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	**incobotulinumtoxinA**
Brand Name	Xeomin®
Dosage Forms	50 units per vial and 100 units per vial, powder for solution for injection
Manufacturer	Merz Therapeutics Canada
Submission Type	**New Submission**
Use Reviewed	For the treatment of chronic sialorrhea associated with neurological disorders in adults
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	Yes, CRR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details: https://www.cadth.ca/sites/default/files/DRR/2021/SR0678%20Xeomin%20-%20CADTH%20Final%20Rec.pdf
Drug Benefit Council (DBC)	The DBC met on November 1, 2021. The DBC considered various inputs including: the final reviews completed by the CADTH, 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 so considered patient input provided to CADTH as well as a Budget Impact Assessment.
Drug Coverage Decision	**Non-Benefit**
Date	February 14, 2023

Reasons	**Drug coverage decision is consistent with the DBC recommendation.** • The drug demonstrated some advantage over placebo with respect to efficacy for reducing salivary flow rate and patient reported impression of change. • At the submitted price, incobotulinumtoxinA was not considered cost-effective for the treatment of chronic sialorrhea associated with neurological disorders in adults. The Ministry of Health participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer which were not able to address the concerns identified by the CDEC and the DBC with respect to cost-effectiveness and value for money. As such, the pCPA negotiations closed without an agreement between the pCPA and Merz Therapeutics Canada and the drug will not be added to the PharmaCare formulary as an eligible benefit.
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

incobotulinumtoxinA (Xeomin®) Merz Therapeutics

Description:
Drug review of **incobotulinumtoxinA (Xeomin®)** for the following Health Canada approved indications:

For the treatment of adults with chronic sialorrhea associated with neurological disorders.

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on September 27, 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 so considered patient input provided to CADTH as well as a Budget Impact Assessment.

Dosage Forms:

Xeomin® is available as incobotulinumtoxinA 50 and 100 units/vial powder for intraglandular injection.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list incobotulinumtoxinA (Xeomin®) at the submitted price for this indication.

Of Note:

- If the Ministry is able to negotiate a significant price reduction, the reimbursement criteria and conditions recommended by CDEC are an appropriate basis for coverage.

Reasons for the Recommendation:

1. **Summary**
- Evidence from one randomized, double-blind, placebo-controlled study in adults with moderate to severe sialorrhea resulting from neurological conditions showed that treatment with incobotulinumtoxinA resulted in a statistically significant reduction in salivary production.
- Based on the manufacturer's submitted prices, Xeomin® in combination with standard of care (SoC) is not considered cost-effective at a willingness to pay of $50,000 per quality-adjusted life year (QALY). CDEC recommended that a price reduction of at least 30% would be needed to ensure Xeomin® is cost-effective.

2. **Clinical Efficacy**

- The DBC considered the CDEC systematic review, which included one randomized, double-blind, placebo-controlled study (SIAXI, N=184) in adults with moderate to severe sialorrhea resulting from neurological conditions.
- The objective of SIAXI was to investigate the efficacy and safety of injection of two doses of incobotulinumtoxinA (75 U or 100 U) into the salivary glands, compared with placebo, in reducing the unstimulated salivary flow rate (uSFR) as well as the frequency and severity of chronic troublesome sialorrhea as evaluated by patients, caregivers and investigators using multiple rating tools.
- The co-primary efficacy outcomes in SIAXI were change in uSFR from baseline to week 4 and patient reported global impression of change scale (GICS) at week 4 of the trial's main period. The secondary outcomes were change in uSFR from baseline to weeks 8 and 12 and patient reported GICS at weeks 1, 2, 8, and 12 of the trial's main period.
- Evidence from SIAXI suggested that injection of incobotulinumtoxinA 100U into the salivary glands of adult patients with neurological disorders resulted in reduced salivary production and improvements in patients' perceptions of frequency and severity of sialorrhea. At 4 weeks post-injection, the mean difference in change from baseline on the uSFR and patient GICS was statistically significant in favour of incobotulinumtoxinA vs. placebo.
- There is considerable uncertainty associated with the results of SIAXI due to limited confidence in the outcome measures used (uSFR, GICS, drooling severity and frequency scales, or modified Radboud oral motor inventory for Parkinson's disease), which were not validated and had no estimated minimal important differences. CDEC noted that these outcomes are not routinely used in clinical practice and are subjective apart from uSFR, which is an impractical outcome in a real-world setting. Thus, post-incobotulinumtoxinA treatment changes in sialorrhea had unclear clinical significance and relevance to the health-related quality of life (HRQoL) of patients.

- There is no comparative evidence on the efficacy of different botulinum neurotoxins for the treatment of chronic sialorrhea associated with neurological disorders and there is a lack of evidence in patients with a variety of neurological conditions.
- For detailed information on the systematic review of Xeomin® please see the CDEC Final Recommendation at: https://www.cadth.ca/incobotulinumtoxina.

3. Safety

- Treatment with incobotulinumtoxinA was tolerated in most patients, and adverse effects were generally manageable, with some infrequent but expected notable harms related to toxin spread (e.g., dry mouth, dysphagia).
- For detailed information on the safety and tolerability of Xeomin®, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The CADTH reanalysis of the manufacturer submission reported the incremental cost-effectiveness ratio (ICER) for incobotulinumtoxinA in combination with SoC was $67,239 per QALY compared with SoC. At this ICER, incobotulinumtoxinA is not cost-effective at a $50,000 per QALY willingness to pay for adult patients with neurological disorders suffering from chronic sialorrhea.

- CADTH recommended a reduction in price of at least 30% would be required for incobotulinumtoxinA to be considered cost-effective.

5. Of Note

- Patient input provided to CADTH indicated that chronic troublesome sialorrhea can lead to speech difficulties, facial skin maceration, bad breath, and infections.
- The most common methods used by individuals living with PD to manage sialorrhea were tissues or cloths to wipe drool (87%), followed by chewing gum (17%) and muscle exercises (16%).
- None of the survey respondents had any previous experience with incobotulinumtoxinA and only one respondent had received other botulism neurotoxins injections.
- Most of the medications used to treat chronic sialorrhea are associated with adverse effects that patients may find difficult to tolerate. Patient input indicated there exists a need for a treatment that effectively reduces the frequency and severity of sialorrhea with minimal adverse effects.