

# 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

<b>Drug</b>	<b>evolocumab</b>
Brand Name	Repatha™
Dosage Forms	140 mg / mL prefilled syringe or autoinjector for subcutaneous injection 420 mg / 3.5 ml automated mini-doser with prefilled cartridge
Manufacturer	Amgen Canada Inc.
<b>Submission Type</b>	<b>New Submission</b>
Use Reviewed	Heterozygous familial hypercholesterolemia (HeFH)
Common Drug Review (CDR)	Yes, CDR recommended: <b>to Reimburse with clinical criteria and/or conditions.</b> Visit the CDR website for more details: <a href="http://www.cadth.ca/sites/default/files/cdr/complete/SR0441_complete_Rapatha-Feb-23_16_e.pdf">www.cadth.ca/sites/default/files/cdr/complete/SR0441_complete_Rapatha-Feb-23_16_e.pdf</a>
Drug Benefit Council (DBC)	DBC met on March 7, 2016. DBC considered various inputs including: final review completed by the CDR on February 19, 2016, which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from two patients, CDR Patient Group Input Submissions, Clinical Practice Reviews from two specialists, a Budget Impact Assessment (BIA), and a December 2015 Canadian Agency for Drugs and Technologies in Health (CADTH) report on Issues in emerging Health Technologies titled “PCSK9 Inhibitor Monoclonal Antibodies for the Treatment of Hypercholesteremia.”
<b>Drug Coverage Decision</b>	<b>Limited Coverage.</b> Access the evolocumab criteria from: <a href="http://www.gov.bc.ca/pharmacarespecialauthority">www.gov.bc.ca/pharmacarespecialauthority</a>
Date	December 18, 2018
Reasons	<b>Drug coverage decision is consistent with the DBC recommendation.</b> <ul style="list-style-type: none"> <li>• Evolocumab, with or without concurrent ezetimibe and statin therapy, demonstrated superiority over placebo in lowering LDL-C levels.</li> <li>• In 2016, DBC reviewed evolocumab and recommended evolocumab not be listed at the submitted price for HEFH and not be listed for patients with clinical atherosclerotic cardiovascular disease (CVD). In 2017, CDR reviewed new evidence for evolocumab for atherosclerotic CVD and this indication is still under review by the Ministry.</li> <li>• BC participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer for HeFH and an agreement was reached and concerns identified by the DBC in 2016 with respect to the cost-effectiveness were addressed.</li> </ul>
Other Information	None

### 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 [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:

For the treatment of high-risk patients with primary hyperlipidemia or mixed dyslipidemia who have experienced a prior cardiovascular event (CV) and who cannot reach the low density lipoprotein cholesterol (LDL-C) target with standard of care.

For the treatment of heterozygous familial hypercholesterolemia (HeFH) patients who are not at the LDL-C target with standard of care.

In their review, the DBC considered the following: final review completed by the Common Drug Review (CDR) on February 19, 2016, which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from two patients, CDR Patient Group Input Submissions, Clinical Practice Reviews from two specialists, a Budget Impact Assessment, and a December 2015 CADTH report on Issues in emerging Health Technologies titled "PCSK9 Inhibitor Monoclonal Antibodies for the Treatment of Hypercholesteremia."

#### **Dosage Forms:**

Repatha™ is available as evolocumab 140 mg/mL prefilled syringe or autoinjector for subcutaneous injection.

### Recommendations:

1. The Drug Benefit Council (DBC) recommends that **evolocumab (Repatha™)** not be listed at the submitted price.
2. If price negotiations are successful and price is reduced, evolocumab could be listed as an adjunct to diet and maximally tolerated statin therapy in adult patients with heterozygous familial hypercholesterolemia (HeFH), who require additional lowering of low density lipoprotein cholesterol (LDL-C), if the following clinical criteria and condition are met:
  - a. Clinical Criteria:
    - i. Patient has a confirmed diagnosis of HeFH.
    - ii. Patient is unable to reach LDL-C target (i.e., LDL-C < 2.0 mmol/L).
    - iii. Patient is currently receiving optimally tolerated standard of care (typically statins with or without ezetimibe).
3. The Drug Benefit Council (DBC) recommends that **evolocumab (Repatha™)** not be listed as an adjunct to diet and maximally tolerated statin therapy in adult patients with clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of LDL-C.

### Reasons for the Recommendation:

#### 1. Summary

- Four double-blind randomized controlled trials (RCT) demonstrated that evolocumab (140 mg every two weeks or 420 mg once per month) was statistically significantly superior to placebo, with or without concurrent ezetimibe and background statin therapy, at lowering LDL-C levels.
- Only the RUTHERFORD-2 study required patients to have HeFH. In RUTHERFORD-2, the evolocumab groups were statistically significantly superior to the placebo groups for reducing LDL-C at 10/12 weeks and 12 weeks.
- The effect of evolocumab on cardiovascular morbidity and mortality has not been determined.
- There is insufficient evidence from the four trials to evaluate the clinical benefit of evolocumab for reducing the risk of cardiovascular events in patients with clinical atherosclerotic CVD. The manufacturer is currently conducting another RCT (FOURIER) to evaluate the impact of evolocumab in combination with statin therapy on major cardiovascular events in patients with CVD.
- The included studies were not powered to assess harms such as adverse events, serious adverse events, or withdrawals due to adverse events.
- At the submitted price, the daily cost of evolocumab is significantly more than statins alone or ezetimibe plus statins.

#### 2. Clinical Efficacy

- The DBC considered the Common Drug Review Clinical Report for evolocumab, which included four double-blind randomized controlled trials (RCTs) (LAPLACE-2, RUTHERFORD-2, DESCARTES, and GAUSS-2) for which the primary

outcome was the percentage change from baseline in LDL-C. All studies were designed to assess the superiority of evolocumab versus either ezetimibe or placebo, depending on the comparator in the study.

- For detailed information on the clinical efficacy of evolocumab, please see the CDEC Final Recommendation at: [https://www.cadth.ca/sites/default/files/cdr/complete/SR0441\\_complete\\_Rapatha-Feb-23\\_16\\_e.pdf](https://www.cadth.ca/sites/default/files/cdr/complete/SR0441_complete_Rapatha-Feb-23_16_e.pdf).

### **3. Safety**

- The included studies were not powered to assess harms such as adverse events, serious adverse events, or withdrawals due to adverse events.
- For detailed information on the safety and tolerability of evolocumab, please see the CDEC Final Recommendation at: [https://www.cadth.ca/sites/default/files/cdr/complete/SR0441\\_complete\\_Rapatha-Feb-23\\_16\\_e.pdf](https://www.cadth.ca/sites/default/files/cdr/complete/SR0441_complete_Rapatha-Feb-23_16_e.pdf).

### **4. Economic Considerations**

- The DBC considered the CDR Pharmacoeconomic Report for evolocumab, which reported that, upon reanalysis of the manufacturer's economic submission, evolocumab is a cost-effective treatment option only for patients with HeFH who are unable to meet target LDL-C levels with currently available therapies.
- At the submitted price, the daily cost of evolocumab is significantly more than statins alone or ezetimibe plus statins.

### **5. Of Note**

- The DBC considered Patient Input Questionnaire responses from two patients who reported having high LDL and high risk for cardiovascular disease. It was not clear if either patient had a confirmed diagnosis of HeFH. Patients wanted a medication that reduced LDL-C, reduced risk of heart attack or stroke, and was more tolerable than statins or ezetimibe.