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	**Amifampridine**
Brand Name	Ruzurgi®
Dosage Form(s)	10 mg tablets
Manufacturer	Médunik Canada
Submission Type	**New Submission**
Use Reviewed	Lambert-Eaton myasthenic syndrome (LEMS)
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: www.cadth.ca/sites/default/files/cdr/complete/SR0660%20Ruzurgi%20-%20CDEC%20Final%20Recommendation%20April%2023%2C%202021_For%20posting.pdf
Drug Benefit Council (DBC)	The DBC met on July 5, 2021. In their review, the DBC considered the following: the final reviews completed by the CRR on April 20, 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 responses from patients, caregivers, or patient groups and thus considered patient input provided to the CRR, and a Budget Impact Assessment.
Drug Coverage Decision	**Limited Coverage Benefit.** Access the amifampridine criteria from **www.gov.bc.ca/pharmacarespecialauthority**
Date	March 28, 2023
Reason(s)	**Drug coverage decision is consistent with the DBC and the CDEC recommendation.** • In one study,amifampridine (Ruzurgi) demonstrated some advantage over placebo in slowing disability progression assotiated with LEMS. • The Ministry participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer which were able to address the concerns identified by the CDEC with respect to 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

Amifampridine (Ruzurgi®)

Médunik Canada Inc.

Description:

Drug review of **amifampridine (Ruzurgi®)** for the following Health Canada approved indications:

> For the symptomatic treatment of Lambert-Eaton myasthenic syndrome (LEMS) in patients 6 years of age and older.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on April 20, 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, and a Budget Impact Assessment.

Dosage Forms:

Ruzurgi® is available as amifampridine 10 mg tablet.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list amifampridine (Ruzurgi®) 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 phase II, double-blind, placebo-controlled withdrawal study of patients with LEMS demonstrated that continuous treatment with amifampridine resulted in less disability progression compared with patients whose amifampridine was withdrawn.
- The cost-effectiveness of amifampridine is unknown due to limitations of the clinical data and methodological issues within the manufacturer's economic model and the amount of a necessary price reduction is likely much greater than the manufacturer's base-case estimate.

2. Clinical Efficacy

- The DBC considered the CADTH systematic review, which included a phase II, double-blind, placebo-controlled withdrawal study (DAPPER), which aimed to confirm the safety and evaluate the efficacy of amifampridine for the treatment of weakness associated with LEMS in adult patients.
- The primary efficacy endpoint in DAPPER was the categorization of the degree of change in the Triple Timed Up and Go (3TUG) test (last observation at the theoretical "peak drug effect", i.e., 2 hours post dose) upon withdrawal of active medication in Stage II of the trial when compared with time matched average of the 3TUG assessments during Stage I. In DAPPER this was categorized as > 30% deterioration in 3TUG time.
- The secondary efficacy endpoint was the Subject Self-Assessment of LEMS-Related Weakness (W-SAS) assessed at the end of Stage II as compared to the baseline.
- The primary efficacy outcome assessment demonstrated that significantly more patients in the taper to placebo arm exhibited a deterioration of 30% or greater on the 3TUG test compared to the continuous amifampridine arm. None of the patients in the continuous amifampridine arm had 30% or greater deterioration in the final (blinded) 3TUG test after withdrawal of study drug (Stage II), compared to 72.2% of patients in the taper to placebo arm.
- The secondary efficacy endpoint, the W-SAS, provided a global self-assessment that demonstrated an increase in weakness in the taper to placebo arm compared to the continuous amifampridine arm. Inference for this secondary outcome is limited as it was not adjusted for multiple comparisons, which prevents firm conclusions from being drawn.

- The effect of amifampridine on health-related quality of life and productivity was not evaluated in DAPPER and remains unknown.
- For detailed information on the systematic review of amifampridine please see the CDEC Final Recommendation at: https://www.cadth.ca/index.php/amifampridine.

3. Safety

- In DAPPER, adverse events excluding LEMS-related signs and symptoms occurred in 5 patients (35.7%) in the continuous amifampridine arm and 12 patients (66.7%) in the taper to placebo arm.
- The most common adverse events were abdominal discomfort and respiratory tract infection, which each occurred in 2 patients (11.1%) in the taper to placebo arm.
- In DAPPER, 1 patient (5.6%) in the taper to placebo arm experienced a serious adverse event of severe pneumonia.
- The duration and design of DAPPER was limited and may not be a true reflection of the harms associated with amifampridine for all patients with LEMS. The patients included in DAPPER were not amifampridine-naive and were required to be on a stable and optimized dose of amifampridine and meet a threshold of responsiveness to amifampridine at baseline.
- For detailed information on the safety and tolerability of amifampridine, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer submitted price, the average annual cost of treatment is between $40,000 and $100,000 per patient.
- The CADTH reanalysis of the manufacturer submission found that limitations of the clinical data and methodological issues within the sponsor's economic model prevented an accurate estimation of the cost-effectiveness of amifampridine.
- The manufacturer estimated an incremental cost-effectiveness ratio (ICER) of $453,809 per quality-adjusted life year (QALY); however, CDEC concluded that this value likely does not reflect the true cost-effectiveness of amifampridine compared to best supportive care (BSC).
- According to the sponsor's base case, there was 0% probability that amifampridine is cost-effective compared to BSC at a $50,000 per QALY willingness-to-pay threshold.

5. Of Note

- Amifampridine has been used for the treatment of LEMS for many years either through Health Canada's Special Access Programme or through compassionate supply provided by the manufacturer.
- Amifampridine was not commercially available in Canada until it was approved for sale in August 2020. As a result, it will no longer be available through the Special Access Programme.
- Patient input provided to CADTH indicated that patients with LEMS hope for a treatment that provides improvements in muscle strength and bodily functions with the goal of performing daily activities with a sense of normalcy.