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	**sebelipase alfa**
Brand Name	Kanuma®
Dosage Form(s)	2 mg/mL concentrate for solution for infusion in 10 mL (20mg) single-use vials
Manufacturer	Alexion Pharma Canada Corp.
Submission Type	**New Submission**
Use Reviewed	For the treatment of lysosomal acid lipase deficiency (LAL-D)
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. CADTH published a Drug Implementation Advice on the use of sebelipase alfa in patients with onset of LAL-D over 6 months of age found here.
Drug Benefit Council (DBC)	The DBC met on November 5, 2018. In their review, the DBC considered the following: the final reviews completed by the CRR of the CADTH on September 26, 2018, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC received and considered Patient Input Questionnaire responses from one Patient Group and also considered patient input provided to the CRR, Other Drug Agencies Review Recommendations document, and a Budget Impact Assessment.

	The DBC recommended that sebelipase alfa not be listed at the submitted price for the treatment of LAL-D.
Drug Coverage Decision	**<u>Infants with confirmed diagnosis and onset of clinical manifestations of LAL-D before 6 months of age:</u>** **Exceptional Case-by-Case Coverage Through the Expensive Drugs for Rare Diseases (EDRD) Process** **<u>Patients with confirmed diagnosis and onset of clinical manifestations of LAL- D after 6 months of age:</u>** **Non-Benefit**
Date	April 5, 2023
Reason(s)	**Drug coverage decision is consistent with the CADTH and DBC recommendations.** • Sebelipase alfa has shown to help infantile patients with an onset of LAL-D at less than 6 months of age survive to 12 months of age compared to past studies showing near certain death by 12 months of age for these patients. • The evidence for patients over 6 months of age was also reviewed but it is unclear how the parameters that were studied would benefit LAL-D patients. • Evidence for both patient populations is uncertain due to limitations of the clinical trials including small sample sizes and lack of long-term follow-up. • Current standard of care is ineffective and other treatment options are risky with limited efficacy. • 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 and the pCPA was able to address the concerns identified by CADTH 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.

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

Sebelipase (Kanuma®)
Alexion Pharmaceuticals Inc.

Description:

Drug review of **sebelipase (Kanuma®)** for the following Health Canada approved indications:

> For the treatment of lysosomal acid lipase deficiency (LAL-D).

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on September 26, 2018, 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 Groups, patient input provided to the CDR, an Other Drug Agencies Review Recommendations document, and a Budget Impact Assessment.

Dosage Forms:

Kanuma® is available as sebelipase 20mg/10mL solution for intravenous (IV) infusion.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that sebelipase (Kanuma®) not be listed at the submitted price.

Reasons for the Recommendation:

1. Summary

- In one trial, 6 of 9 patients survived to 12 months of age. In the historical cohort, 0 of 21 patients survived beyond eight months of age. Results from additional follow-up analyses showed five of the nine patients survived beyond 36 months of age.
- In the other trial, sebelipase alfa therapy resulted in a reduction in multiple disease-related hepatic and lipid abnormalities in some children and adults with LAL-D.
- At the manufacturer-submitted price, the average annual cost for sebelipase alfa in infantile-presentation patients ranges from $892,000 to $4.9 million per patient.

2. Clinical Efficacy

- The DBC considered the CDR clinical review, which included two trials.

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DBC Recommendation and Reasons for Recommendations

- VITAL was a phase II/III, multi-centre, open label, single-arm study of sebelipase alfa in patients with LAL-D with growth failure or other evidence of rapidly progressive disease prior to six months of age. The age range at study entry was 1 month to 6 months. The primary efficacy end point in VITAL was the proportion of patients surviving to 12 months of age.
- ARISE was a phase III, randomized, multi-centre, double-blind, placebo-controlled study of children and adults with LAL-D. The primary efficacy outcome measure in ARISE was the proportion of patients who achieved ALT normalization at the end of the double-blind period (week 20).
- In VITAL, 6 of 9 patients who received any amount of sebelipase alfa, and who were no older than six months when starting sebelipase alfa, survived to 12 months of age. In the historical cohort, 0 of 21 patients survived beyond eight months of age. Results from additional follow-up analyses showed five of the nine patients survived beyond 36 months of age.
- The results of ARISE suggested that sebelipase alfa, as compared with placebo, is associated with statistically significant improvements in ALT levels and some lipid and liver parameters after 20 weeks of treatment. The relationships between many of these biomarker outcomes and clinical outcomes have not been well-established, limiting the usefulness of the trial in determining the efficacy of sebelipase alfa.
- There were no statistically significant between-group differences in health-related quality of life in the ARISE trial.
- Key limitations in both trials were the small sample size and the lack of long-term follow-up. Surrogate outcomes were used instead of hard clinical outcomes in ARISE, and a historical control for the primary outcome was used in VITAL.
- There is no published clinical evidence for the efficacy or safety of sebelipase alfa treatment in children with LAL deficiency with onset of symptoms between age seven months and four years of age.

3. Safety

- The safety profile of sebelipase alfa was similar to placebo in the controlled phase of the trials, with the exception of anti-drug antibodies formation.
- Treatment with sebelipase alfa was not associated with serious adverse events in the short term, beyond infusion-related reactions.
- While there were no apparent differences in safety results for sebelipase alfa between the controlled phase of the studies and the open-label extension, conclusions regarding the long-term safety of sebelipase alfa in patients with LAL deficiency are limited due to the absence of a comparator arm and the short duration of treatment.
- For detailed information on the safety and tolerability of [DRUG], please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer-submitted price, the average annual cost for sebelipase alfa in infantile-presentation patients ranges from $892,000 to $4.9 million per patient.

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DBC Recommendation and Reasons for Recommendations

- The CDR reanalysis of the manufacturer submission estimated the incremental cost-utility ratio (ICUR) for sebelipase alfa compared to best supportive care to be over $4.9 million per QALY and over $2 million per quality adjusted life year (QALY) in infantile- and pediatric/adult-presentations, respectively.
- The CDR estimated that, to reduce the manufacturer and CDR ICURs to $50,000 and $100,000 per QALY, either a price reduction over 96% or a cap on annual drug costs per patient of $50,000 is required.

5. Of Note

- Infantile-onset LAL deficiency is a rare, genetic, life-threatening disease of lipid metabolism with a very high risk of mortality before the age of 12 months. There are no clinically effective drug and non-drug alternative treatments.
- The DBC received patient input from one patient group (the Canadian Liver Foundation BC/Yukon), which emphasized that LAL-D is a genetic, progressive and chronic ultra-rare metabolic disease for which the current standard of care (supplements, low cholesterol and reduced saturated fat diets, and statins) has been shown to be ineffective. Other treatment options, including stem cell therapy and liver transplantation, are risky and have only limited effectiveness. There is an unmet need for an effective and safe treatment that alters the progression of LAL-D.