A Canadian development | Repatha® is the #1 dispensed PCSK9i in Canada[1]

Help your patients reduce the risk of MI, stroke and coronary revascularization[2]

Add on to diet and standard of care therapy

(including moderate- to high-intensity statin therapy alone or in combination with other lipid-lowering therapy)[2]

In patients with atherosclerotic CVD*

Repatha® + statin provided

20% **reduced risk in time to MI, stroke or CV death**

whichever occurred first vs. placebo + statin[2]

Key secondary endpoint

HR 0.80 (95% CI 0.73-0.88; $p<0.0001$)

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

Repatha® 140 mg Q2W (86%) or 420 mg QM

Median follow-up duration 2.2 years

Repatha® (evolocumab) 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.

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.

CV=cardiovascular; CVD=cardiovascular disease; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; MI=myocardial infarction; PAD=peripheral artery disease; PCSK9i=proprotein convertase subtilisin/kexin type 9 inhibitor; Q2W=every 2 weeks; QM=monthly

* FOURIER ardiovascular 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.

Pr Repatha® (evolocumab)

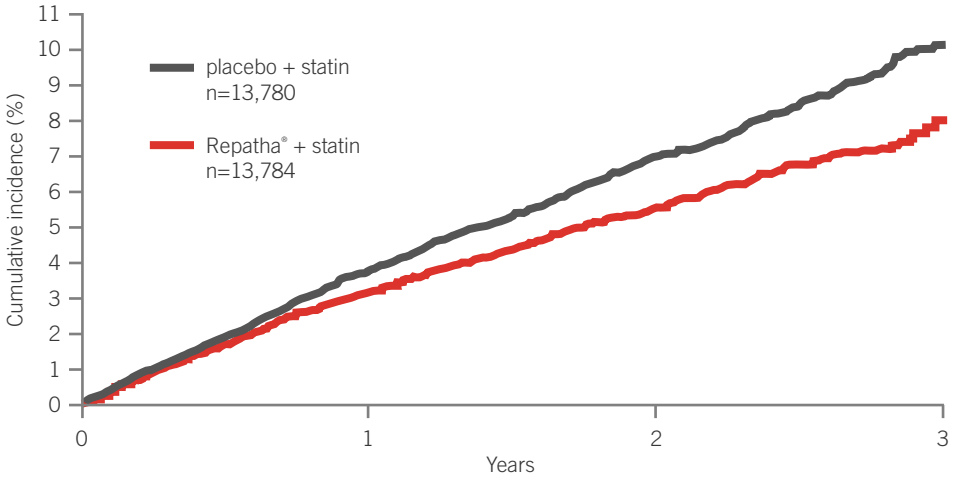
Repatha® + statin

Key secondary endpoint

Demonstrated significant risk reduction in time to MI, stroke or CV death, whichever occurred first vs. placebo + statin[2]

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

Cumulative incidence estimates for key secondary endpoint over 3 years



20% RRR in time to CV death, heart attack or stroke

HR 0.80 (95% CI 0.73-0.88; p<0.0001)

Patients with event: Repatha® 5.92%, placebo 7.35%

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[2]

HR 0.85 (95% CI 0.79-0.92; p<0.0001)

Patients with event: Repatha® 9.75%, placebo 11.34%

Repatha® demonstrated LDL-C reduction[2]

Exploratory endpoint

63% reduction in LDL-C with Repatha® vs. 2% placebo

LS mean % change from baseline at week 12

LS=least squares; RRR=relative risk reduction

Repatha® is a self-administered subcutaneous injection

Biweekly single-use prefilled SureClick® autoinjector (15 sec)[2]

Once-monthly single-use automated mini-doser (9 min)[2]

Repatha®: Clinically equivalent 140 mg Q2W and 420 mg QM dosing[2]

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.

Established safety profile – Over 32,000 patient-years of exposure

The safety profile of Repatha® in the CV outcomes trial was consistent with the known safety profile in patients with primary hyperlipidemia[2]

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

Common adverse reactions reported by ≥5% of patients in either treatment group[2]
(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%

No neutralizing antibodies were observed in Repatha® clinical studies.[2]

The presence of anti-evolocumab binding antibodies did not impact the pharmacokinetic profile, clinical response or safety of Repatha®.

In clinical studies, 0.3% (48/17,992) of patients treated with at least one dose of Repatha® tested positive for the development of anti-evolocumab binding antibodies; 0.2% (39) of these had transient antibodies. Of the patients whose sera tested positive for binding antibodies, who were further evaluated for neutralizing antibodies, none tested positive for neutralizing antibodies.

Repatha® can be stored at room temperature for up to 30 days.[2]

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® + statin

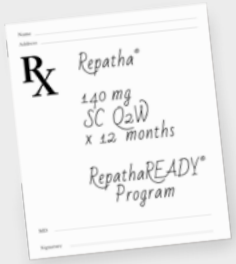
Demonstrated LDL-C reduction[2]

20% **Provided significant risk reduction in time to MI, stroke or CV death,** whichever occurred first vs. placebo + statin (secondary endpoint)[2]

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

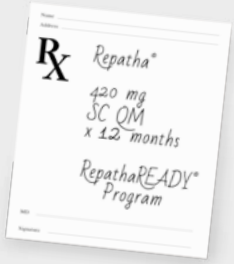
Established safety profile[2]

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%)



RepathaREADY®
PATIENT SUPPORT PROGRAM
YOUR PARTNER IN CARE, EVERY STEP OF THE WAY

- ONE-STEP ENROLMENT
- ACCESS TO REPATHA® NAVIGATION
- GETTING STARTED AND PATIENT REMINDERS



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

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

Other relevant warnings and precautions:
- 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 of Repatha® in patients with severe renal impairment is not recommended
- 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:
Please 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

References: 1. IQVIA. PharmaSTAT Claims database; November 2016 to October 2017. **2.** Repatha® (evolocumab) Product Monograph. Amgen Canada Inc., June 11, 2019. **3.** Sabatine MS, *et al.* Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* 2017;376:1713-22.

Pr Repatha® (evolocumab)

PAAB

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