Cost-Effectiveness of Incobotulinumtoxin-A with Flexible Treatment Intervals Compared to Onabotulinumtoxin-A in the Management of Blepharospasm and Cervical Dystonia

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Abstract

Background: Incobotulinumtoxin-A (Xeomin®, Merz Pharmaceuticals, Sydney, New South Wales) is a formulation of botulinum neurotoxin type A that is free of complexing proteins. Objective: To assess the cost-effectiveness of incobotulinumtoxin-A administered with flexible treatment intervals compared to onabotulinumtoxin-A (Botox®, Sydney, New South Wales) in blepharospasm and cervical dystonia from the perspective of Australian health care providers. Methods: A Markov state transition model was developed to perform a cost-utility analysis to compare the cost and health benefits of incobotulinumtoxin-A to that of onabotulinumtoxin-A. The cost-utility analysis compared incobotulinumtoxin-A treatment, given at minimum intervals of 6 weeks and maximum intervals of 20 weeks, with onabotulinumtoxin-A treatment, given at minimum intervals of 12 weeks and maximum intervals of 20 weeks. The Markov model consisted of three health states and followed patients in weekly cycles for 5 years. Only direct health care costs associated with the acquisition and administration of type A botulinum neurotoxins were included. Utility values were derived from a prospective, open-labeled cohort study. The primary outcome measure was the incremental cost per quality-adjusted life-year. Univariate and probabilistic sensitivity analyses were conducted. Results: Incobotulinumtoxin-A was cost-effective compared to onabotulinumtoxin-A in both blepharospasm and cervical dystonia, with an incremental cost/quality-adjusted life-year gained of A$25,588 and A$23,794, respectively. Conclusions: Incobotulinumtoxin-A administered at flexible treatment intervals determined by the needs of the patient was found to be a cost-effective treatment option when compared to the administration of onabotulinumtoxin-A in the Australian health care system. The option to administer incobotulinumtoxin-A according to the needs of the patient resulted in patients experiencing symptoms for a fewer number of weeks compared to onabotulinumtoxin-A given at minimum 12-week intervals.

Keywords: blepharospasm, cervical dystonia, cost-effectiveness, incobotulinumtoxin-A.

Introduction

Blepharospasm (BLEPH) is a focal dystonia that is characterized by excessive tone in the orbicularis oculi muscle. It causes a sporadic or permanent involuntary closure of the eye, which causes a physical deformity and, with exacerbation of the symptoms, may even lead to visual impairment (functional blindness). BLEPH can cause severe disability to patients in leading their everyday lives. For example, patients are either completely unable to read, watch television, or perform any housework or can only do so with considerable difficulty. Most of the times, they are unable to leave the house without a caregiver. BLEPH is usually bilateral but may be more pronounced on one side than on the other.

Cervical dystonia (CD), also known as spasmodic torticollis, covers a spectrum of involuntary movements with abnormal posture of the head and shoulder/neck region. Patients suffer greatly from CD, which can sometimes make everyday tasks, such as working, cleaning, and eating, impossible to accomplish.

In Australia, the estimated prevalence of BLEPH and CD is 0.0007% and 0.015%, respectively [1,2]. On the basis of the 2012 population estimates from the Australian Bureau of Statistics [3], this equates to 1568 patients for BLEPH and 3360 patients for CD. Medical Benefits Schedule (MBS) [4] and Pharmaceutical Benefits Schedule (PBS) [5] data report that the Commonwealth spent in excess of A$11 million on treatment with onabotulinumtoxin-A for these indications in 2013 and 2014.

In Australia, incobotulinumtoxin-A (Xeomin®, Merz Pharmaceuticals, Sydney, New South Wales) is licensed for the symptomatic management of BLEPH and CD in adults, with the inclusion of flexible treatment intervals (at minimum intervals of 6 weeks and maximum intervals of 20 weeks) to be determined on the actual clinical needs of the individual patient.

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Native botulinum neurotoxin (BoNT) is a high-molecular-weight complex that, in addition to the neurotoxin (150 kD), contains bacterial nontoxic proteins, such as hemagglutinins and nonhemagglutinins (i.e., proteins without any therapeutic effect). In contrast to conventional preparations of BoNT type A (BoNT/A) such as onabotulinumtoxin-A (Botox, Sydney, New South Wales) and abobotulinumtoxin-A (Dysport, Ipsen Biopharmaceuticals, Melbourne, Victoria), incobotulinumtoxin-A contains pure (150 kD) neurotoxin, and because it is free from complexing proteins, it has a low foreign protein content, thereby having a lower immunogenic potential than do other available preparations of BoNT/A, which is a clinical advantage. Such bacterial proteins potentially play a role as a promoter of an immune reaction, resulting in a loss of effect and reduction in duration of activity [6].

Furthermore, the additional clostridial proteins found in conventional BoNT/A formulations are likely to be a risk factor for the formation of neutralizing antibodies [7], which can potentially lead to failure of the treatment. A study that analyzed serum samples of 503 secondary nonresponder patients treated with onabotulinumtoxin-A, abobotulinumtoxin-A, or both found that neutralizing antibodies were detected in 44.5% of the samples tested [8]. This means that repeated application of incobotulinumtoxin-A, even in high doses, does not induce the formation of neutralizing antibodies because of the low content of protein. Therefore, treatment with incobotulinumtoxin-A is able to provide results similar to those achievable with conventional preparations of BoNT/A without the risk of antibody formation, providing long-lasting effects [6].

In addition, conventional BoNT/A preparations, such as onabotulinumtoxin-A and abobotulinumtoxin-A, require refrigeration (2–8°C) during transport and storage. A deviation from these requirements can cause breaks in the cold chain. Advantageously, safety issues or decrease in efficacy due to a break in the cold chain is not a problem with incobotulinumtoxin-A because vials can be stored at room temperature (up to 25°C) for up to 4 years.

Finally, conventional forms of BoNT/A require a minimum 12-week interval before re-treatment compared to incobotulinumtoxin-A, which allows flexible treatment intervals (at minimum intervals of 6 weeks and maximum intervals of 20 weeks). Therefore, incobotulinumtoxin-A can be administered in shorter intervals according to the needs of the patient compared to onabotulinumtoxin-A. A cross-sectional survey on satisfaction with treatment with BoNT/A in patients with CD showed that approximately two-thirds of the patients preferred individualized flexible treatment intervals [9].

The objective of this study was to provide evidence of the cost-effectiveness of incobotulinumtoxin-A when administered with flexible dosing intervals according to the needs of the patient when compared to onabotulinumtoxin-A in patients with BLEPH and CD from the perspective of Australian health care providers.

Methods

Model Structure

The premise underlying the model structure was that patients treated with type A botulinum neurotoxins will experience a re-emergence of symptoms at some point after each injection. The benefit of flexible dosing with incobotulinumtoxin-A at a minimum of 6 weeks is that it can be administered earlier than onabotulinumtoxin-A, thereby sparing the patient these symptoms.

A Markov state transition model was developed to perform a cost-utility analysis to compare the cost and health benefits of incobotulinumtoxin-A flexible dosing given at a minimum interval of 6 weeks and a maximum interval of 20 weeks, with those of onabotulinumtoxin-A delivered at a minimum interval of 12 weeks and a maximum interval of 20 weeks (base case).

The dosage for onabotulinumtoxin-A is consistent with the Australian Product: for BLEPH, “each treatment lasts approximately three months, following which the procedure can be repeated as needed ....”, and similarly for CD, “the duration of therapeutic effect reported in the clinical trials showed ... a typical duration of approximately 12 to 16 weeks, depending on the patient’s individual disease and response” [10].

The Markov model consisted of three health states, with patients in the model transitioning between these health states in weekly cycles for a time horizon of 5 years. The three health states of the Markov model were as follows: 1) patient is receiving treatment (with either incobotulinumtoxin-A or onabotulinumtoxin-A); 2) patient’s symptoms are adequately controlled following treatment; and 3) patient’s symptoms have re-emerged.

Figure 1 illustrates the transition of patients through the Markov model. All patients began in the model by receiving the study treatment. Both treatments were assumed to be effective and patients therefore moved to the “controlled symptoms” health state. At some point over the ensuing weeks, the patients’ symptoms would re-emerge. The rate at which symptoms re-emerged was assumed to be equal between the incobotulinumtoxin-A and the onabotulinumtoxin-A treatment groups because the therapeutic effect was considered comparable between incobotulinumtoxin-A and onabotulinumtoxin-A [11]. Furthermore, there were no significant differences between treatments with regard to the median time to waning of treatment effect: 10 weeks for incobotulinumtoxin-A versus 11 weeks for onabotulinumtoxin-A. Similarly, the time to onset of treatment effect and the duration of treatment effect demonstrated no statistically significant differences between the two treatment groups [12,13].

The model then determined whether the patient was eligible for another treatment on the basis of the time since the patient’s previous injection. If the patient was eligible for treatment, he or she would transit back to the original health state, immediately after which the process began again. If the patient was not eligible for re-treatment, he or she would reside in the health state in which symptoms were present until such time as the necessary treatment interval elapsed. The only difference between the incobotulinumtoxin-A and onabotulinumtoxin-A treatment arms of the economic model was the treatment interval.

The primary outcome measure of the model was incremental cost per quality-adjusted life-year (QALY) gained for incobotulinumtoxin-A compared to that for onabotulinumtoxin-A. All costs and QALYs were discounted at 5% per annum. The model also compared incobotulinumtoxin-A flexible dosing with onabotulinumtoxin-A delivered at fixed 12-week dosing intervals and with onabotulinumtoxin-A delivered at a minimum of 8-week intervals. Finally, the model also compared incobotulinumtoxin-A flexible dosing with incobotulinumtoxin-A delivered at fixed 12-week dosing intervals. Univariate sensitivity analyses were conducted on the base case by substituting the proportion of patients in each injection interval and the cost of incobotulinumtoxin-A. Probabilistic sensitivity analyses (PSA) were conducted on the base case with distributions assigned to the frequency of repeat dosing and to utility valuation of the responder and the non-responder health states. Cost and resource utilization variables were fixed in the PSA because these variables are direct functions of the frequency at which treatment is required.

Clinical Data

Results from published open-label extension studies evaluating the safety and efficacy of repeated injections of incobotulinumtoxin-A in the treatment of BLEPH [14] and CD [15] were used. In both
studies, re-injections of incobotulinumtoxin-A were possible from as early as 6 weeks up to the time whenever the patient expressed the need for a new injection.

In the BLEPH indication, the mean injection interval was 12.6 weeks ± 4.5 weeks (median 12 weeks). In the CD indication, the mean injection interval was 14.0 weeks ± 7.4 weeks (median 13 weeks).

**Costs**

Only direct health care costs associated with the acquisition and administration of BoNT/A treatments were included in the model. All costs were in Australian dollars ($A).

The cost per treatment was determined on the number of 100-unit (U) vials required per treatment and administration costs. The number of vials required was determined by mean doses of incobotulinumtoxin-A and onabotulinumtoxin-A presented in head-to-head clinical trials [12,13]. Each treatment for BLEPH (either unilateral or bilateral) required a single 100-U vial per treatment, whereas each treatment for CD required two 100-U vials per treatment. These doses were consistent with the recommended doses in the approved product information for the respective treatments. The cost per 100-U vial for incobotulinumtoxin-A and onabotulinumtoxin-A was $A 375.00 and $A 415.50, respectively (only 100-U vials were available for BLEPH and CD in Australia at the time of the analysis).

The cost of administering treatment was the same for incobotulinumtoxin-A and onabotulinumtoxin-A and was based on the Australian MBS. These costs were $A 45.05, $A 124.85, and $A 249.75 for unilateral BLEPH, bilateral BLEPH, and CD, respectively (MBS items 18370, 18372, and 18352). Because of the highly purified nature of incobotulinumtoxin-A, the lower immunogenic potential, and the absence of cold chain storage requirements, the assumption made was that there were no costs associated with hospitalizations and adverse events or additional costs associated with the use of incobotulinumtoxin-A relative to onabotulinumtoxin-A. Costs associated with the management of the symptoms of BLEPH or CD were also assumed to be equal across the treatment arms of the model.

**Utility Valuation**

Quality-of-life (QOL) and QALY gains for incobotulinumtoxin-A relative to onabotulinumtoxin-A in the economic model were driven by a reduction in the time with symptoms spent waiting for the minimum treatment interval to expire. Therefore, utility values in the Markov model reflected the QOL for patients experiencing symptoms versus those when the condition was adequately controlled by type A botulinum neurotoxins.

Utility values in the model were derived from a prospective, open-label cohort study by Hilker et al. [16]. Fifty patients with cranial dystonia (including BLEPH) and CD treated long-term with BoNT/A were enrolled in a prospective, open-label cohort study. The health-related QOL was assessed using the EuroQol five-dimensional questionnaire (EQ-SD). Baseline utility values in the study by Hilker et al. [16] were used to represent the utility value for the health state in the economic model in which symptoms had re-emerged. The utility value at the first follow-up visit of 6 weeks in the study by Hilker et al. [16] was used to represent the utility value of patients who were in the health state post-injection but before symptoms had re-emerged.

The baseline utility value for those with BLEPH in the model was 0.59 (standard error [SE] = 0.052), which then increased to 0.66 (SE = 0.056) while symptoms were controlled postinjection. The corresponding utility values for patients with CD were 0.60 (SE = 0.048) and 0.76 (SE = 0.042). Patients in the health state in which treatment was being administered were assumed to have the lower of the two utility values unless the injection was administered before the re-emergence of symptoms.

All Model Variables Are Presented In Table 1.
re-emergence of symptoms before a new injection was permitted over 5 years than did patients who had onabotulinumtoxin-A. In both BLEPH and CD indications, patients who had incobotulinumtoxin-A spent fewer weeks experiencing symptoms, resulting in a QALY gain of 0.0511, than did those on onabotulinumtoxin-A (Table 2).

Univariate Sensitivity Analyses
Table 2 presents the results of univariate sensitivity analyses on the base case. Exploratory post hoc analyses included all incobotulinumtoxin-A injections that were administered with injection intervals of 6 to 20 weeks in the treatment of BLEPH and CD from two prospective, randomized, double-blind, multicenter studies [17,18] and their extension phases [14,15]. In both indications, approximately 45% of the treatments were administered with injection intervals of less than 12 weeks and 55% of the treatments were administered with injection intervals of 12 weeks or more [19]. When these values were used in the model, keeping all other variables as per the base case, incobotulinumtoxin-A continued to be a cost-effective option compared to onabotulinumtoxin-A for both indications (incremental cost per QALY gain of A$ 34,529 for BLEPH and A$ 28,237 for CD).

When the price of incobotulinumtoxin-A increased from A$ 375 to A$ 415.50, keeping all other variables as per the base case, the incremental cost per QALY gained of incobotulinumtoxin-A continued to be a cost-effective option compared to onabotulinumtoxin-A for both indications (incremental cost per QALY gain of A$ 34,529 for BLEPH and A$ 28,237 for CD). The rise in the incremental cost per QALY was driven by the more frequent injections of incobotulinumtoxin-A that were administered over the 5-year time horizon, because these were administered as per the needs of the patient. Despite the increased number of injections, patients administered incobotulinumtoxin-

### Results

**Incobotulinumtoxin-A Flexible Dosing Compared to Onabotulinumtoxin-A Flexible Dosing**

#### Number of Injections

Over the 5-year time horizon, 23.3 injections of incobotulinumtoxin-A were required per patient compared to 20.1 injections of onabotulinumtoxin-A in patients with BLEPH. Similarly in patients with CD, 22.3 injections of incobotulinumtoxin-A were required compared to 19.3 injections of onabotulinumtoxin-A over the 5-year time horizon.

#### Symptoms

In both BLEPH and CD indications, patients who had incobotulinumtoxin-A spent fewer weeks experiencing symptoms over 5 years than did patients who had onabotulinumtoxin-A. Patients with BLEPH who had incobotulinumtoxin-A experienced symptoms for 23.3 weeks, whereas patients with BLEPH who had onabotulinumtoxin-A experienced symptoms for 43.5 weeks over the 5-year time horizon. Patients with CD who had incobotulinumtoxin-A experienced symptoms for 22.3 weeks, whereas patients with CD who had onabotulinumtoxin-A experienced symptoms for 41.3 weeks over the 5-year time horizon.

#### Cost-Effectiveness in BLEPH

The use of incobotulinumtoxin-A was cost-effective compared to that of onabotulinumtoxin-A in patients with BLEPH, with an incremental cost per QALY gained of A$ 25,588. The QALY gain for incobotulinumtoxin-A (0.0242) was achieved because its administration was based on the actual needs of the patients, resulting in patients experiencing symptoms for fewer weeks (Table 2). That is, as soon as a patient experienced a re-emergence of symptoms, it was possible to give a new injection as soon as not after 6 weeks of the last injection but also later than 12 weeks and up to 20 weeks. If a patient taking onabotulinumtoxin-A experienced a re-emergence of symptoms before a new injection was permitted (i.e., before 12 weeks), the patient had to bear the symptoms until a new injection was permitted (at a minimum of 12 weeks). Therefore, patients on incobotulinumtoxin-A experienced symptoms for a shorter time than did those on onabotulinumtoxin-A.

#### Cost-Effectiveness in CD

The use of incobotulinumtoxin-A was cost-effective compared to that of onabotulinumtoxin-A in patients with CD, with an incremental cost per QALY gained of A$ 23,794. Patients on incobotulinumtoxin-A spent less time with symptoms, resulting in a QALY gain of 0.0511, than did those on onabotulinumtoxin-A (Table 2).
Table 2 – Results of the cost-effectiveness of incobotulinumtoxin-A flexible dosing (minimum 6 wk) compared to that of onabotulinumtoxin-A flexible dosing (minimum 12 wk).

<table>
<thead>
<tr>
<th>Type of analysis</th>
<th>BLEPH</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incobotulinumtoxin-A</td>
<td>Onabotulinumtoxin-A</td>
</tr>
<tr>
<td>Doses (n)</td>
<td>23.28</td>
<td>22.12</td>
</tr>
<tr>
<td>Symptoms (wk)</td>
<td>23.28</td>
<td>43.52</td>
</tr>
<tr>
<td>Total costs (A$)</td>
<td>9,961</td>
<td>9,341</td>
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<tr>
<td>QALYs</td>
<td>2.9023</td>
<td>2.8781</td>
</tr>
<tr>
<td>Incremental cost/QALY (A$)</td>
<td>25,588</td>
<td>23,794</td>
</tr>
<tr>
<td>Univariate sensitivity analysis*</td>
<td>1,118</td>
<td>2,016</td>
</tr>
<tr>
<td>Incremental cost (A$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incremental QALYs (A$)</td>
<td>0.0324</td>
<td>0.0714</td>
</tr>
<tr>
<td>Incremental cost/QALY (A$)</td>
<td>34,529</td>
<td>28,237</td>
</tr>
<tr>
<td>Univariate sensitivity analysis†</td>
<td>1,460</td>
<td>2,824</td>
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<tr>
<td>Incremental cost (A$)</td>
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<td></td>
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<tr>
<td>Incremental QALYs (A$)</td>
<td>0.0242</td>
<td>0.0511</td>
</tr>
<tr>
<td>Incremental cost/QALY (A$)</td>
<td>60,244</td>
<td>55,232</td>
</tr>
<tr>
<td>Probabilistic sensitivity analysis</td>
<td>Incobotulinumtoxin-A</td>
<td>Onabotulinumtoxin-A</td>
</tr>
<tr>
<td>Total costs (95% CI) (A$)</td>
<td>9,969 (9,108–10,791)</td>
<td>9,343 (8,965–9,705)</td>
</tr>
<tr>
<td>QALYs (95% CI)</td>
<td>2.9023 (2.9000–2.9047)</td>
<td>2.8780 (2.8644–2.8910)</td>
</tr>
<tr>
<td>NMB‡ (95% CI) (A$)</td>
<td>104 (–224 to 403)</td>
<td>316 (–182 to 731)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BLEPH, blepharospasm; CD, cervical dystonia; CI, credible interval; NMB, net monetary benefit; QALY, quality-adjusted life-year; U, unit.
* Proportion of patients in each injection interval [19].
† Price equal (A$ 415.50).
‡ Assuming a cost per QALY value of A$ 30,000.
A injections spent less time with symptoms than did those administered onabotulinumtoxin-A injections.

Probabilistic Sensitivity Analysis
A PSA was performed using 1000 iterations of the base-case evaluation. Dirichlet distributions for the proportion of the population requiring repeat injections at each time interval and beta distributions for utility values assigned to responders and nonresponders were generated.

The PSA found 23.3 injections (95% credible interval [CI] from the PSA of 22.1–24.6) of incobotulinumtoxin-A were needed per patient compared to 20.1 injections (95% CI 19.6–20.6) of onabotulinumtoxin-A in patients with BLEPH. Similarly, in patients with CD, 22.3 injections (95% CI 21.3–23.3) of incobotulinumtoxin-A were required per patient over 5 years compared to 19.3 injections (95% CI 18.9–19.7) of onabotulinumtoxin-A.

Patients with BLEPH who had incobotulinumtoxin-A experienced symptoms for 23.3 weeks (95% CI 22.1–24.6), whereas
patients with BLEPH who had onabotulinumtoxin-A experienced symptoms for 43.6 weeks (95% CI 37.3–51.2) over 5 years. Patients with CD who had incobotulinumtoxin-A experienced symptoms for 22.3 weeks (95% CI 21.3–23.3), whereas patients with CD who had onabotulinumtoxin-A experienced symptoms for 41.0 weeks (95% CI 35.8–46.3) over 5 years.

Across the 1000 iterations, there was an incremental cost of A$ 626 (95% CI A$ 246–A$ 1080) in patients with BLEPH and A$ 1220 (95% CI A$ 585–A$ 1844) in patients with CD. In addition, incobotulinumtoxin-A was associated with more QALYs than onabotulinumtoxin-A in 100% of the simulations in the BLEPH and CD indications (see Fig. 2A, B), with an incremental QALY gain of 0.0243 (95% CI 0.0179–0.0319) in the BLEPH indication and 0.0512 (95% CI 0.0397–0.0630) in the CD indication.

Cost-effectiveness acceptability curves (Fig. 3) illustrate the probability that the use of incobotulinumtoxin-A will be cost-effective compared to that of onabotulinumtoxin-A at a willingness-to-pay threshold of A$ 30,000 per QALY, which was 85.4% in the BLEPH indication and 98.5% in the CD indication. Use of incobotulinumtoxin-A is almost certainly (100% probability) cost-effective in both indications at a willingness-to-pay threshold of A$ 50,000 per QALY.

Other scenarios
Cost-effectiveness results of incobotulinumtoxin-A flexible dosing (minimum 6 weeks) compared to other scenarios are summarized in Table 3.

When onabotulinumtoxin-A was given at a fixed 12-week interval, incobotulinumtoxin-A flexible dosing (minimum 6 weeks) dominated onabotulinumtoxin-A dosing in patients with BLEPH and CD. Although there was an increase in the number of injections given in the incobotulinumtoxin-A dosing in this scenario, because injections were given more frequently, this improved the QOL more than did the onabotulinumtoxin-A dosing, because patients experienced less time with symptoms by having symptoms taken care of sooner with incobotulinumtoxin-A.

Fig. 3 – Cost-effectiveness acceptability curve (WTP threshold in Australian dollars). BLEPH, blepharospasm; CD, cervical dystonia; WTP, willingness to pay.

### Table 3 – Results of the cost-effectiveness of incobotulinumtoxin-A flexible dosing (minimum 6 wk) compared to other scenarios.

<table>
<thead>
<tr>
<th>Model result</th>
<th>BLEPH</th>
<th>CD</th>
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</thead>
<tbody>
<tr>
<td>Incremental cost (A$)</td>
<td>Onabotulinumtoxin-A fixed 12-wk dosing</td>
<td>−247.48</td>
</tr>
<tr>
<td>Incremental QALYs</td>
<td>0.0264</td>
<td>0.0582</td>
</tr>
<tr>
<td>Incremental cost/QALY</td>
<td>Incobotulinumtoxin-A dominates</td>
<td>0.0045</td>
</tr>
<tr>
<td>Incremental cost (A$)</td>
<td>Onabotulinumtoxin-A flexible dosing (minimum 8 wk)</td>
<td>−491.17</td>
</tr>
<tr>
<td>Incremental QALYs</td>
<td>0.0045</td>
<td>0.0098</td>
</tr>
<tr>
<td>Incremental cost/QALY</td>
<td>Incobotulinumtoxin-A dominates</td>
<td>0.0264</td>
</tr>
<tr>
<td>Incremental cost (A$)</td>
<td>Incobotulinumtoxin-A fixed 12-wk dosing</td>
<td>546.19</td>
</tr>
<tr>
<td>Incremental QALYs</td>
<td>0.2064</td>
<td>0.0582</td>
</tr>
<tr>
<td>Incremental cost/QALY (A$)</td>
<td>Incobotulinumtoxin-A dominates</td>
<td>20.796</td>
</tr>
</tbody>
</table>

BLEPH, blepharospasm; CD, cervical dystonia; QALY, quality-adjusted life-year.
When the minimum dosing interval for onabotulinumtoxin-A dosing was reduced from 12 weeks to 6 weeks, incobotulinumtoxin-A continued to dominate onabotulinumtoxin-A in both indications.

Finally, the model also compared incobotulinumtoxin-A flexible dosing (between 6 and 20 weeks) with a scenario in which incobotulinumtoxin-A was given at fixed doses every 12 weeks. In this situation, incobotulinumtoxin-A flexible dosing was cost-effective compared to incobotulinumtoxin-A fixed 12-week dosing, with an incremental cost per QALY gained of A$ 20,696 in patients with BLEPH and A$ 4,243 in patients with CD.

**Discussion**

The use of incobotulinumtoxin-A provides an alternative treatment option for patients with BLEPH and CD, with flexible dosing intervals of 6 to 20 weeks, determined on actual clinical needs of the individual patient. Incobotulinumtoxin-A can be administered at shorter intervals compared to other preparations of BoNT/A, such as onabotulinumtoxin-A, which have a minimum 12-week dosing interval. Patients will usually reach a steady state at which they would require a re-injection and therefore can develop their own individual treatment schedule in conjunction with their neurologist.

The cost-effectiveness model presented demonstrated that the use of incobotulinumtoxin-A at 6- to 20-week intervals was cost-effective compared to the use of onabotulinumtoxin-A taken at 12- to 20-week intervals in patients with BLEPH and CD. The QALYs gained over the 5-year time horizon were higher for incobotulinumtoxin-A, because patients had the opportunity to alleviate their symptoms as soon as 6 weeks after the initial injection, compared to patients taking onabotulinumtoxin-A, who had to wait till at least 12 weeks. That is, patients had to wait for a minimum of 12 weeks to have a re-treatment even if symptoms re-emerged before 12 weeks.

Because of incobotulinumtoxin-A’s highly purified nature and the reduced immunogenic potential as compared to other available preparations of BoNT/A, the model assumed that there would be no difference in costs associated with hospitalizations or adverse events with the use of incobotulinumtoxin-A relative to onabotulinumtoxin-A and no costs associated with maintaining a cold chain during transportation for incobotulinumtoxin-A. Therefore, this model represented a conservative estimate of cost-effectiveness for incobotulinumtoxin-A.

Incobotulinumtoxin-A is intended to be an alternative to other BoNT/A preparations in Australia. Therefore, every MBS item processed for the administration of incobotulinumtoxin-A will be offset by an equivalent reduction in the number of items processed for the administration of other BoNT/A preparations, such as onabotulinumtoxin-A. Without demanding additional financial resources from the Australian health care system, the use of incobotulinumtoxin-A has the potential to produce cost savings for the Australian health care system compared to the use of onabotulinumtoxin-A.

**Conclusions**

The use of incobotulinumtoxin-A presented to be a more cost-effective treatment option when compared to the use of onabotulinumtoxin-A in the Australian health care system for the treatment of patients with BLEPH and CD. The option to administer incobotulinumtoxin-A at minimum 6-week flexible intervals as per the needs of the patient results in patients experiencing symptoms for less time or overtreatment compared to patients receiving onabotulinumtoxin-A. This increase in utility gain from incobotulinumtoxin-A resulted in incobotulinumtoxin-A being the more favorable treatment option compared to onabotulinumtoxin-A for patients with BLEPH and CD.

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**References**