# Drug Coverage Decision for B.C. PharmaCare

**About PharmaCare** B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

**Details of Drug Reviewed**

| | |
|---|---|
| **Drug** | **evolocumab** |
| Brand Name | Repatha® |
| Dosage Forms | 140 mg/mL prefilled syringe or autoinjector for subcutaneous injection<br>420 mg/3.5 mL automated mini-doser with prefilled cartridge |
| Manufacturer | Amgen Canada Inc. |
| **Submission Type** | **New Indication** |
| Use Reviewed | Clinical artherosclerotic cardiovascular disease (ASCVD) |
| Common Drug Review (CDR) | Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: www.cadth.ca/sites/default/files/cdr/complete/SR0515_Repatha_Resubmission_complete_Nov_24_17.pdf |
| Drug Benefit Council (DBC) | DBC met on December 4, 2017. DBC considered the following: final review completed by the CDR on November 22, 2017, which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). DBC also considered Clinical Practice Reviews from two specialists and one general practitioner, a budget impact assessment (BIA) and patient input questionnaire responses from seven patients and three caregivers. |
| **Drug Coverage Decision** | **No- benefit** |
| Date | March 10, 2020 |

| | |
|---|---|
| Reasons | **Drug coverage decision is consistent with the CDEC and DBC recommendations.**<br>• Evolocumab, with optimized statin therapy, demonstrated superiority over placebo in reducing some major cardiovascular (CV) events, but the absolute reductions were relatively small and there was no reduction in the risk of death.<br>• In 2017, DBC recommended evolocumab not be listed for ASCVD.<br>• At the submitted price, evolocumab was not considered cost-effective for ASCVD. The Ministry participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer which were not able to address the concerns identified by the CDEC with respect to the cost-effectiveness and value for money. |
| Other Information | Evolocumab is a Limited Coverage drug for heterozygous familial hypercholesterolemia (HeFH). |

**The Drug Review Process in B.C.**

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry. The DBC looks at:

- whether the drug is safe and effective
- advice from a national group called the Common Drug Review (CDR)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit The Drug Review Process in B.C. - Overview and Ministry of Health - PharmaCare for more information.

**This document is intended for information only.**
It does not take the place of advice from a physician or other qualified health care provider.

# Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation
# FINAL

**Evolocumab (Repatha™) Amgen Canada Inc.**

**Description:**
Drug review of **evolocumab (Repatha™)** for the following Health Canada approved indications:

> As an adjunct therapy for lowering of low density lipoprotein cholesterol (LDL-C) in adults with clinical atherosclerotic cardiovascular disease (ASCVD).

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on November 22, 2017, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 7 patients and 3 caregivers, patient input to the CDR review from one Patient Group, Clinical Practice Reviews from two specialists and one general physician, and a Budget Impact Assessment.

**Dosage Forms:**

Repatha™ is available as evolocumab 140 mg/mL prefilled autoinjectors for subcutaneous injection.

**Recommendations:**

1. The Drug Benefit Council (DBC) recommends that evolocumab (Repatha™) not be listed for lowering of LDL-C in adults with clinical ASCVD.

**Reasons for the Recommendation:**

**1. Summary**

- Two double-blinded randomized controlled trials (DB RCTs) found evolocumab was superior to placebo in reducing some major cardiovascular (CV) events, but the absolute reductions were relatively small and there was no reduction in the risk of death.
- The annual cost of evolucumab is significantly more than most other comparators, including statins and cholesterol-lowering agents, and there is a high risk of off-label use in other populations requiring reductions in LDL-C.

**2. Clinical Efficacy**

- The DBC considered the CDEC clinical review, which included two DB RCTs (FOURIER and GLAGOV) that compared evolocumab to placebo in patients with ASCVD not at LDL-C target despite maximized statin therapy.
- The primary outcome of FOURIER was a composite of major CV events: CV death, myocardial infarction (MI), stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary outcome was a composite of CV death, MI or stroke. Other secondary outcomes were all-

cause mortality, as well as individual components of the composite, and other composites such as CV death or hospitalization for worsening heart failure and ischemic fatal or non-fatal stroke or transient ischemic attack.

- FOURIER demonstrated superiority of evolocumab over placebo for the primary composite endpoint, as well as the key secondary composite of CV death, MI or stroke. However, the treatment effect was small for each of these endpoints (an absolute difference between evolocumab and placebo of 1.5% for each endpoint), and the clinical significance of such a difference is not clear.
- The DBC noted that the large reduction in LDL-C seen in FOURIER resulted in relatively small reductions in major CV events and no reduction in the risk of death.
- The primary outcome of GLAGOV was the change from baseline to week 78 in percent atheroma volume, and secondary outcomes included the nominal change in total atheroma volume to week 78, or participants with plaque regression at 78 weeks. While GLAGOV met its primary outcome, demonstrating superiority of evolocumab over placebo for reduction in percent atheroma volume, the clinical significance of this finding is less clear.
- For detailed information on the systematic review of Repatha™ please see the CDEC Final Recommendation at: https://www.cadth.ca/evolocumab-0.

**3. Safety**

- There was no clear difference between evolocumab and placebo with respect to serious adverse events or adverse events in either study. Notable harms such as neurocognitive, muscle-related and hepatic events were also similar between evolocumab and placebo. There was a slight numerical increase in risk of injection site reactions with evolocumab over placebo, which is not uncommon with monoclonal antibodies.
- The duration of follow up (which for FOURIER was a median of 26 months, and for GLAGOV was 78 weeks) is likely not adequate to assess long term safety of PCSK9 inhibition.
- The relative efficacy and harms of evolocumab versus other available therapies such as alirocumab or ezetimibe is currently unknown. For detailed information on the safety and tolerability of Repatha™, please see the CDEC Final Recommendations at the link above.

**4. Economic Considerations**

- At the manufacturer submitted price, the annual cost of therapy with evolocumab is comparable to alirocumab, but is significantly more expensive than the statins or ezetimibe.
- The CDR re-analysis of the manufacturer's economic submission found that, at the recommended dose, the incremental cost utility ratio (ICUR) for evolocumab plus standard of care (SOC) vs. SOC is $1,007,961 per quality-adjusted life year (QALY), while the ICUR for evolocumab plus SOC vs. ezetimibe plus SOC is $1,478,417 per QALY. The CDR concluded a price reduction of more than 90% would be required for the ICUR for evolocumab to fall to $50,000 per QALY when compared to statins alone or ezetimibe plus statins.

**5. Of Note**

- Several of the patient responses were from people who has tried evolocumab. Some patients had experienced difficulty reaching LDL-C targets using statins, or had intolerable responses to statins (severe muscle pain was the most commonly reported reason), and found evolocumab enabled them to reach LDL-C targets without experiencing severe adverse events.