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	**icosapent ethyl**
Brand Name	Vascepa®
Dosage Forms	0.5 mg and 1 mg capsules
Manufacturer	HLS Therapeutics Inc.
Submission Type	**New Submission**
Use Reviewed	for prevention of cardiovascular events in statin-treated patients
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	Yes, the CRR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details: www.cadth.ca/sites/default/files/cdr/complete/SR0619%20Vascepa%20-%20CDEC%20Final%20Recommendation%20July%2020%2C%202020_for%20posting.pdf
Drug Benefit Council (DBC)	The DBC met on August 10, 2020. The DBC considered various inputs including: the final reviews completed by the CRR on July 16, 2020, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups. The DBC also considered Clinical Practice Reviews from one specialist, and a Budget Impact Assessment.
Drug Coverage Decision	**Non-Benefit**
Date	July 6, 2023.
Reasons	Drug coverage decision is consistent with the DBC recommendation: • Icosapent ethyl demonstrated a reduction in major cardiovascular events in patients with established cardiovascular disease. • The Ministry participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer but was not able to complete a product listing agreement.
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 Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews(CRR)
- 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.

Appendix

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Icosapent ethyl (Vascepa®)

HLS Therapeutics Inc.

Description:

Drug review of **icosapent ethyl (Vascepa®)** for the following Health Canada approved indications:

> For risk reduction of ischemic cardiovascular events in statin-treated patients with elevated triglycerides, patients with established cardiovascular disease (CVD), or patients at high risk of CVD.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on July 16, 2020, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups, and the CDR similarly received no patient input. The DBC also considered Clinical Practice Reviews from one specialist, and a Budget Impact Assessment.

Dosage Forms:

Vascepa® is available as icosapent ethyl 0.5 mg and 1 mg capsules.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that icosapent ethyl (Vascepa®) not be listed at the submitted price.
2. If a significant price reduction is achieved, the DBC recommends the following coverage criteria:

Initiation Criteria

1. Patients aged 45 years or older with established cardiovascular disease (CVD) (secondary prevention population).
2. Patients must have a fasting TG of 1.7 mmol/L or greater and lower than 5.6 mmol/L at baseline, measured within the preceding three months before starting treatment with icosapent ethyl.
3. Patients must have a low-density lipoprotein cholesterol (LDL-c) greater than 1.0 mmol/L and lower than 2.6 mmol/L at baseline and be receiving a maximally tolerated statin dose, targeted to achieve an LDL-c lower than 2 mmol/L, for a minimum of four weeks.

Prescribing Conditions

1. Icosapent ethyl should be prescribed in conjunction with a statin

Reasons for the Recommendation:

1. Summary

- In one double-blind, randomized controlled trial (RCT) (REDUCE-IT), icosapent ethyl demonstrated a statistically significant reduction in major CV events in patients with established CVD (secondary prevention), a fasting triglycerides (TG) measurement of 1.7 or greater and lower than 5.6 mmol/L, and a low-density lipoprotein cholesterol (LDL-c) greater than 1.0 and lower than 2.6 mmol/L at baseline, who were treated with icosapent ethyl 4 g per day added to statin therapy compared with those treated with statin therapy plus placebo.
- At the manufacturer-submitted price, the estimated incremental cost-utility ratio (ICUR) for icosapent ethyl plus statin compared with statin therapy alone for the full population studied in REDUCE-IT (i.e., primary and secondary prevention) is $105,053 per quality-adjusted life-year (QALY) A price reduction of at least 43% would be required to achieve an ICUR of $50,000 per QALY.

2. Clinical Efficacy

- The DBC considered the CADTH systematic review, which included two RCTs, REDUCE-IT and ANCHOR.
- REDUCE-IT evaluated 4 g per day orally of icosapent ethyl versus placebo in patients aged 45 years or older with established CV risk, and those aged 50 years or older with diabetes in combination with one additional risk factor for CVD, with a median follow-up of 4.9 years.

- The primary outcome in REDUCE-IT was the time from randomization to the first occurrence of any of the composite outcome events of CV death, non-fatal MI, non-fatal stroke, coronary revascularization, and unstable angina requiring hospitalization. Secondary outcomes included a secondary composite end point of time from randomization to any of CV death, non-fatal MI, or non-fatal stroke; a composite of CV death or non-fatal MI; fatal or nonfatal MI; emergency or urgent revascularization; CV death; hospitalization for unstable angina; fatal or non-fatal stroke; a composite of total mortality, non-fatal MI (including silent MI), or non-fatal stroke; and total mortality.
- ANCHOR included patients aged 18 years or older with fasting TG levels of 2.3 mmol/L or greater and 5.6 mmol/L or lower, who were receiving a stable dose of statin therapy (with or without ezetimibe), and who were at high risk for CVD. ANCHOR included three treatment groups: placebo, icosapent ethyl 2 g daily, and icosapent ethyl 4 g daily, but only the icosapent ethyl 4 g daily dosage group was included because that is the Health Canada dosage. ANCHOR evaluated the percent change in TG levels from baseline to week 12 as the primary outcome. Secondary end points included the percent change in non-lipoprotein cholesterol, LDL-c, apolipoprotein B, very low-density lipoprotein, and lipoprotein-associated phospholipase A2 from baseline to week 12. CV events and other clinically important outcomes were not assessed.
- REDUCE-IT demonstrated a statistically significant reduction in major CV events (composite of CV mortality, non-fatal MI, non-fatal stroke, coronary revascularization, and hospitalization for unstable angina) in patients with established CVD (secondary prevention), a fasting TG of 1.7 or greater and lower than 5.6 mmol/L, and an LDL-c greater than 1.0 and lower than 2.6 mmol/L at baseline, who were treated with icosapent ethyl 4 g per day added to statin therapy compared with those treated with statin therapy plus placebo.
- The results of REDUCE-IT have limited generalizability because the patients enrolled were a selective subset of the patient population for whom this drug is likely to be prescribed in practice
- ANCHOR demonstrated that icosapent ethyl 4 g orally per day reduced TGs, LDL-c, and high-sensitivity C-reactive protein from baseline when compared with placebo in a population of adults already receiving a stable dose of statin therapy (with or without ezetimibe) and at high risk for CVD.
- ANCHOR did not examine the effects of icosapent ethyl on clinical outcomes and therefore could not be used to verify the results observed in REDUCE-IT.
- For detailed information on the systematic review of icosapent ethyl please see the CDEC Final Recommendation at: https://www.cadth.ca/icosapent-ethyl.

3. Safety

- Adverse events, serious adverse events, and withdrawals due to adverse events occurred at similar frequencies between the icosapent ethyl and placebo groups in both REDUCE-IT and ANCHOR.
- For detailed information on the safety and tolerability of icosapent ethyl, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The CADTH reanalysis of the manufacturer's submission reported the ICUR for icosapent ethyl plus statins was $105,053 per QALY gained when compared with statins alone. A price reduction of 43% would be required for icosapent ethyl plus statin therapy to be cost-effective at a willingness-to-pay threshold of $50,000 per QALY.
- The cost-effectiveness of icosapent ethyl in a broader clinical population beyond what has been studied in REDUCE-IT is unknown.

5. Of Note

- The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups, and the CDR similarly received no patient input.