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	**caplacizumab**
Brand Name	Cablivi®
Dosage Form(s)	Powder for solution for intravenous or subcutaneous injection (11mg/vial)
Manufacturer	Sanofi Aventis
Submission Type	**New Submission**
Use Reviewed	Treatment of adults with acquired thrombotic thrombocytopenic purpura in combination with plasma exchange and immunosuppressive therapy
Common Drug Review (CDR)	Yes, CDR recommended: **Do Not Reimburse**. Visit the CDR website for more details: https://www.cadth.ca/caplacizumab-0
Drug Benefit Council (DBC)	Caplacizumab was reviewed by the Drug Benefit Council in 2020 which included a review of clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee. The DBC also considered Patient Input Questionnaire responses from two patients, one caregiver, and one Patient Group, patient input provided to the CDR, Clinical Practice Reviews from one specialist, and a Budget Impact Assessment. The DBC recommended that caplacizumab not be listed.
Drug Coverage Decision	Non-benefit
Date	May 26, 2023
Reason(s)	• The drug did not demonstrate advantages over standard of care with respect to efficacy and 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.

	• The pan-Canadian Pharmaceutical Alliance decided not to negotiate collectively or individually at the provincial-territorial level with the manufacturer of caplacizumab.
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 Common Drug Review (CDR)
- 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.

Drug Benefit Council Recommendation and Reasons for Recommendation

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Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Caplacizumab (Cablivi™)
Sanofi Genzyme, a division of Sanofi-Aventis Canada Inc.

Description:

Drug review of **caplacizumab (Cablivi™)** for the following Health Canada approved indications:

> For the treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP).

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on August 26, 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 two patients, one caregiver, and one Patient Group, patient input provided to the CDR, Clinical Practice Reviews from one specialist, and a Budget Impact Assessment.

Dosage Forms:

Cablivi™ is available as caplacizumab 11 mg powder for solution for IV or SC injection.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list caplacizumab (Cablivi™).

Reasons for the Recommendation:

1. **Summary**

- Results from one double-blind randomized controlled trial demonstrated that caplacizumab in addition to standard of care (SOC) statistically significantly reduced the time to normalization of platelet count compared to placebo in addition to SOC.
- The trial was of short-term duration (6 months), did not assess health-related quality of life, nor was it designed to assess the effects of caplacizumab on clinically important

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outcomes such as survival, reduction in organ damage, health care use, or long-term recurrence of aTTP.

- Patients receiving caplacizumab will still have to undergo treatment with plasma exchange (PEX) and corticosteroids, as well as other immunosuppressive drugs.
- Limitations in the design of the reviewed studies preclude determining whether the addition of caplacizumab to PEX plus immunosuppressive therapy provides clinically meaningful value compared with PEX plus immunosuppressive therapy alone.
- The price of caplacizumab would need to be reduced by approximately 75% to be considered cost-effective at a willingness-to-pay of $50,000 per quality-adjusted life year (QALY).

2. Clinical Efficacy

- The DBC considered the CDEC systematic review of caplacizumab, which included one phase III, double-blind randomized controlled trial (RCT) (HERCULES) that evaluated the efficacy and safety of caplacizumab in adult patients with aTTP. Eligible participants were randomized to receive caplacizumab 11 mg or placebo, in addition to SOC, which consisted of plasma exchange (PEX) and corticosteroid treatment, as well as other immunosuppressive drugs.
- The primary efficacy outcome of HERCULES was time to platelet count response. Other efficacy outcomes included prevention of recurrence of aTTP, prevention of refractory aTTP, prevention of major thromboembolic event, normalization of organ damage markers, and intensive care unit (ICU) or hospital stay related to aTTP episodes. A composite end point including aTTP-related death, recurrence of aTTP, or a thromboembolic event during the treatment period were assessed as well.
- Health-related quality of life was not assessed. HERCULES was also not designed to assess the effects of caplacizumab on the clinically important outcomes of survival, reduction in organ damage, health care use, or long-term recurrence of aTTP.
- HERCULES demonstrated that caplacizumab statistically significantly reduced the time to normalization of platelet count. CDEC could not determine the clinical magnitude of the correlation between time to normalization of platelet count with the aforementioned clinical outcomes.
- Limitations in the design of the reviewed studies precluded CDEC from determining whether caplacizumab provides clinically meaningful value compared with PEX plus immunosuppression alone.
- HERCULES and a supportive phase II RCT (TITAN) provided data on the effects of caplacizumab versus placebo for up to two aTTP episodes only. As such, CDEC could not determine caplacizumab's benefit, if any, beyond the duration of the trials.
- The variability in the natural history of aTTP and the limitations in the design and analysis of HERCULES prevented CDEC from identifying a subpopulation of patients with aTTP that is most likely to benefit from treatment with caplacizumab.
- For detailed information on the systematic review of caplacizumab please see the CDEC Final Recommendation at: https://www.cadth.ca/caplacizumab.

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3. **Safety**

- During the overall study period of HERCULES, almost all patients reported adverse events: 97.2% in the caplacizumab group and 97.3% in the placebo group. The most common adverse events reported in the caplacizumab group were epistaxis, headache, gingival bleeding, urticaria, pyrexia, fatigue, nausea, and aTTP episodes.
- There were fewer serious adverse events with caplacizumab compared with placebo during the overall study period. aTTP episodes were the most commonly reported serious adverse event, and the incidence of aTTP episodes was higher in the placebo group than in the caplacizumab group.
- Five patients (7.0%) treated with caplacizumab and nine patients (12.3%) treated with placebo withdrew from the study or treatment due to adverse events.
- For detailed information on the safety and tolerability of caplacizumab, please see the CDEC Final Recommendations at the links above.

4. **Economic Considerations**

- In CADTH's base-case analysis, the incremental cost-effectiveness ratio (ICER) associated with caplacizumab plus SOC compared to SOC alone was $237,053 per QALY.
- At a willingness-to-pay of $50,000 per QALY, the price of caplacizumab would need to be reduced by approximately 75% to be considered cost-effective.
- There is uncertainty associated with the cost-effectiveness of caplacizumab plus SOC as CADTH was unable to consider future aTTP episodes, specifically the potential impact of caplacizumab on reducing or delaying them, or the costs associated with further treatment for acute episodes

5. **Of Note**

- According to survey results compiled by the patient group, patients want options to improve the likelihood of success of PEX and to reduce the risk of future relapse.
- None of the patients who responded to the request for input had been treated with caplacizumab, although three of the patients from Canada who provided information through a Patient Group survey had received treatment with caplacizumab as part of a clinical trial. Patients who had received caplacizumab reported faster response and faster increase in platelet counts following PEX treatment.

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