications:

- Hypersensitivity to Repatha® or to any ingredient in the formulation, including any non-medicinal ingredient or component of the container
- Refer to the Contraindications section of the relevant product monographs of any concomitant lipid-lowering medications

Relevant warnings and precautions:

- Refer to the Warnings and Precautions section of the relevant product monographs of any concomitant lipid-lowering medications
- Hypersensitivity reactions (e.g., rash, urticaria, angioedema) have been reported. If signs or symptoms of serious allergic reactions occur, discontinue Repatha® and treat according to standard of care and monitor until signs and symptoms resolve
- No studies have been conducted with Repatha® in pregnant women or nursing women and relevant data from clinical use are very limited
- There is no information regarding the presence of evolocumab in human milk, the effects on the breastfed infant, or the effects on milk production; a risk to breastfed infants cannot be excluded
- Statin product monographs recommend discontinuation when a patient becomes pregnant, therefore Repatha® should also be discontinued
- Data on efficacy and safety in HoFH patients aged 10-11 years are limited
- Efficacy and safety have not been established in pediatric patients <10 years of age with HeFH, HoFH or in pediatric patients with other types of hyperlipidemia
- Use with caution in patients with severe renal impairment
- Use with caution in patients with severe hepatic impairment
- Needle cap of the SureClick® autoinjector contains dry natural rubber, which may cause an allergic reaction in latex-sensitive patients
- Effects of Repatha® in patients with or at risk of hepatitis C virus infection remain uncertain

For more information:

Please consult the Product Monograph at www.amgen.ca/Repatha_PM.pdf for further details regarding the Warnings and Precautions, as well as important information relating to adverse reactions, drug interactions and dosing information which have not been mentioned in this piece.

The Product Monograph is also available by calling Amgen at 1-866-502-6436.

SC=subcutaneous
# AMGEN Entrust is our unified patient support services platform, built on the legacy of our branded support programs.
** Coverage support does not include pharmacy acquisition cost mark-up or dispensing fee.

AMGEN Entrust® RepathaREADY®

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MEMBER OF INNOVATIVE MEDICINES CANADA

AMGEN Cardiovascular

CAN-145-0822-80006-25E

Electronic Certificate

Version: 4 . 0

Document Number: CAN-145-0822-80006

Document Name: Repatha Core Leave Behind

Country: Canada

Product: Repatha

Branding: Branded

Type: GRP Material

Sub Type: Advertisement

Classification:

Material Intent: Promotional

Expiration Date: 31 Dec 2025

Certification Statement
We certify that the final electronic form of this material is in accordance with the regulations set forth by the health authority (where applicable) for the country of this document, and is a fair and truthful presentation of the facts about the product.

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