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	**dapagliflozin**
Brand Name	Forxiga®
Dosage Form(s)	10 mg oral tablet
Manufacturer	AstraZeneca Canada Inc.
Submission Type	**New Submission**
Use Reviewed	For the treatment of heart failure with reduced ejection fraction (HFrEF)
Common Drug Review (CDR)	Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: https://www.cadth.ca/dapagliflozin-1
Drug Benefit Council (DBC)	DBC met on February 1, 2021. DBC considered the following: the final reviews completed by the Common Drug Review (CDR), which included clinical and pharmacoeconomic evidence review material and the recommendations from the CDEC. The DBC also considered Patient Input Questionnaire responses from 6 patients, 17 caregivers, and one patient groups, as well as patient input provided to the CDR, Clinical Practice Reviews from two specialists, and a Budget Impact Assessment (BIA).
Drug Coverage Decision	**Limited Coverage Benefit. Access the dapagliflozin criteria from www.gov.bc.ca/pharmacarespecialauthority**
Date	**January 11, 2022**
Reason(s)	**Drug coverage decision is consistent with CDEC and DBC recommendations (see Appendix A).** • CDEC and DBC recommended that dapagliflozin be reimbursed for the treatment of HFrEF, as an adjunct to standard of care (SOC) therapy only in adults with New York Heart Association

	(NYHA) class II and III heart failure (HF). SOC therapies include beta-blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, plus a mineralocorticoid receptor antagonist. • In one randomized controlled trial (RCT) in adults with symptomatic HFrEF who received dapagliflozin as add-on therapy to SOC therapies, the time to occurrence of cardiovascular death, HF hospitalization or urgent HF visits was greater for the dapagliflozin-treated patients relative to placebo. • Based on economic considerations and the submitted list price, dapagliflozin is likely to be cost-effective for treatment of patients in NYHA Class II HF but is not likely to be cost-effective in NYHA Class III and IV HF. • At the submitted list price, the annual treatment cost for dapagliflozin is more expensive than the annual treatment cost for beta-blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or mineralocorticoid receptor antagonists. • The Ministry led successful negotiations for dapagliflozin on behalf of the pan-Canadian Pharmaceutical Alliance (pCPA).
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 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 A

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Dapagliflozin (Forxiga®)
AstraZeneca Canada Inc.

Description:

Drug review of **dapagliflozin (Forxiga®)** for the following Health Canada approved indications:

> As an adjunct to standard of care (SoC) therapy, for the treatment of heart failure with reduced ejection fraction (HFrEF) to reduce the risk of cardiovascular (CV) death, hospitalization for heart failure (HF) and urgent HF visit.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on December 23, 2020, 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 6 patients, 17 caregivers, and one patient groups, as well as patient input provided to the CDR, Clinical Practice Reviews from two specialists, and a Budget Impact Assessment.

Dosage Forms:

Forxiga® is available as dapagliflozin 5 mg and 10 mg oral tablet. The recommended dose is 10 mg once daily for the treatment of HFrEF to reduce the risk of CV death, hospitalization for HF and urgent HF visit, in adults.

Recommendations:

- The Drug Benefit Council (DBC) recommends listing dapagliflozin (Forxiga®) as an adjunct to SoC therapies in adults with New York Heart Association (NYHA) class II and III heart failure. SoC therapies include beta-blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, plus a mineralocorticoid receptor antagonist.

Reasons for the Recommendation:

1. **Summary**

- In one randomized controlled trial (RCT) in adults with symptomatic HFrEF who received dapagliflozin as add-on therapy to guideline recommended drug therapies, the time to occurrence of CV death, HF hospitalization or urgent HF visits was greater for the dapagliflozin-treated patients relative to placebo.
- There was no direct evidence comparing dapagliflozin to other second line therapies for HFrEF.

- At the manufacturer-submitted price, dapagliflozin is likely to be cost effective for treatment of patients in NYHA Class II HF but is not likely to be cost effective in NYHA Class III and IV HF as there is a high degree of uncertainty about the clinical efficacy of dapagliflozin in patients with Class III and IV HF.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included two double-blind randomized placebo-controlled trials of patients with HFrEF: DAPA-HF and DEFINE-HF.
- The pivotal trial, DAPA-HF, evaluated the efficacy of dapagliflozin 10 mg daily versus placebo as add-on to standard of care therapy in adults with HFrEF. The median follow-up duration of this event driven trial was 18.2 months, with > 99% of patients completing the study. The primary outcome in DAPA-HF was the time to first occurrence of CV death, hospitalization for HF, or an urgent HF visit.
- Because the co-primary outcomes in DEFINE-HF included biomarker and health status measures that were not outcomes of interest according to the systematic review protocol, the CDR concentrated on DAPA-HF.
- Both trials enrolled adults ≥18 years of age with a documented diagnosis of HFrEF (left ventricular ejection fraction [LVEF] ≤40% and NYHA class II to IV. All patients were required to receive SoC therapies for HF including either an ACEI, ARB or sacubitril/valsartan in combination with a beta-blocker, and, if appropriate, a mineralocorticoid receptor antagonist at baseline and during the study period
- In DAPA-HF, 16.3% of patients in the dapagliflozin group and 21.2% of patients in the placebo group reported a composite primary outcome event of CV death, HF hospitalization or urgent HF visit. The time to occurrence of the composite of primary events was greater for the dapagliflozin-treated patients relative to placebo. Similar treatment effects were noted for the analysis of time to first occurrence of CV death or HF hospitalization. For each component of the primary outcome, the time to first event was greater for dapagliflozin-treated patients.
- The total number of CV deaths or HF hospitalizations was lower in the dapagliflozin versus placebo groups (average 16.3 events per 100 person years [PYs] versus 21.6 events per 100 PYs, respectively) with a rate ratio of 0.75.
- According to clinical experts consulted by the CDR, the between-group differences in CV death and HF hospitalizations were clinically important, particularly considering that patients were already receiving guideline-recommended treatment for HF.
- The DAPA-HF trial population excluded patients with more advanced disease including those with recent HF hospitalization or CV events, and those with poor or worsening renal function. Most patients in DAPA-HF were NYHA class II (68%) and less than 1% had NYHA class IV HF.
- There was no direct evidence comparing dapagliflozin to other add-on therapies such as sacubitril/valsartan or ivabradine.
- For detailed information on the systematic review of dapagliflozin for HFrEF, please see the CDEC Final Recommendation at: https://www.cadth.ca/dapagliflozin-1.

3. Safety

- No new safety signals were identified in patients with HFrEF; however, the pivotal DAPA-HF study did not collect data for all nonserious adverse events.
- For detailed information on the safety and tolerability of dapagliflozin, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The CDR reanalysis of the manufacturer submission found that, for patients in NYHA class II, the incremental cost-effectiveness ratio (ICER) for dapagliflozin plus SoC versus SoC alone was $8,760 per quality adjusted life-year (QALY).
- For patients in NYHA class III and IV, dapagliflozin plus SoC was dominated by SoC, meaning that dapagliflozin plus SoC was more costly and associated with fewer QALYs than SoC. This suggests that dapagliflozin is likely cost-effective for patients in NYHA II class, but not cost-effective in NYHA class III and IV.
- Given the absence of evidence of a mortality benefit in NYHA class III and IV in the DAPA-HF trial, an ICER below $50,000 per QALY for dapagliflozin plus SoC versus SoC could not be achieved with any level of price reduction for dapagliflozin.

5. Of Note

- Patients who responded to the Patient Input Questionnaires expressed the hope that treatments for HF will reduce their symptoms, improve their quality of life, prevent hospitalizations, reduce mortality, and have fewer adverse effects or at least more tolerable adverse effects than other treatments.
- Several patients and caregivers reported experience with dapagliflozin for HF. Patients reported quality of life improvements including increased energy, reduced shortness of breath and improved mobility.