Drug Coverage Decision for BC PharmaCare

About PharmaCare BC PharmaCare is a publicly funded drug plan that helps B.C. residents pay for most prescription drugs and pharmacy services, and some medical devices and supplies.

Details of Drug Reviewed

Drug	mavacamten
Brand name	Camzyos™
Dosage form(s)	2.5 mg, 5 mg, 10 mg, and 15 mg capsules
Manufacturer	Bristol Myers Squibb
Submission type	**New Submission**
Indication reviewed	For the treatment of symptomatic obstructive hypertrophic cardiomyopathy (oHCM) of New York Heart Association (NYHA) Class II-III in adult patients.
Canada's Drug Agency (CDA-AMC) Clinical Reimbursement Reviews (CRR)	CDA-AMC recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more mavacamten | CDA-AMC
Drug Benefit Council (DBC)	The DBC met on June 5, 2023. The DBC considered various input, including clinical and pharmacoeconomic evidence review material and the recommendations of the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from one patient and one patient groups, as well as patient input provided to the CRR, Clinical Practice Reviews from a specialist, and a Budget Impact Assessment
Drug Coverage Decision	**Limited Coverage benefit** Access the mavacamten criteria from **www.gov.bc.ca/pharmacarespecialauthority**
Date	November 26, 2024

Reason(s)	**Drug coverage decision is consistent with the CDEC and DBC recommendations.** • Two phase III, randomized, double-blind, placebo-controlled trials demonstrated that treatment with mavacamten resulted in added clinical benefit in adult patients with symptomatic oHCM. • Mavacamten may address some of the needs that are important to patients, by reducing HCM symptoms and improving patients' health related quality of life (HRQoL). • At the submitted price, mavacamten was not considered cost-effective for this indication. The Ministry participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer which were able to address the concerns identified by the CDEC and DBC with respect to the cost-effectiveness and value for money.

The drug review process in B.C.

A manufacturer submits a request to the Ministry of Health (the Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry by considering:

- whether the drug is safe and effective
- advice from a national group called Canada's Drug and Health Technology Agency (CADTH)
- what the drug costs and whether funding it provides good value to the province
- ethical considerations of covering and not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes a BC PharmaCare coverage decision by taking into account:

- existing BC PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- drugs already covered by BC PharmaCare that treat similar medical conditions
- the overall cost of covering the drug

Visit BC PharmaCare and Drug reviews for more information.

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It does not take the place of advice from a physician or other qualified health care provider.

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Drug Benefit Council (DBC)
Recommendation and Reasons for Recommendation

FINAL

Mavacamten (Camzyos™)
Bristol Myers Squibb

Description:

Drug review of **mavacamten (Camzyos™)** for the following Health Canada approved indications:

> For the treatment of symptomatic obstructive hypertrophic cardiomyopathy (oHCM) of New York Heart Association (NYHA) class II to III in adult patients.

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on April 14, 2023, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC also considered Patient Input Questionnaire responses from one patient and one patient groups, as well as patient input provided to the CDR, Clinical Practice Reviews from a specialist, and a Budget Impact Assessment.

Dosage Forms:

Camzyos™ is available as mavacamten 2.5 mg, 5 mg, 10 mg, and 15 mg capsules.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list mavacamten (Camzyos™) at the submitted price.

Of Note:

- If a significant price reduction is achieved, the reimbursement criteria and conditions recommended by CADTH are an appropriate basis for coverage, with the DBC recommending the following revision:
    - In the second recommended reimbursement condition ("Patients must be receiving beta-blocker or calcium-channel blocker therapy and experience clinical deterioration in symptoms or echocardiography while receiving either of these treatments"), remove the requirement for a clinical deterioration of symptoms or echocardiography.

Reasons for the Recommendation:

1. **Summary**

- Two phase III, randomized, double-blind, placebo-controlled trials demonstrated that treatment with mavacamten resulted in added clinical benefit in adult patients with symptomatic oHCM.
- In one trial, mavacamten was statistically significantly more efficacious than placebo in improving the NYHA class and exercise capacity (pVO2) in patients with symptomatic oHCM of NYHA class II to III.
- Mavacamten is a second-line treatment option after beta-blockers or calcium channel blockers.
- At the manufacturer submitted price, mavacamten is not cost-effective at a $50,000 per quality-adjusted life-year (QALY) willingness to pay (WTP) threshold for adult patients with symptomatic oHCM of NYHA Class II–III.

2. **Clinical Efficacy**

- The DBC considered the CADTHY systematic review, which included two trials: EXPLORER-HCM and VALOR-HCM.
- EXPLORER-HCM (N = 251) evaluated the efficacy and safety of once-daily orally administered treatment with mavacamten (starting dose 5 mg) in adult patients with symptomatic oHCM with an left ventricular outflow tract (LVOT) peak gradient ≥ 50 mmHg at rest, after Valsalva maneuver, or post exercise, documented LVEF ≥ 55%, a maximum septal wall thickness determined by a core laboratory ≥ 15 mm or ≥ 13 mm with family history of HCM, and with NYHA functional class II or III symptoms.
- The primary outcome of EXPLORER-HCM was composite functional response at week 30, defined as achieving an improvement of ≥ 1.5 mL/kg/min increase in peak oxygen consumption (pVO2) and ≥ 1 NYHA functional class reduction or ≥ 3.0 mL/kg/min in pVO2 without NYHA class worsening. Secondary outcomes prespecified in the statistical hierarchy included changes in post-exercise LVOT peak gradient, pVO2, NYHA class, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ CSS), and Hypertrophic Cardiomyopathy Symptom Questionnaire Shortness of Breath (HCMSQ SoB) domain score.
- VALOR-HCM (N = 112) evaluated the efficacy and safety of once-daily orally administered treatment with mavacamten (starting dose 5 mg) in adult patients with symptomatic oHCM with a dynamic LVOT gradient at rest or with provocation (i.e., Valsalva or exercise) of 50 mmHg or greater, a documented LVEF ≥ 60%, a maximum septal wall thickness determined by a core laboratory ≥ 15 mm or ≥ 13 mm with family history of HCM and NYHA functional class III, IV, or class II with exertional syncope or near syncope.
- The primary outcome of VALOR-HCM was a composite of the decision to proceed with septal reduction therapy (SRT) prior to or at week 16 or be considered guideline eligible for SRT at week 16. Secondary outcomes prespecified in the statistical hierarchy included changes in post-exercise LVOT peak gradient, ≥ 1 class of NYHA

improvement, changes in KCCQ CSS, and changes in N-terminal pro b-type natriuretic peptide (NT-proBNP) and cardiac troponin I biomarkers.

- In EXPLORER-HCM, a total of 37% of patients on mavacamten versus 17% of patients on placebo met the primary endpoint at week 30 with a between group difference of 19.4%. In regards to key secondary outcomes tested in the statistical hierarchy from baseline to week 30, patients in the mavacamten group compared to those in the placebo group had: greater reductions in post-exercise LVOT gradient, greater increases in pVO2, more patients improving by ≥ 1 NYHA class (65% of patients in the mavacamten group vs 31% of patients in the placebo group), greater improvement in scores on the KCCQ-23 CSS, and greater reductions in severity of HCM symptoms as assessed by the HCMSQ SoB domain score.
- In VALOR-HCM, for the primary composite outcome, after 16 weeks treatment, 17.9% of mavacamten treated patients continued to meet guideline criteria for SRT or elected to undergo the procedure compared to 76.8% of placebo treated patients, with a treatment difference of 58.9% favouring mavacamten. In regard to key secondary outcomes tested in the statistical hierarchy from baseline to week 16, patients in the mavacamten group compared to those in the placebo group had: a greater reduction in post-exercise LVOT gradient, more patients with ≥ 1 class of NYHA functional class improvement, greater improvement in scores on the KCCQ CSS, and greater reductions in NT-proBNP and in cardiac troponin I.
- For detailed information on the systematic review of mavacamten please see the CDEC Final Recommendation at: https://www.cadth.ca/mavacamten.

3. Safety

- In EXPLORER-LTE, 62.9% of patients in the treatment cohort experienced at least 1 adverse event (AE). The most common adverse events (frequency ≥ 3%) were atrial fibrillation, diarrhea, fatigue, nasopharyngitis, dizziness, headache, dyspnea, and pain in extremity. One death, due to bacterial endocarditis, occurred, which was deemed unrelated to mavacamten by the investigator. The most common serious adverse events (SAEs) among patients were cardiac failure (1.3%), pneumonia (0.9%), and atrial fibrillation (0.9%).
- In VALOR-HCM trial, through to week 32, the rate of SAEs was similar between the original mavacamten group and the placebo crossover group. There were no reported deaths, myocardial infarctions, or strokes in either group.
- For detailed information on the safety and tolerability of mavacamten, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The ICER for mavacamten plus beta-blocker or calcium-channel blocker is $576,295 when compared with beta-blocker or calcium-channel blocker alone. A price reduction of at least 73% for mavacamten would be required for mavacamten plus beta-blocker or calcium-channel blocker to achieve an ICER of $50,000 per QALY gained compared to beta-blocker or calcium-channel blocker alone.

5. Of Note

- HCM is a common genetic cardiomyopathy that occurs in 1 in 500 individuals that is a major cause of sudden cardiac death for people under the age of 30. Common symptoms of HCM include chest pain, palpitations, shortness of breath, fatigue and fainting. HCM often results in the need for invasive procedures such as surgery or ablation and can lead to heart failure, end stage heart failure, and ultimately the need for a heart transplant.
- The patient who completed the questionnaire had not tried the drug under review, and the patient group representative reported that none of the patients they represent had tried the drug under review.
- Patients indicated that currently available treatments (including beta-blockers, calcium channel blockers and antiarrhythmics) may have intolerable side effects and mavacamten offers another option for patients.