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	**eculizumab**
Brand Name	Soliris®
Dosage Form(s)	10 mg/mL parenteral solution for intravenous infusion in 30 mL (300 mg) single-use vials
Manufacturer	Alexion Pharma Canada Corp.
Submission Type	**New Indication**
Use Reviewed	Treatment of generalized myasthenia gravis (gMG) in adult patients.
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (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 November 2, 2020. In their review, the DBC considered the following: the final reviews completed by the CRR on October 19, 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 one caregiver, patient input provided to the CRR, a Clinical Practice Report from one clinical expert, and a Budget Impact Assessment. The DBC recommended that eculizumab not be listed for the treatment of gMG in adults.
Drug Coverage Decision	**Non-Benefit**
Date	February 10, 2023

Reasons	**Drug coverage decision is consistent with the CADTH and DBC recommendations.** • The effects of eculizumab on health-related quality of life and exacerbations of gMG are uncertain because of limitations associated with the analysis of these outcomes in the trial. • Based on economic considerations and the submitted product price, the drug was not cost effective and did not offer optimal value for money. • B.C participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer; however, the pCPA was not able to address the concerns identified by CADTH with respect to the cost-effectiveness and value for money. The negotiations concluded without an agreement on December 12, 2022.
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 :

- 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

Eculizumab (Soliris®)
Alexion Pharma Canada Corp.

Description:

Drug review of **eculizumab (Soliris®)** for the following Health Canada approved indications:

> For the treatment of refractory generalized myasthenia gravis (gMG) in adult patients.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on October 19, 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 one caregiver, patient input provided to the CDR, a Clinical Practice Report from one clinical expert, and a Budget Impact Assessment.

Dosage Forms:

Soliris® is available as eculizumab 10 mg/mL parenteral solution for intravenous infusion in 30 mL (300 mg) single-use vials.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list eculizumab (Soliris) for treatment of gMG in adult patients.

Reasons for the Recommendation:

1. Summary

- In one double-blind, placebo-controlled randomized trial comparing eculizumab to placebo, eculizumab failed to demonstrate a statistically significant benefit in the primary outcome, change from baseline to week 26 in the MG—ADL score, a measurement of activities of daily living.

- The effects of eculizumab on health-related quality of life (QoL) and exacerbations of MG are uncertain because of limitations associated with the analysis of these outcomes in the trial.
- Several other medications are available in British Columbia that are used for treatment of gMG.
- At the manufacturer-submitted price, eculizumab would not be considered a cost-effective treatment option for gMG.

1. Clinical Efficacy

- The DBC considered the CDEC systematic review, which included one double-blind, placebo-controlled, 26-week RCT, ECU-MG-301 (the REGAIN study), which randomized a total of 125 patients to receive eculizumab or placebo.
- REGAIN showed no statistically significant difference in its primary outcome, the change from baseline to week 26 in MG-ADL score between eculizumab and placebo based on the worst-rank analysis of covariance (ANCOVA) approach.
- Sensitivity analyses using less conservative techniques than ANCOVA showed statistically significant differences in favour of eculizumab versus placebo. None of the differences between groups in the sensitivity analyses were considered clinically meaningful based on the reported minimal important difference for the MG-ADL.
- QoL measures (measured using the Myasthenia Gravis Quality of Life 15-item scale, the Quality of Life in Neurological Disorders-Fatigue scale, and EuroQoL 5-Dimensions scale) were not interpretable based on a higher-order comparison for the Myasthenia Gravis Composite score not being statistically significant per the pre-specified hierarchical analysis plan.
- For detailed information on the systematic review of eculizumab for gMG, please see the CDEC Final Recommendation at: https://www.cadth.ca/eculizumab-16.

2. Safety

- Within the relatively small REGAIN population, there were no serious indications of harm beyond those already identified in the product monograph for eculizumab.
- Eculizumab has been associated with significant but rare harms in other populations, including anemia, high blood pressure, and meningococcal infections. The product monograph for eculizumab recommends all patients be vaccinated with meningococcal vaccines prior to, or at the time of, initiating eculizumab.
- For detailed information on the safety and tolerability of eculizumab, please see the CDEC Final Recommendations at the links above.

3. Economic Considerations

- The CADTH reanalysis of the manufacturer's economic submission estimated the incremental cost-effectiveness ratio (ICER) of eculizumab for gMG to be $1,505,712 per quality-adjusted life year (QALY) compared to standard of care alone.

- At the manufacturer's submitted price ($6,742 per 300 mg single-use vial for IV injection; annual cost of $728,136 per patient after the first year), eculizumab is not considered to be a cost-effective treatment option.
- A price reduction of 91% would be required for eculizumab plus SOC to achieve an ICER below $50,000 per QALY gained.

1. Of Note

- The DBC received no patient or patient group responses, and only one caregiver response, to the request to provide input for the review. Patient input received by the CDR indicated that refractory gMG is a rare and chronic condition with significant impacts on patient functioning, and that patients with refractory gMG have few treatment options after SOC.
- Patient input indicated that intravenous immunoglobulin (IVIg) and plasma exchange (PLEX) are not effectively meeting treatment goals for patients with refractory gMG.
- REGAIN did not include rituximab as a comparator. A panel of clinical experts consulted by CADTH indicated that rituximab is used in clinical practice as an off-label treatment.