



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application 1272 – Intravesical Injection of Botulinum Toxin Type A (BOTOX®) into the Bladder Wall for Urinary Incontinence due to Idiopathic Overactive Bladder

Sponsor/Applicant/s: Allergan Australia Pty Ltd

Date of MSAC meeting: 28 November 2013

1. Purpose of application

On 5 April 2013, a minor submission requesting Medicare Benefits Schedule (MBS) listing of the procedure to inject botulinum toxin type A (BOTOX®) for the treatment of urinary incontinence due to idiopathic overactive bladder (IOAB) was received from Allergan Australia Pty Ltd. This MSAC application was co-dependent on an application to the Pharmaceutical Benefits Advisory Committee (PBAC) for Pharmaceutical Benefits Scheme (PBS) listing of the medicine component of the service.

The proposed procedure involves twenty 100 U injections of botulinum toxin into the muscle of the bladder wall at 1 cm intervals using a rigid or flexible cystoscope. Clinical improvement occurs within 2 weeks and the median time to retreatment (in clinical trials) was approximately 6 months. Delivery of the service is proposed to be restricted to approved urologists and urogynaecologists. Generally, the procedure is performed in hospital on day-admitted patients.

2. Background

At the April 2013 meeting, MSAC supported MBS listing for a similar procedure to inject botulinum toxin type A (BOTOX®) for urinary incontinence due to neurogenic detrusor overactivity (NDO) - Application 1221.

3. Prerequisites to implementation of any funding advice

BOTOX® is TGA approved for the (broader) indication of overactive bladder (OAB).

In addition, BOTOX® is also TGA approved for the treatment of strabismus, blepharospasm, cervical dystonia, focal spasticity, severe primary hyperhidrosis of the axillae, spasmodic dysphonia, and chronic migraine.

4. Proposal for public funding

The submission proposed a fee of \$229.85 for the intravesical injection of botulinum toxin type A for urinary incontinence due to IOAB. This is consistent with the fee proposed in the

Final DAP for Application 1272 (February 2013) and the fee for intravesical injection of botulinum toxin type A for urinary incontinence due to neurogenic detrusor overactivity (57th MSAC Meeting minutes, Application 1221).

The following MBS item was proposed:

Applicant proposed wording and fee for the requested MBS item

<p>Group T11 – Botulinum toxin</p> <p>Division 2.42A of the General Medical Services Table</p>
<p>MBS item no: TBA (within Group T11)</p> <p>BOTULINUM TOXIN (Botox), intravesical injection of, for the treatment of urinary incontinence due to idiopathic overactive bladder, including cystoscopy and all injections in one day, but not provided on the same occasion as a service described in item 11900, in patients aged 18 years or older who have failed or are intolerant to anti-cholinergic medications, and who are willing and able to self-catheterise. (Anaes-)</p> <p>(See para T11.1 of explanatory notes to this Category)</p> <p>MBS Fee: \$229.85 Benefit: 75% = \$172.40</p>

As noted in the final DAP, the MBS item would be aligned with the PBAC-recommended PBS listing. MSAC noted that the proposed item descriptor would limit botulinum toxin type A injection to patients older than 18 years with ≥ 14 episodes of urinary incontinence due to IOAB per week who have failed or are intolerant of two or more anticholinergics and who are willing and able to self-catheterise.

The proposed PBS restriction is shown below. Under the proposed PBS restriction, treatment would be discontinued if the patient does not show a response ($\geq 50\%$ reduction in incontinence episodes) after the first treatment.

The Minor Submission proposed the following wording of the PBS Section 100 listing for botulinum toxin type A for IOAB:

Applicant Proposed wording of the PBS Section 100 listing for botulinum toxin type A for IOAB

<p><u>Section 100 Botulinum Toxin Program</u></p> <p><i>Authority Required</i></p> <p>Treatment of urinary incontinence due to idiopathic overactive bladder in patients who have ≥ 14 episodes/week, are willing to self-catheterise, and are not adequately managed by 2 or more anti-cholinergics.</p> <p>Inadequate management by anti-cholinergic therapy is shown by an insufficient response or if the patient experiences intolerable side effects necessitating withdrawal from treatment.</p> <p>Treatment should be discontinued if the patient does not show response after the first treatment.</p> <p>Treatment response is defined as a 50% or greater reduction from baseline in urinary incontinence frequency 6–12 weeks after the first treatment.</p>
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5. Consumer Impact Statement

Nil.

6. Proposed intervention’s place in clinical management

As specified in the Final DAP and consistent with the recommendation of botulinum toxin type A for NDO, botulinum toxin type A for IOAB is proposed as a second-line conservative

treatment for patients who are intolerant of, or fail, first-line conservative management (i.e. best supportive care). This includes lifestyle modifications (e.g. pad use, portable urinals, clean intermittent catheterisation) and anti-cholinergic medication.

As noted in the PSD for Application 1221, sacral nerve stimulation (SNS) is a more expensive and invasive treatment option (requiring implantation of a system that delivers electrical stimulation to the sacral nerve), and may be utilised less frequently as a result of listing botulinum toxin type A injections on the PBS and MBS (insofar as the medicine may displace SNS as a second-line treatment option).

7. Other options for MSAC consideration

Nil.

8. Comparator to the proposed intervention

The submission nominated best supportive care (BSC) as the appropriate main comparator.

PASC agreed that existing MBS item 36851 was the most appropriate benchmark to set the MBS fee.

9. Comparative safety

A systematic literature review was conducted and identified five relevant trials:

- Two pivotal Phase III randomised controlled trials (*Studies 095 and 520*) examining the efficacy and safety of botulinum toxin type A for IOAB patients refractory to anti-cholinergics.
- Two supportive trials, consisting of a Phase II RCT (*Study 077*) and a publication of a small investigator-initiated RCT (Jabs 2010).
- A long-term follow-up trial of the two pivotal trials (*Study 096*).

The key safety outcomes relating to the procedure were reported in the Phase III pivotal RCTs. MSAC noted there was no significant difference in incidence of injection/procedural pain reported in the pivotal trials; incidence: botulinum toxin type A 0.9%, Placebo 0.7%.

PBAC considered the comparative safety of the medicine.

Consistent with the MSAC minutes for Application 1221, overall, the adverse events were consistent with the known pharmacology for botulinum toxin type A with no unexpected safety issues associated with the treatment of IOAB.

10. Comparative effectiveness

The overall comparative effectiveness of the proposed service was considered by PBAC. This approach was consistent with consideration of comparative effectiveness evidence for Application 1221 (botulinum toxin type A for NDO).

11. Economic evaluation

The economic evaluation to determine the cost-effectiveness of the proposed service was considered by PBAC.

As the proposed service would only be provided 'in-hospital', there will be no Extended Medicare Safety Net (EMSN) financial implications.

12. Financial/budgetary impacts

The expected utilisation and costs associated with botulinum toxin type A treatment, under the proposed listing for IOAB, were estimated using an epidemiological approach.

The results indicated that a total of between 10,000 – 50,000 patients are expected to initiate treatment during Year 1.

The net cost to the MBS was estimated to be less than \$10 million in Year 1, increasing to between \$30 - \$60 million in Year 5.

13. Other significant factors

Nil.

14. Key issues for MSAC from ESC

Nil.

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

MSAC considered an application requesting Medicare Benefits Schedule (MBS) listing of intravesical injection of botulinum toxin type A for the treatment of urinary incontinence due to IOAB. This was a co-dependent application with the Pharmaceutical Benefits Advisory PBAC, which assessed the safety, effectiveness and efficacy, cost-effectiveness and safety of botulinum toxin type A injection for treating this condition. MSAC's role was to consider the wording of the MBS item descriptor, the MBS fee and the financial implications of publicly funding the intravesical injection procedure.

The proposed procedure involves twenty 100 U injections of botulinum toxin type A into the muscle of the bladder wall at 1 cm intervals using a rigid or flexible cystoscope. Clinical improvement happens within 2 weeks and the median time to retreatment was approximately 6 months in clinical trials. The delivery is proposed to be restricted to approved urologists and urogynaecologists. Generally the procedure is performed in hospital on day-admitted patients.

The proposed item descriptor would limit botulinum toxin injections to patients >18 years with ≥ 14 episodes of urinary incontinence due to IOAB per week who have failed or are intolerant of two or more anticholinergics and who are willing and able to self-catheterise. MSAC noted that the proposed item descriptor does not provide for general anaesthesia. The applicant stated that (**redacted information**)% of patients will require local anaesthesia only. However, this would leave a subset of patients that do require anaesthesia with extended out-of-pocket costs. MSAC noted that the lack of an anaesthesia requirement may result in procedures being performed in specialist's clinics rather than in hospital. MSAC accepted that the delivery of anaesthesia differed in patients with IOAB compared with patients with urinary incontinence due to neurogenic detrusor overactivity (NDO) considered in April 2013; general anaesthesia is needed in NDO patients to help prevent spasms occurring during the procedure.

MSAC considered the costs of this listing to the MBS which was estimated at \$123 million over 5 years. MSAC considered that this cost estimate may not be accurate. The epidemiological approach adopted as the basis for estimating costs to the MBS raised a concern that this may be an underestimate. This is because the percentage of patients currently not adequately managed, and therefore potentially eligible for this treatment, was

based on expert opinion and unweighted means from four clinical trials. According to these trials, the failure rate of anticholinergics may range from 35% to 58% of the IOAB population. At 58%, the 5-year cost to the MBS would increase to \$192 million. The financial model also assumed that **(redacted information)**% of patients who have failed on anticholinergics would seek botulinum toxin treatment; if this rose to **(redacted information)**% the 5-year cost to the MBS would be greater than \$100 million.

However, MSAC also noted the constraints in the health care system which suggests that the projected numbers of intravesical injections may be well beyond the current capacity of the limited number of specialists and hospitals able to render the service. In addition, the estimates do not account for the split of services provided to private patients rendered in private or public hospitals (and so eligible for MBS funding) and public patients in public hospitals (and so not eligible for MBS funding).

MSAC concluded that there remains considerable uncertainty about the financial impact of publicly funding intravesical injections of botulinum toxin type A for IOAB. Based on the submitted estimates, it appears that the net cost to the MBS will be substantial or very substantial.

MSAC noted that the proposed Schedule fee aligns with current MBS cystoscopy injection item 36851 and with April 2013 MSAC advice on injecting botulinum toxin for NDO.

Lay Summary

MSAC considered an application to include injection of botulinum toxin (BOTOX[®]) into the muscle wall of the bladder as a treatment for urinary incontinence due to idiopathic overactive bladder. This application was coordinated with a PBAC consideration of botulinum toxin for listing in the PBS for the same population.

MSAC advised that the injection should be publicly funded, and that this should be coordinated with the listing of the medicine on the PBS. MSAC also expressed concerns that the estimated net cost to the MBS may not be accurate.

16. MSAC's advice to the Minister

MSAC supported public funding via the proposed MBS item with the wording of the item descriptor and timing of implementation coordinated with the PBS listing of botulinum toxin type A.

Draft new MBS item	Category 3 – Group T11 – botulinum toxin injections
New item 18379	<p>Botulinum toxin type A (Botox), intravesical injection of, with cystoscopy, for the treatment of urinary incontinence, including all such injections on any one day, if:</p> <ul style="list-style-type: none"> (a) the urinary incontinence is due to idiopathic overactive bladder in a patient: <ul style="list-style-type: none"> (i) who is at least 18 years of age; and (ii) the patient has urinary incontinence that has been inadequately controlled by at least two alternative anti-cholinergic agents, as manifested by having experienced at least 14 episodes of urinary incontinence per week before commencement of treatment with botulinum toxin type A; and (b) the patient is willing and able to self-catheterise; and (c) the requirements relating to botulinum toxin type A under the Pharmaceutical Benefits Scheme are complied with; and

	<p>(d) treatment is not provided on the same occasion as a service described in item 104, 105, 110, 116, 119, 11900 or 11919</p> <p>For each patient—applicable not more than once, except if the patient achieves at least a 50% reduction in urinary incontinence episodes from baseline at any time during the period of 6 to 12 weeks after first treatment</p> <p>(Anaes.) (H)</p> <p>MBS fee: \$229.85* Benefit: 75% = \$172.40</p>
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*MBS fee and benefit (rebate) are at the 1 November 2012 rate. Fee and benefit from 1 November 2014 will be at the 1 July 2014 indexed rate (e.g. \$234.00 and \$175.50 respectively).

MSAC noted that the flow-on implications for MBS costs were large and highly uncertain and supported the Department undertaking further work to refine these estimates.

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

No comment.

18. Context for decision

This advice was made under the MSAC Terms of Reference.

MSAC is to:

Advise the Minister for Health 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.