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	**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 neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.
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 September 14, 2020. In their review, the DBC considered the following: the final reviews completed by the CRR on August 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 Patient Group, patient input provided to the CRR, Clinical Practice Reviews from two specialists, and a Budget Impact Assessment. The DBC recommended that eculizumab not be listed for the treatment of NMOSD in adults.

Drug Coverage Decision	**Non-Benefit**
Date	February 10, 2023
Reasons	**Drug coverage decision is consistent with the CADTH and DBC recommendations.** • Eculizumab did not demonstrate a statistically significant benefit on disability status versus placebo, and limitations of the trial meant no conclusions could be made on the effects of eculizumab on important subsequent endpoints, such as functional status and health-related quality of life. • 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 (pCPA) 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.
Provided to: Jason Locklin
Title: Director, Global Value, Access & Policy
Date: November 4, 2020

Description:

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

> For the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on August 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 Patient Group, patient input provided to the CDR, Clinical Practice Reviews from two specialists, 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 NMOSD.

Reasons for the Recommendation:

1. Summary

- One double-blind, randomized controlled trial (RCT) demonstrated that compared with placebo, eculizumab resulted in a statistically significant reduction in the risk of adjudicated on-trial relapse in a selected population of patients with NMOSD who were anti-AQP4 antibody positive.
- Eculizumab did not demonstrate a statistically significant benefit on disability status (change in EDSS) versus placebo, and limitations of the trial meant no conclusions could be made on the effects of eculizumab on important subsequent endpoints, such as functional status and health-related quality of life.
- At the manufacturer's submitted price, a price reduction of 96% would be required for the drug to achieve an incremental cost-effectiveness ratio (ICER) below $50,000 per quality adjusted life year (QALY) gained.

2. Clinical Efficacy

- The DBC considered the CDR clinical review, which included one phase III, time-to-event, multicenter, double-blind, placebo controlled RCT (PREVENT) conducted in 143 patients 18 years of age and older with a diagnosis of neuromyelitis optica (NMO) or NMOSD.
- The primary objective of PREVENT was to assess the efficacy of eculizumab treatment, as compared with placebo, in relapsing NMOSD patients based on time to first relapse and relapse risk reduction.
- The primary efficacy outcome in PREVENT was time to first adjudicated on-trial relapse where adjudication of on-trial relapses was based on consensus of an independent relapse adjudication committee consisting of two neurologists and one neuro-ophthalmologist.
- Secondary endpoints in PREVENT included: adjudicated on-trial annualized relapse rate (ARR), change from baseline in Expanded Disability Status Scale (EDSS) score, Modified Rankin Scale (mRS) score, European Quality of Life Health 5-Dimension Questionnaire (EQ-5D) score, and Hauser Ambulation Index (HAI) score.
- In PREVENT, eculizumab statistically and clinically significantly improved the time to first adjudicated on-trial relapse and adjudicated on-trial ARR compared to placebo, regardless of concurrent immunosuppressive therapy use.
- Eculizumab did not demonstrate a statistically significant benefit on disability status (change in EDSS) versus placebo. The lack of a statistically significant difference for the change from baseline on the EDSS precluded drawing conclusions on the effects of eculizumab on subsequent endpoints in the hierarchical testing sequence, such as functional status and health-related quality of life.

Key limitations of PREVENT were the disproportionately higher percentage of patients who discontinued treatment prematurely in the eculizumab group compared with the placebo group, the likely underestimation of the ARR in both treatment groups related to censoring of patients after the primary outcome event, limited

- efficacy assessments based on clinically relevant subgroups , and inability to interpret findings related to functional status and health-related quality of life because the hierarchical statistical analysis failed at a higher order comparison.
- The trail design of PREVENT (a time to event trial, where patients completed the trial after having a relapse) inherently emphasizes the efficacy of eculizumab on the first relapse, but is not designed to assess its efficacy on subsequent relapses. In PREVENT, patients were censored per the primary outcome analysis of time to relapse, and therefore subsequent relapses would not have been captured, thereby likely underestimating the ARR. The effectiveness of eculizumab on subsequent relapses remains largely unknown.
- For detailed information on the systematic review of eculizumab please see the CDEC Final Recommendation at: https://www.cadth.ca/eculizumab-17.

1. Safety

- Adverse events occurred similarly in patients in the eculizumab group (91.7%) and placebo group (95.7%) in PREVENT. Serious adverse events were more frequently reported in patients treated with placebo (55.3%) than in the eculizumab group (31.3%); however, the difference in events was largely eliminated when worsening of NMOSD was excluded.
- The comparative safety of eculizumab to other treatments for NMOSD could not be assessed based on the use of a placebo comparator in PREVENT and the absence of relevant indirect treatment comparisons.
- For detailed information on the safety and tolerability of eculizumab, please see the CDEC Final Recommendations at the links above.

2. Economic Considerations

- At the sponsor's submitted price of $6,742 per 300 mg vial, the annual cost of eculizumab was $728,136 in the first year and $701,168 thereafter, based on the recommended dosage for NMOSD.
- The DBC considered the CDR reanalysis of the manufacturer's economic submission, which reported an incremental cost-effectiveness ratio (ICER) for eculizumab plus standard of care (SoC) of $1,508,152 per quality-adjusted life-year (QALY) compared to SoC alone.
- Eculizumab is not considered to be a cost-effective treatment option at the submitted price. CADTH recommended that a price reduction of 96% would be required for eculizumab plus SoC to achieve an ICER below $50,000 per QALY gained.

3. Of Note

- The DBC considered patient input received from one patient group, the MS Society, which provided results from an online survey from March 3, 2020 to March 13, 2020,

- in both English and French. Of the 11 respondents (both patients and caregivers), none had experience with eculizumab.
- NMOSD is a rare autoimmune disorder which causes damage to the optic nerves and the spinal cord, leading to painful inflammation and loss of vision and weakness or paralysis in the legs or arms, loss of sensation, and problems with bladder and bowel function. NMOSD inevitably leads to disability (blindness, inability to walk,
- Patients noted that disease modifying therapies for MS are not beneficial in NMOSD and when administered have been shown to cause NMSOD disease to worsen. Patients who had used other therapies used for NMOSD reported they were of limited effectiveness or had severe side effects.
- Eculizumab is the first therapy approved for treatment of NMOSD. Other commonly used therapies such as azathioprine and rituximab are off-label drugs. Patients expressed there is a need for a drug that provides a reduction or avoidance of disease attacks and the consequent accrued disability from the attacks.