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	**luspatercept**
Brand Name	**Reblozyl®**
Dosage Forms	25 mg and 75 mg lyophilized powder for solution for subcutaneous injection
Manufacturer	Cellgene Inc.
Submission Type	**New Submission**
Use Reviewed	Red blood cells (RBC) transfusion-dependent anemia associated with beta-thalassemia
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	Yes, CRR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details: www.cadth.ca/sites/default/files/attachments/2021-06/CADTH_reimbursement_recommendation_luspatercept_%28reblozyl%29.pdf
Drug Benefit Council (DBC)	The DBC met on July 5, 2021 and the DBC considered various inputs including: the final reviews completed by the Common Drug Review (CDR) on June 8, 2021, 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 thus considered patient input provided to the CDR, Clinical Practice Reviews from one specialist, and a Budget Impact Assessment.
Drug Coverage Decision	**Limited Coverage Benefit.** Access the luspatercept criteria from **www.gov.bc.ca/pharmacarespecialauthority**
Date	March 14, 2023
Reasons	**Drug coverage decision is consistent with the CDEC and DBC recommendations.** • Luspatercept was superior to placebo in terms of reducing transfusion burden in adult patients with transfusion-dependent anemia associated with beta-thalassemia. • The Ministry participated in the pan-Canadian Pharmaceutical Alliance 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.

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

luspatercept (Reblozyl®)

Celgene Inc., a Bristol Myers Squibb Company

Description:

Drug review of **luspatercept (Reblozyl®)** for the following Health Canada approved indications:

> For the treatment of adult patients with red blood cell transfusion-dependent anemia associated with beta(β)-thalassemia associated anemia.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on June 8, 2021, 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 thus considered patient input provided to the CDR, Clinical Practice Reviews from one specialist, and a Budget Impact Assessment.

Dosage Forms:

Reblozyl® is available as luspatercept 25 mg and 75 mg powder for subcutaneous injection.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list luspatercept (Reblozyl®) at the submitted price.

Of Note:

- If a significant price reduction is achieved, the CDEC recommendation included detailed reimbursement criteria and conditions that could be used as the basis for Special Authority criteria.

Reasons for the Recommendation:

1. Summary

- One ongoing phase III, multicentre, double-blind randomized placebo-controlled study showed that treatment with luspatercept was superior to placebo in terms of reducing transfusion burden by at least 33% during fixed week 13 to week 24 in adult patients with transfusion-dependent anemia associated with beta-thalassemia.
- Treatment with luspatercept has been shown to reduce but not remove the need for transfusions and iron chelations.
- Luspatercept did not show a benefit in terms of health-related quality of life (HRQoL) when evaluated against the placebo group.
- A price reduction of 85% of the manufacturer's submitted price would be required for luspatercept to be cost-effective at a willingness-to-pay threshold of $50,000 per quality-adjusted life year (QALY).

2. Clinical Efficacy

- The DBC considered the CADTH systematic review, which included one ongoing phase III, multicentre, double-blind randomized placebo-controlled study (BELIEVE) evaluating the efficacy and safety of luspatercept in adult patients with transfusion-dependent anemia associated with beta-thalassemia.
- The primary efficacy outcome of BELIEVE was the proportion of patients who achieved an erythroid response of greater than or equal to 33% reduction from baseline in transfusion burden (defines as units of red blood cells/time) with a reduction of at least 2 units, in a fixed 12-week period from week 13 to week 24.
- The three key secondary endpoints were the proportion of patients who achieved an erythroid response of greater than 33% in a fixed 12-week period from week 37 to 48; by 50% during fixed week 13 to week 24 and fixed week 37 to week 48.
- The primary and secondary endpoints of the study were found to be clinically meaningful by the clinical experts consulted by CADTH.
- Treatment with luspatercept was superior to placebo in terms of reducing transfusion burden by at least 33% during fixed week 13 to week 24 in adult patients with transfusion-dependent anemia associated with beta-thalassemia.
- Treatment with luspatercept was superior to placebo in reducing transfusion burden by at least 33% during week 37 to 48 and by 50% during fixed week 13 to week 24 and week 37 to week 48 in adult patients with transfusion-dependent anemia associated with beta-thalassemia.
- HRQoL was an outcome noted as important to patients, but the effect of luspatercept on HRQoL outcomes was uncertain due to a lack of control for multiplicity and major limitations around the data. Overall, luspatercept did not show benefit in terms of HRQoL when evaluated against the placebo treatment group.
- For detailed information on the systematic review of luspatercept please see the CDEC Final Recommendation at: https://www.cadth.ca/luspatercept.

3. Safety

- Thromboembolic events, hypertension, hepatic and renal adverse events, bone pain, and neoplasms were identified as safety concerns associated with luspatercept, and these events occurred more frequently in the luspatercept group than in the placebo group in the BELIEVE study.
- For detailed information on the safety and tolerability of luspatercept, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer's submitted price, CADTH estimated the incremental cost-effectiveness ratio (ICER) of luspatercept compared with best supportive care (BSC) to be $659,395 per quality-adjusted life-year (QALY), with a 0% probability of being cost-effective at a $50,000 per QALY willingness-to-pay threshold.
- A price reduction of 85% would be required for luspatercept to be cost-effective at this threshold.

5. Of Note

- The current standard of care for managing beta-thalassemia requires clinic visits every 2 to 4 weeks for RBC transfusions and iron chelation therapy, and there are no other treatments available that address the underlying disease state.
- It should be noted that treatment with luspatercept reduces but does not remove the need for transfusions and iron chelations.