BRITISH COLUMBIA | Ministry of Health

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	**pegcetacoplan**
Brand Name	Empaveli™
Dosage Form(s)	1080mg/20mL (54mg/mL) solution for subcutaneous infusion
Manufacturer	Sobi Canada Inc.
Submission Type	**New Submission**
Use Reviewed	For the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH) who have an inadequate response to, or are intolerant of, a C5 inhibitor
Canada's Drug and Health Technology Agency's (CADTH) Reimbursement Review (CRR)	Yes, the CRR recommended **to Reimburse with clinical criteria and/or conditions.** Visit the CRR website for more details.
Drug Benefit Council (DBC)	The DBC met on May 1, 2023. In their review, the DBC considered the following: the final reviews completed by the CRR of CADTH on March 20, 2023, 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 two patient groups, patient input provided to CADTH, and a Budget Impact Assessment. The DBC recommended that pegcetacoplan be listed as a Limited Coverage benefit.

pegcetacoplan (Empaveli™)

Drug Coverage Decision	Case-by-Case Coverage Through the Expensive Drugs for Rare Diseases (EDRD) Process
Date	March 6, 2024
Reason(s)	**Drug coverage decision is consistent with the CDEC and DBC recommendations.** • Evidence suggests that pegcetacoplan treatment is associated with a statistically and clinically significant improvement in hemoglobin levels relative to eculizumab. Transfusion avoidance was also more commonly observed among pegcetacoplan patients than eculizumab patients. • Adverse events were similar among pegcetacoplan and eculizumab patients. • BC participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer and the pCPA was able to address the concerns identified by CADTH and DBC with respect to the cost-effectiveness and value for money.
Other Information	See the DBC Recommendation & Reasons

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.

Appendix

CONFIDENTIAL

Drug Benefit Council (DBC)
Recommendation and Reasons for Recommendation

FINAL

Pegcetacoplan (Empaveli®)
Sobi Canada, Inc.

Description:

Drug review of **pegcetacoplan (Empaveli®)** for the following Health Canada approved indications:

> For the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH) who have an inadequate response to, or are intolerant of, a C5 inhibitor.

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on March 20, 2023, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC also considered Patient Input Questionnaire responses from two patient groups, patient input provided to CADTH, and a Budget Impact Assessment.

Dosage Forms:

Empaveli® is available as pegcetacoplan 54mg/mL solution for subcutaneous infusion in 20 mL (1080mg) single-dose vials.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that pegcetacoplan (Empaveli®) be listed as a Limited Coverage benefit.
2. The reimbursement criteria and conditions recommended by CADTH are an appropriate basis for coverage.

Of Note:

- The Ministry of Health should negotiate a price reduction for pegcetacoplan.

Reasons for the Recommendation:

1. **Summary**

- One phase III, open-label, randomized controlled trial (RCT) demonstrated that treatment with pegcetacoplan was associated with a statistically significant and

clinically meaningful improvement in change in hemoglobin level from baseline at week 16 compared with eculizumab.
- Transfusion avoidance, an important outcome according to patients and the clinical experts, was more commonly observed with pegcetacoplan than with eculizumab.
- At manufacturer list price, pegcetacoplan is not cost-effective at a willingness-to-pay (WTP) threshold of $50,000 per quality-adjusted life-year (QALY) for adult patients with PNH who have an inadequate response to C5 inhibitors.

2. Clinical Efficacy

- The DBC considered the CADTH systematic review, which identified one pivotal phase III, open-label RCT comparing pegcetacoplan (1,080 mg twice weekly via subcutaneous infusion) versus eculizumab (at patients' established dosage regimen via IV infusion) in adult patients with PNH who continued to have hemoglobin levels of less than 105 g/L despite treatment with eculizumab at a stable dosage for at least 3 months (PEGASUS, N = 80).
- The primary outcome in PEGASUS was change from baseline (before the run-in period) at week 16 in hemoglobin (primary end point). Key secondary end points were transfusion avoidance, change in baseline at week 16 in absolute reticulocyte count (ARC), lactate dehydrogenase (LDH, a marker of intravascular hemolysis), and the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score.
- The least square (LS) mean change from baseline at week 16 in hemoglobin level (censored for transfusion) was 23.7 g/L (standard error [SE] = 3.6 g/L) in the pegcetacoplan arm and −14.7 g/L (SE = 6.7 g/L) in the eculizumab arm, with a between-group difference of 38.4 g/L in favour of pegcetacoplan.
- Transfusion avoidance was achieved in 85.4% of patients in the pegcetacoplan arm, and 15.4% in the eculizumab arm, with an adjusted risk difference of 62.5% in the intention-to-treat (ITT) analysis. The lower bound of the 95% CI for risk difference was greater than the noninferiority margin (NIM) of −20% in both the ITT and per-protocol (PP) analysis sets, supporting noninferiority of pegcetacoplan versus eculizumab.
- Change from baseline at week 16 in the FACIT-Fatigue score was a key secondary end point but was not tested for non-inferiority nor superiority due to prior failure in the testing hierarchy.
- For detailed information on the systematic review of pegcetacoplan please see the CDEC Final Recommendation at: https://www.cadth.ca/pegcetacoplan.

3. Safety

- Treatment-emergent adverse events (TEAEs) were reported in 87.8% of patients in the pegcetacoplan arm and 87.2% of patients in the eculizumab arm. There was a similar incidence of serious TEAEs in both arms (pegcetacoplan: 17.1%; eculizumab 15.4%). No deaths were reported in either arm.
- Withdrawal from study treatment due to TEAE occurred in 3 (7.3%) patients in the pegcetacoplan arm, all due to breakthrough hemolysis. No patients in the eculizumab withdrew from study treatment due to a TEAE.

- The incidence of injection site–related TEAEs (36.6%) was higher in the pegcetacoplan arm than the eculizumab arm (2.6%). Breakthrough hemolysis was less frequently reported with pegcetacoplan (9.8%) relative to eculizumab (23.1%).
- For detailed information on the safety and tolerability of pegcetacoplan, please see the CDEC Final Recommendation at the links above.

4. Economic Considerations

- At the manufacturer list price, the incremental cost-effectiveness ratio (ICER) for pegcetacoplan was $62,144 per quality-adjusted life-year (QALY) gained compared with ravulizumab. CADTH recommended a price reduction of at least 0.9% would be required for pegcetacoplan to achieve an ICER of $50,000 per QALY gained compared with C5 inhibitors.

5. Of Note

- Patient group input expressed a need for treatments that can effectively control intravascular hemolysis (IVH), reduce extravascular hemolysis (EVH), improve anemia, reduce or eliminate transfusion requirements, and improve fatigue and quality of life. Pegcetacoplan appears to meet some of these needs.