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

<table>
<thead>
<tr>
<th>Drug</th>
<th>ezetimibe</th>
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</thead>
<tbody>
<tr>
<td>Brand Name</td>
<td>Ezetrol and generics</td>
</tr>
<tr>
<td>Dosage Form</td>
<td>10 mg tablets</td>
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<tr>
<td>Manufacturer</td>
<td>Merck Canada Inc. and generic manufacturers</td>
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</table>

Submission Type: Ministry initiated submission

Use Reviewed: Heterozygous Familial Hypercholesterolemia (HeFH) and hypercholesterolemia

Common Drug Review (CDR): No, CDR did not review ezetimibe.


Drug Coverage Decision

Limited Coverage. Access the ezetimibe criteria from www.gov.bc.ca/pharmacarespecialauthority

Regular Benefit for Plan W: December 18, 2018

Reasons

Drug coverage decision is consistent with the DBC recommendation.

- Ezetimibe, when added to statin therapy, demonstrated advantage over placebo in reducing low density lipoprotein cholesterol (LDL-C) and improved cardiovascular outcomes.
- Cost of ezetimibe at generic price is similar to cost of least costly statins.

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

Ezetimibe (Ezetrol® and generics)
Merck Canada Inc. and various generic manufacturers

Description:

Drug review of ezetimibe (Ezetrol® and generics) for the following Health Canada approved indications:

Heterozygous Familial Hypercholesterolemia (HeFH) and hypercholesterolemia.

In their review, the DBC considered the following: the Ezetrol® product monograph, the results of the Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) published June 3, 2015 in the New England Journal of Medicine; the 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult; a Systematic Literature Review published November 25, 2016 by the Centre for Population Health Research; and a Budget Impact Assessment.

The DBC was asked to provide an answer to the question: based on the evidence provided, what is your recommendation to the British Columbia Ministry of Health (the Ministry) regarding the PharmaCare coverage status of ezetimibe (Ezetrol® and generics) for the treatment of:

1. Heterozygous Familial Hypercholesterolemia (HeFH); and
2. hypercholesterolemia

Dosage Forms:
Ezetimibe (Ezetrol and generics) Continued...

Ezetimibe is available as 10 mg tablet.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that ezetimibe (Ezetrol® and generics) should be listed as a benefit.

Reasons for the Recommendation:

1. Summary
   - Ezetimibe monotherapy significantly reduced low density lipoprotein cholesterol (LDL-C) concentrations compared with placebo, and significant potentially favourable changes were also observed in total cholesterol and high density lipoprotein cholesterol (HDL-C).
   - When added to statin therapy, ezetimibe resulted in incremental lowering of LDL-C levels and improved cardiovascular outcomes.
   - At current manufacturer list prices, the annual cost of ezetimibe monotherapy is similar to most statins and significantly lower than evolocumab and alirocumab. The annual cost of ezetimibe in combination with a statin is still significantly lower than evolocumab and alirocumab.

2. Clinical Efficacy
   - The Systematic Literature Review provided by the Centre for Population Health Research (which included meta-analyses of eight studies for LDL-C and nine studies for HDL-C) concluded that ezetimibe monotherapy significantly reduced LDL-C concentrations compared with placebo, and significant potentially favourable changes were also observed in total cholesterol and HDL-C.
   - The combination of ezetimibe with a statin significantly reduced LDL-C and significantly increased HDL-C. Results of the studies that up-titrated the statin doses to achieve LDL-C targets generally showed that the co-administration of ezetimibe and statin was more effective in reducing LDL-C than statin monotherapy.

3. Safety
   - Ezetimibe monotherapy appeared to be well tolerated with a safety profile similar to placebo. Ezetimibe in combination with a statin has a similar safety profile to a statin monotherapy.

4. Economic Considerations
   - At current manufacturer list prices, the annual cost of ezetimibe monotherapy is similar to most statins and significantly lower than evolocumab and alirocumab. The annual cost of ezetimibe in combination with a statin is still significantly lower than evolocumab and alirocumab.
   - Listing ezetimibe as a PharmaCare benefit would most likely result in a modest budget impact.
5. Of Note

- Ezetimibe, administered alone or with a statin, is indicated for the reduction of elevated total cholesterol, LDL-C, apolipoprotein B, and triglycerides and to increase HDL-C in patients with primary (heterozygous familial and non-familial) hypercholesterolemia.

- Ezetimibe, administered with a statin, is indicated for the reduction of elevated total cholesterol and LDL-C levels in patients with HoFH as an adjunct to treatments such as LDL apheresis or if such treatments are not possible.