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.[1]

Primary hyperlipidemia (including HeFH)

Repatha® is indicated for the reduction of elevated low-density lipoprotein cholesterol (LDL-C) in adult patients with primary hyperlipidemia (including heterozygous familial hypercholesterolemia [HeFH]) 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.

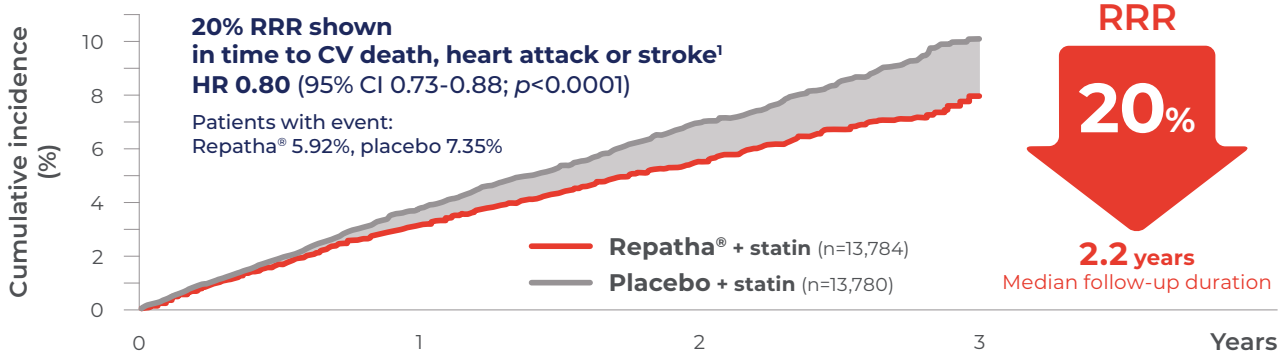
Repatha®
evolocumab injection

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

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 32,000 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., October 30, 2020. **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):1870-83. **3.** Sabatine MS, *et al.* Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017;376:1713-22. **4.** 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. **5.** Amgen letter, August 18, 2012; IQVIA. Compuscript. National TRX Volume; claims database, July 2020-June 2021. **6.** Amgen Data on File – RepathaREADY® Assist card coverage, October 10, 2019. **7.** Amgen letter, October 16, 2019. **8.** Amgen letter, June 1, 2021.

Repatha®
evolocumab injection

Canadian Cardiovascular Society 2021

Select recommendations for intensification of lipid-lowering therapy for secondary prevention ASCVD patients

LDL-C threshold for treatment intensification: ≥1.8 mmol/L[4]*
(or non-HDL-C ≥2.4 mmol/L or ApoB ≥0.7 g/L)

For patients **appropriate for PCSK9 inhibitor therapy** in whom LDL-C remains **≥1.8 mmol/L** on maximally tolerated statin dose, e.g., those with recent acute coronary event (ACS) (hospitalized index ACS to 52 weeks post index ACS):

- Add PCSK9 inhibitor +/- ezetimibe[4]

For **all secondary prevention patients** in whom LDL-C remains **≥1.8 mmol/L** on maximally tolerated statin dose:

- Add ezetimibe +/- PCSK9 inhibitor[4]

Additional lipid-lowering therapy with ezetimibe and PCSK9 inhibitors may also be considered for **ASCVD patients with an LDL-C <1.8 mmol/L, especially for patients considered to be at high risk for recurrent ASCVD events**.[4]

ApoB=apolipoprotein B; ASCVD=atherosclerotic cardiovascular disease; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; PCSK9=proprotein convertase subtilisin/kexin type 9

Repatha® is a self-administered subcutaneous injection

Convenience of at-home self-injection[1]*

Biweekly single-use
prefilled SureClick® autoinjector (15 sec)[1]

Once-monthly
single-use automated mini-doser[1]

Repatha®: Clinically equivalent 140 mg Q2W and 420 mg QM dosing

Repatha® can be stored at room temperature for up to 30 days.[1]

As standard practice, Repatha® should be stored in the refrigerator (2°C to 8°C) in the original carton. If removed from the refrigerator, Repatha® should be kept at controlled room temperature up to 25°C in the original carton and must be used within 30 days. Protect from direct light and temperatures above 25°C. Do not freeze. Do not shake.

Please see the Product Monograph for complete dosing and drug interaction information.

Fixed dose for your Repatha® patients
140 mg Q2W or 420 mg QM

* Repatha® is intended for patient self-administration after proper training. Administration should be performed by an individual who has been trained to administer the product.[1]

A Canadian development

Repatha® is the #1 dispensed PCSK9i in Canada[5]

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

RepathaREADY® Assist card provides up to 30% copay support for your patients[6,7]

With the RepathaREADY® Assist card, the majority of Private Insurance patients have $0 out-of-pocket costs.[8]

Enrol your patients and follow their treatment journey through the RepathaREADY® PatientCare Portal

Contraindications:

- Hypersensitivity to Repatha® or to any ingredient in the formulation 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 and relevant data from clinical use are very limited
- Statin product monographs recommend discontinuation when a patient becomes pregnant, therefore Repatha® should also be discontinued
- Not recommended for use in nursing women or in pediatric patients with primary 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; there is no dry natural rubber in the automated mini-doser with prefilled cartridge
- Effects of Repatha® in patients with or at risk of hepatitis C virus infection remain uncertain

For more information:

Consult the Product Monograph at www.amgen.ca/Repatha_PM.pdf for important information relating to adverse reactions, drug interactions and dosing information which have not been discussed in this piece.

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

SC=subcutaneous

* AMGEN Entrust is our new unified patient support services platform, built on the legacy of our branded support programs.

AMGEN Entrust™ RepathaREADY®

REVIEWED BY PAAB

MEMBER OF INNOVATIVE MEDICINES CANADA

AMGEN® Cardiovascular

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