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	**ivabradine**
Brand Name	Lancora™
Dosage Forms	5 mg and 7.5 mg film - coated tablets
Manufacturer	Servier Canada Inc.
Submission Type	**New Submission**
Use Reviewed	Heart Failure NYHA class II to III
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/SR0506_complete_Lancora-Jun15-17_e.pdf
Drug Benefit Council (DBC)	DBC met on June 5, 2017. DBC considered various inputs including: 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 patient input from two patients.
Drug Coverage Decision	**Limited Coverage Benefit.** Access the ivabradine criteria at **www.gov.bc.ca/pharmacarespecialauthority**
Date	October 30, 2018.
Reason(s)	**Drug coverage decision is consistent with the DBC recommendation. See complete DBC Recommendation and Reasons below.** • One double-blind, randomized controlled trial demonstrated that treatment with ivabradine reduced the risk of cardiovascular mortality or hospitalisation for heart failure compared with placebo. • At the submitted price ivabradine is considered cost-effective and its annual cost is lower than the annual cost of comparator drug, sacubitril-valsartan for heart failure. • BC participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with manufacturer and an agreement was reached.
Other Information	None

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Ivabradine hydrochloride (Lancora™)
SERVIER Canada Inc.

Description:

Drug review of **ivabradine hydrochloride (Lancora™)** for the following Health Canada approved indication:

> For the treatment of stable chronic heart failure (HF) with reduced left ventricular ejection fraction (LVEF) (≤ 35%) in adult patients with New York Heart Association (NYHA) Classes II or III who are in sinus rhythm with a resting heart rate ≥ 77 beats per minute (bpm), to reduce the incidence of cardiovascular (CV) mortality and hospitalisations for worsening HF, administered in combination with standard chronic HF therapies.

In their review, the DBC considered the following: final review completed by the Common Drug Review (CDR) on May 24, 2017, 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. No caregivers or patient groups responded to the request for input. CDR patient input was also considered, as were Clinical Practice Reviews from two specialists and one general physician, and a Budget Impact Assessment.

Dosage Forms:

Lancora™ is available as ivabradine hydrochloride 5 mg and 7.5 mg film-coated tablets.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that **ivabradine hydrochloride (Lancora™)** be listed as a benefit according to the Health Canada approved indication with the following criteria:
    a. Patients with NYHA class II to III symptoms despite at least four weeks of treatment with a stable dose of an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin II receptor antagonist (ARB) in combination with a beta blocker and, if tolerated, a mineralocorticoid receptor agonist (MRA);
    b. Patient resting heart rate must be documented to be ≥ 77 bpm on average using either an ECG on at least three separate visits or by continuous monitoring;
    c. Patient with at least one hospitalization due to heart failure in the last year;
    d. Treatment with ivabradine should be initiated by a specialist, but may be titrated by a GP or a specialist.

Reasons for the Recommendation:

1. Summary

- One large event-driven double blind, Phase III randomized placebo-controlled trial demonstrated a statistically significant improvement compared with placebo in the primary composite end point (CV mortality and hospitalization for worsening heart failure) and in some secondary outcomes such as fewer all-cause deaths, deaths related to heart failure, all-cause hospitalizations, and CV hospitalizations, all in the pre-specified subgroup of patients with a baseline heart rate of ≥ 77 bpm.
- A slightly lower percentage of patients have experienced treatment emergent adverse events (TEAEs) and fewer patients have experienced serious adverse events (SAEs) in the ivabradine treatment group compared to the placebo group. The percentage of patients who stopped treatment due to adverse events was similar between the two groups.
- The CDR analysis found, despite major limitations, that ivabradine was of reasonable cost-effectiveness.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included one event-driven double blind, Phase III randomized placebo-controlled trial designed to assess the superiority of ivabradine versus placebo in patients with heart rate ≥ 70 bpm (the SHIfT trial).
- In accordance with the manufacturer request and the Health Canada-approved indication, the CDR review focused primarily on the results from a pre-specified subgroup of patients (i.e., patients with a heart rate ≥ 77 bpm).
- Ivabradine demonstrated a statistically significant improvement compared with placebo in the primary composite end point (CV mortality and hospitalization for worsening heart failure) in the pre-specified subgroup of patients with a baseline heart rate of ≥ 77 bpm. The primary composite end point was statistically significant for both cardiovascular mortality and for hospitalization for worsening heart failure.
- Ivabradine also demonstrated a statistically significant improvement compared with placebo in the same pre-mentioned subgroup of patients for some secondary outcomes of interest such as fewer all-cause deaths, deaths related to heart failure, all-cause hospitalizations, and CV hospitalizations.
- For detailed information on the systematic review of ivabradine please see the CDEC Final Recommendation at: https://www.cadth.ca/ivabradine.

3. Safety

- TEAEs were experienced by slightly fewer patients in the ivabradine group compared to the placebo group during the SHIfT trial. The most common TEAEs were cardiac failure, bradycardia (symptomatic and asymptomatic), atrial fibrillation, and inadequately controlled blood pressure.
- SAEs were experienced by fewer patients in the ivabradine treatment group than in the placebo group. The most common SAEs were cardiac failure and atrial fibrillation.
- The percentage of patients who stopped treatment due to adverse events was similar between the ivabradine and placebo groups, where sudden death, atrial fibrillation, unstable angina, pneumonia, cardiac failure, and sudden cardiac death were the most commonly reported reasons for stopping treatment.
- Notable harms that were more commonly reported in the ivabradine group than in the placebo group included bradycardia, asymptomatic bradycardia (i.e., heart rate decreased), and patients experiencing visual abnormalities (phosphenes). The percentage of patients experiencing atrial fibrillation, hypotension, and renal failure were similar between the ivabradine and placebo treatment groups.
- For detailed information on the safety and tolerability of ivabradine, please see the CDEC Final Recommendation at the links above.

4. Economic Considerations

- Ivabradine is expected to be administered as an add-on therapy to patients receiving ACEI or ARB, beta-blocker, and MRA triple therapy.
- The CDR reanalysis of the manufacturer's cost-utility analysis found an estimated incremental cost utility ratio (ICUR) of $12,895 per quality-adjusted life-year (QALY) for ivabradine plus standard of care (SOC) compared with SOC alone, and up to $16,729 per QALY in patients receiving 100% or more of the target beta-blocker dose.

5. Of Note

- Patient and caregiver input, including from patients who had tried ivabradine, indicated that patients experienced significant reductions in morbidity and mortality when on the drug.

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.