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	**onabotulinumtoxinA**
Brand Name	Botox ®
Dosage Form(s)	50 units/vial, 100 units/vial and 200 units/vial powder for solution for injection
Manufacturer	Allergan Inc.
Submission Type	**New Submission**
Use Reviewed	For the treatment of overactive bladder (OAB)
Common Drug Review (CDR)	Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: https://www.cadth.ca/sites/default/files/cdr/complete/cdr_complete_SR0362_Botox-OAB_nov14_2014.pdf
Drug Benefit Council (DBC)	DBC met on November 17, 2014. DBC considered various inputs including: final review completed by the Common Drug Review (CDR), which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from one Patient Group, Clinical Practice Reviews from two specialists, Manufacturer comments on the CDEC recommendation, as well as a Budget Impact Assessment (BIA) and a DBC Recommendation and Reasons for Recommendation regarding the Overactive Bladder Therapeutic Review from the September 9, 2013 meeting.
Drug Coverage Decision	**Limited Coverage: Access the clostridium botulinum neurotoxin type A, with complexing proteins, also known as onabotulinumtoxinA criteria from www.gov.bc.ca/pharmacarespecialauthority**
Date	February 26, 2019
Reason(s)	**Drug coverage decision is consistent with the DBC recommendation.** • The drug demonstrated some advantage over placebo in patients with inadequate response to or are intolerant of anticholinergic medication with respect to efficacy and quality of life but was associated with more adverse events. • Based on economic considerations and the submitted product price, the drug was not cost-effective. • 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 the cost-effectiveness and 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 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 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 (DBC) Recommendation and Reasons for Recommendation

FINAL

OnabotulinumtoxinA (Botox®)
Allergan Inc.

Description:

Drug review of **onabotulinumtoxinA (Botox®)** for the following Health Canada approved indication:

> For the treatment of refractory urinary incontinence due to overactive bladder.

In their review, the DBC considered the following: final review completed by the Common Drug Review (CDR) on November 12, 2014, which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from one Patient Group, Clinical Practice Reviews from two specialists, Manufacturer comments on the CDEC recommendation, as well as a Budget Impact Assessment and a DBC Recommendation and Reasons for Recommendation regarding the Overactive Bladder Therapeutic Review from the September 9, 2013 meeting.

Dosage Forms:

Botox® is available as onabotulinumtoxinA 50, 100 and 200 units per vial for intradetrusor injection.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that **onabotulinumtoxinA (Botox®)** be listed with the following criteria:
    a. For use in patients who have had an adequate trial of at least two other pharmacological treatments for OAB (MBPSD to determine a definition for an adequate trial);
    b. Prescribing be restricted to urologists;
    c. Funding should be limited to treatment with one dose to establish efficacy, and it should be discontinued in non-responders (i.e., those who fail to achieve a reduction of at least 50% in the frequency of urinary incontinence episodes with one dose);

d. Limit to a maximum of three doses per year in responders, at a frequency of no more than once every 12 weeks.

2. Of note: the Ministry of Health is encouraged to negotiate an acceptable price (i.e. no more than the current cost of onabotulinumtoxinA for treatment of urinary incontinence due to neurogenic detrusor overactivity resulting from neurogenic bladder associated with multiple sclerosis or subcervical spinal cord injury).

Reasons for the Recommendation:

1. Summary

- In 2 randomized controlled trials (RCTs) involving patients who were nonresponsive to one or more anticholinergic agents, onabotulinumtoxinA was demonstrated to be more effective than placebo in terms of percentages of patients with incontinence episodes, number of episodes of micturition for 24 hours, and proportion achieving continence.
- Urinary tract infections, urinary retention, and dysuria are significantly more common with onabotulinumtoxinA than with placebo.
- Use of this agent requires specialized expertise and administration via an invasive procedure.
- At the proposed price, the cost-effectiveness of onabotulinumtoxinA is unattractive.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included four multicentre, double-blind RCTs comparing onabotulinumtoxinA injection of 100 U with placebo. Two studies were phase 3 trials of up to 39 weeks duration but the placebo-controlled comparison was limited to 12 weeks, after which all patients could receive treatment with onabotulinumtoxinA. Two studies were phase 2 studies of 36 weeks and 6 months duration, respectively.
- Three studies enrolled patients aged ≥ 18 years with symptoms of idiopathic OAB with urge incontinence and who were not adequately managed with anticholinergic therapy. One study enrolled patients with symptoms of idiopathic OAB with episodes of urgency with or without urge incontinence and who are refractory, or had contraindications to, or discontinued anticholinergics because of adverse events. CDEC primarily focused the deliberations on the results of the two phase 3 trials.
- Patients treated with onabotulinumtoxinA had a greater decrease from baseline in the number of daily incontinence episodes at week 12 compared with placebo.
- In two studies patients treated with onabotulinumtoxinA had a greater decrease from baseline in the number of daily urge incontinence episodes at week 12 compared with placebo.
- Compared with placebo, at week 12 patients treated with onabotulinumtoxinA had a greater decrease from baseline in the number of daily urgency episodes, a greater decrease from baseline in the number of micturitions per 24 hours, and a greater decrease from baseline in the number of daily nocturia episodes.

- Two studies reported statistically significant and clinically important improvements in disease-specific health-related quality of life measures for patients treated with onabotulinumtoxinA versus placebo.

3. Safety

- In the two studies CDEC focused upon, the proportions of patients with at least one serious adverse event, at least one adverse event, and who withdrew due to adverse events, was greater in the onabotulinumtoxinA groups compared with placebo.
- The most frequent adverse events associated with onabotulinumtoxinA were urinary tract infection, dysuria, urinary retention, bacteriuria, and increased residual urine volume.
- The proportion of patients who required the use of clean intermittent catheterization for urinary retention was significantly greater compared to placebo.

4. Economic Considerations

- The manufacturer submitted a cost-utility analysis onabotulinumtoxinA plus best supportive care (BSC), which included incontinence pads and treatment for adverse events such as skin and urinary tract infections, compared to BSC alone for the treatment of refractory urinary incontinence in adults with OAB.
- The CDR re-analysis of the manufacturer analysis found that, accounting for limitations, the incremental cost-utility ratio (ICUR) for onabotulinumtoxinA compared with BSC ranged from $56,932 to $60,451 per quality-adjusted life-year (QALY) gained, with a most likely estimate of $59,388 per QALY gained.
- At the submitted price, and depending on frequency of re-treatment, the annual drug cost of onabotulinumtoxinA varies from $357 to $1,428 per year. When administration costs are also considered, the total annual cost of onabotulinumtoxinA is significantly greater that of second-line anticholinergics

5. Of Note

- Patient Input Questionnaire response from one Patient Group indicated that patients who had received treatment with onabotulinumtoxinA experienced good results with regards to effectiveness, tolerability, and frequency of leakage episodes. The Patient Group noted that other OAB treatments are associated with side effects including severe dry mouth, which often leads to patients discontinuing them.