



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1221 – Intravesical injection of BOTOX[®] (botulinum toxin) for the treatment of urinary incontinence due to neurogenic detrusor overactivity (NDO)

Sponsor/Applicant/s: Allergan Australia Pty Ltd

Date of MSAC consideration: 5 April 2013

1. Purpose of application

In August 2011, an application to the Medical Services Advisory Committee (MSAC) was received from Allergan Australia Pty Ltd, requesting Medicare Benefits Schedule (MBS) listing of intravesical* injection of BOTOX[®] for the treatment of urinary incontinence due to neurogenic detrusor overactivity (NDO). This MSAC application is co-dependent on an application to the Pharmaceutical Benefits Advisory Committee (PBAC) for Pharmaceutical Benefits Scheme (PBS) listing of the drug component of the service.

* Please note: Terminology used in the original title of this application was ‘transurethral injection of BOTOX[®]’, but expert clinical opinion recommended changing it to ‘intravesical injection’.

Prior to the procedure, the patient is usually given a local anaesthetic, with light sedation administered by an anaesthetist, or may occasionally be provided general anaesthesia. A rigid or flexible cystoscope is inserted through the urethra and into the bladder to allow visualisation of the bladder wall. Reconstituted BOTOX[®] (200 U in 30 mL) is injected into the inner muscular layer of the bladder wall (detrusor). Clinical improvement generally occurs within 2 weeks. Time to re-treatment is approximately nine months.

Injecting BOTOX[®] into the bladder wall has not been formally approved for funding via the MBS. Expert clinical opinion confirmed that the service was currently being performed under MBS item 36851 (cystoscopy with injection into the bladder wall) and patients pay for the drug in the absence of PBS subsidy. Item 36851 was not originally listed for such use; it was mainly intended for bulking agent injections into the bladder.

Urinary incontinence due to NDO is described as incontinence resulting from an underlying neurologic disorder, such as multiple sclerosis (MS) or spinal cord injury (SCI). In patients with NDO, spontaneous detrusor contractions lead to increased bladder pressure, reduced storage volume and incontinence.

2. Background

At its November 2012 meeting, after considering the strength of the available evidence in relation to the safety, clinical effectiveness and cost-effectiveness of the injection of botulinum toxin in the treatment of urinary incontinence related to neurogenic detrusor overactivity, MSAC deferred the application until its responses to PBAC's requests, its other advice, and further information from the applicant, were considered by PBAC. If PBAC was to refer more matters to MSAC for advice, or the applicant had reason to disagree with the MSAC advice given, MSAC would support an expedited process for reconsideration. If PBAC was subsequently to recommend to the Minister that botulinum toxin be listed on the PBS for the treatment of urinary incontinence related to neurogenic detrusor overactivity, MSAC would support an expedited process for reconsideration, to align MSAC support for public funding of the injection of botulinum toxin according to the circumstances recommended by PBAC. The purpose of this reconsideration would be to align the proposed MBS item descriptor with the proposed PBS restriction; consider the exclusion of other items to be billed to the patient on the same occasion of service; and consider changes in the estimates of costs to the MBS. MSAC also advised the Minister that the current MBS item 36581 should be rewritten to exclude its use for injecting botulinum toxin at a time considered reasonable.

A re-application for PBS listing of BOTOX® for this indication was considered at the March 2013 PBAC meeting. MSAC was advised that, as a subsequent out-of-session decision, PBAC recommended the listing of botulinum toxin type A (BOTOX®) for this indication.

3. Prerequisites to implementation of any funding advice

BOTOX® was approved by the Therapeutic Goods Administration (TGA) for the treatment of urinary incontinence due to NDO in March 2012. The TGA approved indication is "Treatment of urinary incontinence due to neurogenic detrusor overactivity resulting from a defined neurological illness (such as spinal cord injury or multiple sclerosis) and not controlled adequately by anticholinergic agents. This does not include idiopathic overactive bladder."

4. Proposal for public funding

Applicant's proposed MBS item descriptor to the November 2012 MSAC meeting

GROUP T11 – BOTULINUM TOXIN INJECTIONS (<i>Division 2.42A of the General Medical Services Table (GMST) Regulations</i>)
BOTULINUM TOXIN (Botox), transurethral injection of, for the treatment of urinary incontinence due to neurogenic detrusor overactivity in patients who have failed or are intolerant to anti-cholinergic therapy, including cystoscopy and all injections in one day. Injections can only be performed on patients willing to self-catheterise if necessary, and may be performed on an in-hospital or out-of-hospital basis. (Anaes.)

The corresponding requested PBS restriction to the March 2013 PBAC meeting was:

Section 100 Botulinum Toxin Program

Eligibility criteria:

Treatment of urinary incontinence due to neurogenic detrusor overactivity in patients with multiple sclerosis, spinal cord injury or adult spina bifida, as demonstrated by an urodynamic study, in a patient who is not adequately managed by anti-cholinergic therapy. Patients must experience ≥ 14 urinary incontinence episodes per week, and be willing and able to self-catheterise.

Inadequate management by anti-cholinergic therapy is shown by an insufficient response or if the patient experiences intolerable side effects necessitating withdrawal from treatment.

Continuation criteria:

Treatment should be discontinued if the patient does not show response after the first treatment. Treatment response is defined as a 50% or greater reduction from baseline in urinary incontinence infrequency 6–12 weeks after the first treatment.

Maximum number of treatments per year is two, with no less than six months to elapse between treatments.

The PBAC recommended PBS restriction was:

Condition/Indication:	Urinary incontinence
Restriction:	Section 100 Botulinum Toxin Program
Clinical criteria:	<p>The condition must be due to neurogenic detrusor overactivity, as demonstrated by urodynamic study</p> <p>AND</p> <p>The condition must be inadequately controlled by anti-cholinergic therapy</p> <p>AND</p> <p>Patient must have experienced at least 14 episodes of urinary incontinence per week prior to commencement of treatment with botulinum toxin.</p> <p>AND</p> <p>The treatment must not continue if the patient does not achieve a 50% or greater reduction from baseline in urinary incontinence episodes 6-12 weeks after the first treatment.</p>
Population criteria:	<p>Patient must have multiple sclerosis; OR Patient must have a spinal cord injury; OR Patient must be aged 18 years or older and have spina bifida</p> <p>AND</p> <p>Patient must be willing and able to self-catheterise.</p>

5. Consumer Impact Statement

Not applicable.

6. Proposed intervention’s place in clinical management

BOTOX[®] injections are proposed as a second-line conservative treatment for patients who are unsuitable for, or fail, first-line conservative management or best supportive care (BSC) e.g. lifestyle modifications including: pad use, portable urinals, clean intermittent catheterisation (CIC) or the use of anti-cholinergic drugs.

7. Other options for MSAC consideration

At its November 2012 meeting, MSAC foreshadowed its intention to advise that the definition of eligible patients should be aligned with any PBAC-recommended PBS restriction, preferring to include the ability to self-catheterise as a prerequisite to botulinum toxin therapy and the term “intravesical injection” rather than “transurethral injection”. This advice has since been accepted by both the applicant and PBAC.

8. Comparator to the proposed intervention

In November 2012, MSAC accepted that the comparator (MBS item 36851, “cystoscopy, with injection into the bladder wall”, which is the item currently being billed for administering botulinum toxin) proposed in the Final Decision Analytic Protocol (DAP) served as a relevant benchmark for setting an MBS item fee to inject the drug. MSAC also accepted that the comparator proposed in the SBA report (best supportive care) was appropriate. This aligned with PBAC’s assessment of the drug.

9. Comparative safety

In November 2012, MSAC advised that there was no evidence to suggest that any variation in injecting performance across trained and experienced urologists (or other subspecialists such as urogynaecologists) would be likely to have important consequences for patient safety or for the safety of botulinum toxin in the proposed indication.

10. Comparative effectiveness

In November 2012, MSAC advised that there was no evidence to suggest that any variation in injecting performance across trained and experienced urologists (or other subspecialists such as urogynaecologists) would be likely to have important consequences for the effectiveness of botulinum toxin in the proposed indication.

11. Economic evaluation

In November 2012, MSAC agreed with PBAC that the economic evaluation of botulinum toxin in the proposed indication was a matter to be considered by PBAC, subject to MSAC advice on the cost of MBS-funded health care resources.

MSAC further advised that, in the context of proposed MBS items to inject proposed PBS listings of botulinum toxin, the relative influence of MBS costs on the overall economic evaluation for the PBS proposal is greater than usual. For this reason, MSAC advised PBAC and the applicant that the average fee charged in these tables should be included in the economic evaluation to reflect its opportunity cost from the health care system perspective (rather than the MBS fee as is recommended in PBAC’s Manual of Resource Items and their Unit Costs).

The minor resubmission to the March 2013 PBAC meeting appropriately added non-MBS related hospital costs for injecting botulinum toxin to cover the hospital facility, operating room, and admission costs. It estimated these as \$532 per injection with reference to the National Efficient Price for the appropriate Australian Refined Diagnosis Related Group (AR-DRG) of L41Z (“Cystourethroscopy, same day”) by subtracting out the components related to the medical provider.

It provided three revised economic evaluations (as incremental cost-effectiveness analyses):

- based on the previous approach using the entire AR-DRG unit cost;
- based on the non-MBS related hospital costs derived from the AR-DRG unit cost and then adding costs for MBS related items using MBS fees; and
- based on the non-MBS related hospital costs derived from the AR-DRG unit cost and then adding costs for MBS related items using the actual fees charged.

In relation to the second evaluation, the minor resubmission to PBAC argued “the inclusion of out-of-pocket fees is out of step with most other PBAC submissions and does not facilitate fair cross-comparison of submissions”.

In November 2012, MSAC also advised that unit costs for other MBS items, including consultation item(s) likely to be required to assess and reassess each patient would be MBS item 104 (noting that urologists, who are nominated to inject botulinum toxin for urinary incontinence, are specialists) for an initial assessment if referred for this purpose and MBS item 105 for an initial assessment for this purpose (if part of the ongoing management by the urologist, having been referred earlier) and also for subsequent reassessments. In addition, MSAC included a number of points of advice to PBAC and the applicant in relation to the model considered by PBAC in July 2012 and by MSAC in November 2012.

The minor resubmission to PBAC maintained the previous position that the listing of botulinum toxin for this indication would not change any other consultation rates.

12. Financial/budgetary impacts

At its November 2012 meeting, MSAC advised that it would support \$229.85 as the MBS fee for injecting botulinum toxin in urinary incontinence with reference to the benchmark MBS item 36851: “cystoscopy, with injection into the bladder wall”. This advice has since been accepted by both the applicant and PBAC.

MSAC further recommended \$315.60 as the MBS rebate per injection in total and \$36.30 as the rebate per MBS item for MBS item 23 (used in the minor resubmission to PBAC to estimate the cost of treating urinary tract infections (UTIs)).

Based on the estimated utilisation presented in the minor resubmission, the net financial cost to the MBS is estimated to be less than \$0.5 million in Year 5. This includes the cost of the injection fee and the cost to MBS for the treatment of UTIs.

13. Key issues from ESC to MSAC

Not applicable.

14. Other significant factors

MSAC advised that the wording of the descriptor for MBS item 36851, “cystoscopy, with injection into the bladder wall” be amended to exclude injection of any botulinum toxin product.

15. Summary of consideration and rationale for MSAC’s advice

MSAC noted that the applicant and PBAC had accepted MSAC’s previous advice in relation to the proposed item descriptor and MBS fee to inject botulinum toxin type A for the proposed indication. MSAC also noted that the applicant had included two sensitivity analyses of its economic evaluation, one involving the average fee charged and the other involving the MBS fee. MSAC re-affirmed its November 2012 advice that the average fee charged was the appropriate basis for the economic evaluation and noted that PBAC had accepted this advice despite the applicant’s preference that the MBS fee be used for this purpose.

MSAC noted PBAC’s recommended restriction for botulinum toxin type A and considered that it would be appropriate to ensure that the population eligible for an MBS medical service to inject the medicine should be identical to the population eligible for the medicine via the PBS. MSAC also noted that the current review of existing MBS items to inject botulinum toxin products for other purposes would probably raise similar issues of consistency between eligibility for the MBS and the PBS.

MSAC noted that in the absence of a minor resubmission for the MBS service from the applicant, its secretariat had effectively created a basis for MSAC reconsideration. The Committee requested that any future major submissions for Botox to PBAC, which rely on MSAC's November 2012 advice on appropriate MBS fees, should be accompanied by a minor resubmission to MSAC to ensure that the applicant and MSAC are in direct communication. This applies to both the resubmission to the July 2013 PBAC meeting for refractory migraine and the expected submission to the November 2013 PBAC meeting for urinary incontinence due to idiopathic overactive bladder.

16. MSAC's advice to the Minister

After considering the strength of available evidence in relation to the safety, clinical effectiveness and cost-effectiveness of the injection of botulinum toxin type A (BOTOX®), MSAC supports public funding for the treatment of certain patients with urinary incontinence due to neurogenic detrusor overactivity.

MSAC further advised that:

- the existing item 36851 should be amended to exclude its use for injecting any botulinum toxin product;
- the proposed fee for the new MBS item is \$229.85;
- no Extended Medicare Safety Net (EMSN) issues arise (as this is an in-hospital service only);
- the new item should only be an inpatient service (as for the existing benchmark item 36851);
- it is assumed that the new item is usually accompanied by anaesthesia (local anaesthetic with light sedation, through to full general anaesthetic, depending on the patient);
- the new MBS item should exclude the possibility of a specialist consultation item being billed on the same occasion of service as the item to inject botulinum toxin;
- the eligible population and conditions of use written into the MBS item descriptor should reflect those of the corresponding PBS restriction, and should refer to "intravesical injection" rather than "transurethral injection"; and
- the wording of the proposed item descriptor may need to be reviewed in the context of the current review of existing item descriptors.

MSAC suggested the following MBS item descriptor:

<p>GROUP T11 – BOTULINUM TOXIN INJECTIONS</p> <p>BOTULINUM TOXIN TYPE A (Botox™), intravesical injection of, for the treatment of urinary incontinence due to neurogenic detrusor overactivity as demonstrated by urodynamic study in patients:</p> <ul style="list-style-type: none"> • with multiple sclerosis or spinal cord injury or be aged 18 years or older and have spina bifida <p>AND</p> <ul style="list-style-type: none"> • who are inadequately controlled by anti-cholinergic therapy as manifested by having experienced at least 14 episodes of urinary incontinence per week prior to commencement of treatment with botulinum toxin type A and continued in patients who have responded to prior botulinum toxin type A as shown by achieving a 50% or greater reduction from baseline in urinary incontinence episodes 6-12 weeks after the first treatment <p>AND</p> <ul style="list-style-type: none"> • are willing and able to self-catheterise; <p>in accordance with requirements relating to access to botulinum toxin type A under the Pharmaceutical Benefits Scheme (PBS), including cystoscopy and all injections in one day, and not provided on the same occasion as a service described in any of items 104, 105, 110, 116, 119, 11900 and 11919. (H) (Anaes.)</p>

17. Applicant's comments on MSAC's Public Summary Document

The sponsor had no comment.

18. Context for decision

This advice was made under the MSAC Terms of Reference.

MSAC is to:

Advise the Minister for Health and Ageing on medical services that involve new or emerging technologies and procedures and, where relevant, amendment to existing MBS items, in relation to:

- the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;
- whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
- the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;
- the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
- other matters related to the public funding of health services referred by the Minister.

Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.

MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

19. Linkages to other documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au.