Drug Coverage Decision for BC PharmaCare

About PharmaCare BC PharmaCare is a publicly funded drug plan that helps B.C. residents pay for most prescription drugs and pharmacy services, and some medical devices and supplies.

Details of Drug Reviewed

Drug	**avalglucosidase alfa**
Brand name	Nexviazyme™
Dosage form(s)	10 mg/mL in 100 mg vial, lyophilized powder for intravenous infusion
Manufacturer	sanofi-aventis Canada Inc.
Submission type	**New Submission**
Use reviewed	Late-onset Pompe disease (LOPD)
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	CRR recommendation: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for details.
Drug Benefit Council (DBC)	The Drug Benefit Council (DBC) met on May 1, 2023, and considered the following: the CADTH final review, which included clinical and pharmacoeconomic evidence review material; the CADTH recommendations; responses from three patient input questionnaires; patient, caregiver and patient group input provided to the CRR; a clinical practice review from a specialist; and a budget impact assessment. The DBC recommended that Nexviazyme be reimbursed with criteria as a first-line agent for LOPD only if certain pricing conditions are met.
Drug Coverage Decision	**Non-benefit**
Date	October 25, 2023
Reason(s)	**The drug coverage decision is consistent with the DBC and CADTH recommendations to only reimburse Nexviazyme if certain pricing conditions are met.**

	• One clinical trial demonstrated that Nexviazyme did not demonstrate significant clinical advantages over alglucosidase alfa (Myozyme®) in addressing patients' unmet needs. • The Ministry of Health participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer and attempted to address some concerns identified by CADTH and the DBC with respect to the cost-effectiveness and value for money. The negotiations concluded without an agreement on September 29, 2023, after inability to achieve the value required by the pCPA.

The drug review process in B.C.

A manufacturer submits a request to the Ministry of Health (the Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry by considering:

- whether the drug is safe and effective
- advice from a national group called the Canadian Agency for Drugs and Technologies in Health (CADTH)
- what the drug costs and whether funding it provides good value to the province
- ethical considerations of covering and not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes a BC PharmaCare coverage decision by taking into account:

- existing BC PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- drugs already covered by BC PharmaCare that treat the same or similar medical conditions
- the overall cost of covering the drug

Visit Ministry of Health - PharmaCare and BC PharmaCare – Drug reviews 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

CONFIDENTIAL

Drug Benefit Council (DBC)
Recommendation and Reasons for Recommendation

FINAL

Avalglucosidase alfa (Nexviazyme®)
Sanofi-Aventis Canada Inc.

Description:

Drug review of **avalglucosidase alfa (Nexviazyme®)** for the following Health Canada approved indications:

> For the long-term treatment of patients with late-onset Pompe disease (LOPD).

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on July 5, 2022, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC also considered Patient Input Questionnaire responses from three patients, as well as patient, caregiver and patient group input provided to the CDR, a Clinical Practice Review from a specialist, and a Budget Impact Assessment.

Dosage Forms:

Nexviazyme® is available as avalglucosidase alfa lyophilized powder of 100 mg/vial for intravenous infusion.

Recommendations:

1. The Drug Benefit Council (DBC) recommends listing avalglucosidase alfa (Nexviazyme®) as a first-line benefit for patients with late-onset Pompe disease.
2. The Ministry of Health should negotiate to achieve a lower price.
3. The reimbursement criteria and conditions recommended by CADTH are an appropriate basis for coverage, with the DBC recommending three revisions: the requirement that patients be treatment-naïve should be removed; the assessment of treatment response should be reviewed at 12 months, rather than 6 months; and the discontinuation criterion requiring declining motor or respiratory function *at a similar rate as prior to therapy* should be removed. The revised criteria are below:

    1. Treatment with avalglucosidase alfa should be reimbursed when initiated in patients with all the following:
        1.1. a confirmed diagnosis of late-onset Pompe disease, and
        1.2. ambulatory,

2. Treatment with avalglucosidase alfa must not be reimbursed when initiated in patients with any of the following:
   2.1. known Pompe-specific cardiac hypertrophy,
   2.2. have severe disease, and
   2.3. unable to perform repeated FVC [% predicted] measurements between 30% and 85%.
3. Assessment of treatment response should be conducted at 12-month intervals. Treatment with avalglucosidase alfa can be renewed as long as the patient does not meet any of the discontinuation criteria.
4. Treatment with avalglucosidase alfa must be discontinued if the patient develops any of the following:
   4.1. Severe untreatable infusion-related reactions.
   4.2. Declining motor or respiratory function to the point of loss of ambulation or the need for permanent invasive ventilation.
5. The patient must be under the care of a clinician experienced in treating lysosomal storage diseases or other types of neuromuscular diseases.

Reasons for the Recommendation:

1. Summary

- In one randomized controlled trial (RCT), treatment with avalglucosidase alfa was non-inferior to alglucosidase alfa in the primary outcome, mean difference of change in forced vital capacity (FVC % predicted) between treatment groups at week 49.
- Secondary and exploratory outcomes, including the 6-minute walk test (6MWT), aligned with the non-inferiority result observed in the primary outcome.
- At the manufacturer's submitted price, avalglucosidase alfa was less costly per patient but not less effective than alglucosidase alfa.

2. Clinical Efficacy

- The DBC considered the CADTH review, which included one multicentre, double blind, active control, phase III RCT (COMET, N = 100) designed to evaluate the efficacy and safety of avalglucosidase alfa 20 mg/kg body weight given every other week for the treatment of LOPD.
- The primary outcome of COMET, FVC (% predicted) in the upright position, was used to test the noninferiority of avalglucosidase alfa to alglucosidase alfa using a noninferiority margin of -1.1%. Sequential testing continued with superiority testing for FVC (% predicted) followed by the key secondary outcome of distance walked and % predicted on the 6MWT.
- In COMET, patients in the modified intention-to-treat (mITT) population, which was equivalent to the intention-to-treat (ITT) population, demonstrated a least squares (LS) mean change in FVC (% predicted) in the upright position from baseline to Week 49 of 2.89% for the avalglucosidase alfa arm and 0.46% for the alglucosidase alfa arm. The mean difference of change between treatment groups was 2.43%, for which the lower bound of the 95% confidence interval (CI) did not exceed the

noninferiority margin of -1.1%, indicating that the criteria for noninferiority of avalglucosidase alfa compared to alglucosidase was demonstrated.

- Analysis of the per protocol population had similar results with a FVC (% predicted) LS mean change from baseline to Week 49 of 2.87% and 0.19% for the avalglucosidase alfa and alglucosidase alfa groups, respectively. The mean difference of change between treatment groups was 2.69%.
- The mean change from baseline to Week 49 for the 6MWT distance was 32.21 metres for the avalglucosidase alfa group and 2.19 metres for the alglucosidase alfa group.
- For detailed information on the systematic review of avalglucosidase alfa (Nexviazyme®), please see the CDEC Final Recommendation at: https://www.cadth.ca/avalglucosidase-alfa.

3. Safety

- In COMET, the number of adverse events, serious adverse events and withdrawals due to adverse events were similar in the avalglucosidase alfa and alglucosidase alfa treatment arms.
- For detailed information on the safety and tolerability of avalglucosidase alfa, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer's list price, avalglucosidase alfa is less costly per patient per year than alglucosidase alfa.

5. Of Note

- Patients with Pompe disease who responded to the questionnaire indicated their condition can cause heart problems, breathing problems, and muscle weakness. Many patients will need to use wheelchairs and ventilators as the disease progresses.
- Patients expressed a desire for a treatment that halted the progression of the disease, rather than slowing it. It should be noted that neither avalglucosidase alfa nor alglucosidase alfa have been shown to halt the progression of the disease.
- All of the patients who completed the Patient Input Questionnaire had received treatment with alglucosidase alfa (Myozyme), and none had tried avalglucosidase alfa.