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1272

Final Decision  
Analytic Protocol  
(DAP) to guide the  
assessment of  
intravesical injection  
of BOTOX®  
(botulinum toxin) for  
the treatment of  
urinary incontinence  
due to idiopathic  
detrusor overactivity  
(IDO)

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February 2013

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## MSAC and PASC

The Medical Services Advisory Committee (MSAC) is an independent expert committee appointed by the Minister for Health and Ageing (the Minister) to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister on the evidence relating to the safety, effectiveness, and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

The Protocol Advisory Sub-Committee (PASC) is a standing sub-committee of MSAC. Its primary objective is the determination of protocols to guide clinical and economic assessments of medical interventions proposed for public funding.

### Purpose of this document

This document is intended to provide a draft decision analytic protocol that will be used to guide the assessment of an intervention for a particular population of patients. The draft protocol will be finalised after inviting relevant stakeholders to provide input to the protocol. The final protocol will provide the basis for the assessment of the intervention.

The protocol guiding the assessment of the health intervention has been developed using the widely accepted "PICO" approach. The PICO approach involves a clear articulation of the following aspects of the research question that the assessment is intended to answer:

**P**atients – specification of the characteristics of the patients in whom the intervention is to be considered for use;

**I**ntervention – specification of the proposed intervention

**C**omparator – specification of the therapy most likely to be replaced by the proposed intervention

**O**utcomes – specification of the health outcomes and the healthcare resources likely to be affected by the introduction of the proposed intervention

## Purpose of application

An application requesting MBS listing of intravesical<sup>1</sup> injection of BOTOX® (botulinum toxin) for the treatment of urinary incontinence due to idiopathic overactive bladder (IOAB)<sup>2</sup> was received from Allergan Australia Pty Ltd by the Department of Health and Ageing in May 2012.

This is distinct from the previous MSAC submission (Application 1221), which, as noted by PASC, is specifically for urinary incontinence due to neurogenic detrusor overactivity (NDO). The MSAC submission for Application 1221 was submitted on 14<sup>th</sup> June 2012 and is co-dependent to a PBAC submission for BOTOX® (which was considered at the July 2012 PBAC meeting).

In accordance with instructions from MSAC, Allergan adapted the Final DAP from MSAC Application 1221 (transurethral injection of BOTOX® for the treatment of incontinence due to NDO, May 2012) to produce DAP 1272 to guide the assessment of the safety, effectiveness and cost-effectiveness of intravesical injection of BOTOX® for the treatment of urinary incontinence due to IDO (in order to inform MSAC's decision-making regarding public funding of this intervention).

In November 2012, MSAC considered Application 1221 (urinary incontinence due to NDO) and agreed on the provision of information to the Pharmaceutical Benefits Advisory Committee (PBAC) regarding:

- (i) the MBS item descriptor;
- (ii) the recommended MBS fee for the service;
- (iii) patient out-of-pocket costs; and
- (iv) Extended Medicare Safety Net risk.

MSAC has suspended its final decision on public funding for the MBS service, pending PBAC's decision on funding (and associated restrictions) for BOTOX® for the treatment of incontinence due to NDO.

## Intervention

### Description

There is no consensus on either the definition of urinary incontinence or the measurement of the severity of urinary incontinence. Consequently, the reported rates of urinary incontinence in Australia vary. AIHW, for example, estimated in 2006 that 545,000 of the Australian adult population experience severe incontinence, 723,100 Australians experience moderate urinary incontinence and

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<sup>1</sup> The term 'transurethral' (used in application 1221) was replaced with the term 'intravesical' (in the present application, 1272) on the advice of Clinical Experts.

<sup>2</sup> The initial application was for the indication of overactive bladder (OAB), although the applicant later gave approval to modify this to idiopathic overactive bladder (IOAB). In conjunction with Clinical Experts, PASC determined that botulinum toxin is only beneficial for patients who have urinary incontinence due to idiopathic detrusor overactivity (IDO), because the mechanism of action of botulinum toxin is mediated through its effect on the detrusor muscle. Effectiveness of botulinum toxin is thus less biologically plausible for patients who have the broader indication of idiopathic urinary incontinence due to overactive bladder (IOAB), without detrusor involvement.

2,877,500 Australians experience slight urinary incontinence (AIHW, 2006). These population prevalence rates, however, do not differentiate by type of incontinence: stress incontinence (typically occurring during activities such as coughing, laughing, sneezing or exercise), overactive bladder or urge incontinence (result of bladder spasms or contractions), and obstruction incontinence (typically due to benign prostatic hyperplasia, bladder stones, bladder or pelvic tumours, urethral stricture, etc).

Overactive bladder (OAB) is a clinical syndrome comprising urinary urgency, frequency of voiding with or without nocturia and with or without urinary urge incontinence. It is caused by a dysfunction in the coordinated mechanisms that provide controlled storage and voiding of urine. This can lead to sudden urgency to urinate, which may be difficult to suppress, and sometimes leads to the involuntary loss of urine (incontinence). Bladder overactivity is also associated with increased pressure within the bladder, which can infrequently lead to upper urinary tract complications and renal damage. However, OAB, even if idiopathic OAB, (IOAB) is not identical to IDO; the latter requires confirmation by urodynamic studies that the symptoms are a result of the activity of an overactive detrusor. In patients with OAB due to IDO, the cause of the bladder dysfunction itself is unknown (unlike in patients with OAB due to NDO, where the cause is the underlying neurological condition). The goal of the treatment is to improve patients' quality of life by restoring continence, as well as to maintain normal pressure within the bladder during storage.

Botulinum toxin (BOTOX<sup>®</sup>) is produced by the gram-positive anaerobic bacterium *Clostridium botulinum*; it is among the most potent biologic neurotoxins. BOTOX<sup>®</sup>'s primary mechanism of action is inhibition of acetylcholine release at the presynaptic cholinergic junction. This results in a reduction of type Ia/II intrafusal muscle fibre afferent conduction, affecting the spinal stretch reflex and decreasing muscle tone and contractility without affecting muscle strength. BOTOX<sup>®</sup> is thought to have a direct effect on detrusor motor innervations, as well as on intrinsic bladder reflexes (Smaldone et al, 2010). BOTOX<sup>®</sup> also affects the transmission of afferent stimuli and reduces the appreciation of urgency. Consequently, the clinical experts estimate that approximately 10-20% of IDO patients will require self-catheterisation in the first 6 months post-injection. At baseline, less than 2% of IDO patients self-catheterise.

The intravesical injection of BOTOX<sup>®</sup> for the treatment of urinary incontinence due to IDO may be performed with local anaesthetic (with or without sedation) or under general anaesthesia. BOTOX<sup>®</sup> is injected into multiple sites in the muscular layer of the bladder wall.

## **Administration, dose, frequency of administration, duration of treatment**

The patient may be given local anaesthetic with or without sedation, or general anaesthesia, prior to the procedure. A rigid or flexible cystoscope is inserted through the urethra and into the bladder to allow visualisation of the bladder wall. 100 U<sup>3</sup> of BOTOX<sup>®</sup> is injected into the inner muscular layer of

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<sup>3</sup> The Applicant proposed 100U on the basis of two phase III trials. However, a variety of doses are reported in the literature. Clinical experts favour doses of 150U or 200U to be effective at 6 to 12 month intervals (usually 9 months), although the precise protocol used is dependent on clinical judgement and personal experience of the clinician. The Cochrane Collaboration has published a review of 'Botulinum toxin injections for adults with

the bladder wall (detrusor). The needle is inserted approximately 2 mm into the detrusor, and 20 injections are spaced approximately 1 cm apart. Clinical improvement generally occurs within 2 weeks.

The effect of BOTOX<sup>®</sup> wears off over time; in the two Phase III pivotal trials, the median time to retreatment was 24.1 weeks (approximately 6 months). The applicant proposes that a more accurate estimation of duration of treatment effect will be obtained from an integrated analysis of the two Phase III pivotal studies and the long-term extension study, which will be presented in the MSAC submission for this MBS listing application.

Delivery could be restricted to certain specialties, including urologists and potentially also gynaecologists or subspecialties of gynaecology (e.g. urogynaecologists).<sup>4</sup> The procedure is performed in a theatre or procedure room on a 100% in-hospital basis – generally on patients who are day-admitted (occasionally, patients are overnight-admitted if there are significant co-morbidities). As the service is provided only to admitted in-hospital patients, PASC determined that Extended Medicare Safety Net (EMSN) risk is negligible. (Other attendance items that may be performed in connection with this service have EMSN caps.)

## Co-administered interventions

Urodynamic studies (MBS item 11919) are a standard part of patient assessment. They are typically performed when the patient first presents for initial treatment, in order to diagnose detrusor involvement. Repeat urodynamic studies would not be required at the time the patient would become eligible for BOTOX<sup>®</sup> injections. According to a clinical expert, a urodynamic study assesses the function of the lower urinary tract, and involves a measurement of: the urinary flow (including the measurement of the urine flow rate, voided volume, and voiding pattern), bladder and perineal ultrasound or fluoroscopy (assesses residual urinary volume and urethral mobility), cystometry (assesses bladder filling, storage and pressures) and stress testing (to diagnose urodynamic stress incontinence) and a pressure-flow study to assess emptying.

The additional health care resources required on the same day as the injection may include: hospital admission costs, anaesthesia cost, intravenous antibiotics, needle cost (Williams needle for rigid cystoscope and flexible needle if flexible cystoscope is used<sup>5</sup>), and BOTOX<sup>®</sup> cost.<sup>6</sup> With the exception of the BOTOX<sup>®</sup> cost, these resources would also be incurred on the day of sacral nerve stimulation.

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overactive bladder syndrome' (The Cochrane Library, 2011, Issue 12), which provides some insight into safe and effective doses.

<sup>4</sup> Letters of support have been received from the Urological Society of Australia and New Zealand, as well as from the Urogynaecological Society of Australasia. It needs to be noted, however, that although the letters quote application 1272 and provide support for injections for 'urinary incontinence', IDO is not mentioned specifically.

<sup>5</sup> Expert clinical opinion is that the cost for either of these needles is approximately \$50.

<sup>6</sup> In line with expert clinical opinion, a urine flow study (MBS item 11900) should be restricted from being performed on the same day as the injection of botulinum toxin (if a urine flow study is needed on the same day as the procedure, it should form part of the botulinum toxin service). The urine flow study should still be included as a relevant health care resource, as it may still be performed, but only on a separate occasion of service.

Patients being considered for BOTOX<sup>®</sup> injections will have failed or will be intolerant to anticholinergic therapy and/or smooth muscle relaxants. However, some patients may remain on these therapies during treatment with BOTOX<sup>®</sup>.

Anticholinergic drugs currently in use include: oxybutynin (PBS item number 8039D), propantheline (PBS item number 1953T), imipramine (PBS item number 2420J), tolterodine (not PBS-listed), darifenacin (not PBS-listed), solifenacin (not PBS-listed), extended-release patch version of oxybutynin (PBS item number 9454N) and extended release version of tolterodine (not PBS-listed). Oxybutynin is the most widely used anticholinergic, although propantheline is an older drug still sometimes used in Australia (Kuteesa and Moore, 2006).

According to a clinical expert, the smooth muscle relaxant currently in use is oxybutynin (PBS item number 8039D).

Clinical experts advise that, in current practice, the patient would typically start therapy with oxybutynin. Subsequently, either oxytrol patches, or solifenacin, or darifenacin, or tolterodine would be tried. Propantheline is seldom used in current practice, on account of its side effects. Any of the anti-muscarinics can be augmented in effect by tricyclic antidepressants such as imipramine.

## Background

### Current arrangements for public reimbursement

BOTOX<sup>®</sup> injection for overactivity incontinence is currently available to patients visiting an urologist or urogynaecologist through patient self-pay (for drug costs), and, less frequently, through private hospital funding or private health insurance. Co-dependent with the current MSAC application, Allergan will be seeking PBS funding of BOTOX<sup>®</sup> for the treatment of urinary incontinence due to idiopathic overactive bladder (IOAB), through Section 100 of the PBS.

The injection of BOTOX<sup>®</sup> into the bladder is currently being claimed using MBS items 36851 (predominantly) or 37339 (infrequently). Clinical experts indicated that item 37339 is unlikely to be used for BOTOX<sup>®</sup> injections, as it is predominantly used for injections of collagen, macroplastique or deflux into the urethral wall.

The number of claims processed per calendar year under item 36851 has increased from fewer than 100 in 2000/2001, to 661 in 2010/2011, whereas the numbers of claims under item 37339 has fluctuated but remained fairly constant over time (537 claims were processed in 2000/2001 and 564 were processed in 2010/11). It is not possible to differentiate the proportion of claims under items 36851 (or 37339) that would be attributed to botulinum toxin. Although data on items 36851 (and 37339) may provide some guidance, it is important to note that the data would be masked by appropriate usage for the purpose originally approved for each item.

#### MBS 36851

CYSTOSCOPY, with injection into bladder wall

(Anaes.)

Fee: \$229.85

MBS 37339

PERIURETHRAL OR TRANSURETHRAL INJECTION of materials for the treatment of urinary incontinence, including cystoscopy and urethroscopy

(Anaes.)

Fee: \$239.85

## Regulatory status

BOTOX® (a trademark of Allergan) is currently TGA-registered for a number of indications under TGA entries 172264 and 67311. The applicant informs that TGA assessment of BOTOX® for the indication of OAB is underway (i.e. the indication is not limited to IDO). The complete TGA submission was lodged in early July 2012.<sup>7</sup>

The currently approved indications (under entries 172264 and 67311) include:

- 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.
- Prophylaxis of headaches in adults with chronic migraine (headache on at least 15 days per month of which at least 8 days are with migraine);
- Treatment of strabismus in children and adults;
- Treatment of blepharospasm associated with dystonia, including benign blepharospasm and VII nerve disorders (specifically hemifacial spasm) in patients twelve years and over;
- Treatment of cervical dystonia (spasmodic torticollis);
- Treatment of focal spasticity of the upper and lower limbs, including dynamic equinus foot deformity, due to juvenile cerebral palsy in patients two years of age and older;
- Treatment of severe primary hyperhidrosis of the axillae;
- Treatment of focal spasticity in adults;
- Treatment of spasmodic dysphonia.

BOTOX (Botulinum Toxin Type A) Purified Neurotoxin Complex is indicated for the following cosmetic indications:

- Temporary improvement in the appearance of upper facial rhytides (glabellar lines, crows' feet and forehead lines) in adults.

An alternative clostridium botulinum type A toxin (Dysport) is also TGA-registered for a more limited list of indications. Under TGA entries 74124 and 170651, Dysport is specified for the treatment of:

- Spasticity of the upper limb in adults following a stroke;
- Spasmodic torticollis in adults;
- Dynamic equinus foot deformity due to spasticity in ambulant paediatric cerebral palsy patients, two years of age or older;

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<sup>7</sup> As of 31 January 2013, the TGA approval has not yet been granted.

- Blepharospasm in adults;
- Hemifacial spasm in adults;
- Moderate to severe glabellar lines in adults.

As noted by TGA, there is a lack of interchangeability between botulinum toxin products due to the lack of a standardised international unit. As such, BOTOX® is not therapeutically equivalent to any other botulinum toxin type A preparations.

## Patient population

The applicant is seeking MBS and PBS funding for patients with urinary incontinence due to idiopathic overactive bladder (IOAB) - which is a broader population than idiopathic detrusor overactivity (IDO) - in patients who have failed or are contraindicated for first-line conservative therapy, including anti-cholinergic medications. (Patients must be willing and able to self-catheterise.) The patient population associated with MBS funding would be aligned with any PBAC-recommended PBS listing.

Although the population to be eligible for PBS subsidy of botulinum toxin is a matter for PBAC, PASC noted that:

- Expert clinical opinion is that botulinum toxin is only beneficial for patients with urinary incontinence due to IDO. This is because the mechanism of action of botulinum toxin is mediated through its effect on the detrusor muscle. Effectiveness of botulinum toxin is less biologically plausible for patients who have the broader indication of urinary incontinence due to IOAB, without detrusor involvement. IOAB patients may not benefit from botulinum toxin treatment and the service may be unsustainable on the MBS, given the large population of people with IOAB. IDO requires urodynamic confirmation (MBS item 11919) that the patient's symptoms are a result of the activity of an overactive detrusor.
- There are many reasons for (and different severities of) urinary incontinence, and caution is needed when recommending botulinum toxin for people under the age of 18. Botulinum toxin would not be appropriate for many of these patients. Patients under 18 who may benefit from botulinum toxin would most likely fall within the eligible population of Application 1221 (NDO).

For these reasons, PASC recommends that, in the context of the proposed PBAC submission, PBAC consider restricting the use of botulinum toxin to IDO (as demonstrated by a urodynamic study), and to adults 18 years of age and older. PASC upheld the previous recommendation that administration of the drug (for IDO and NDO) should be restricted to patients who are willing and able to self-catheterise.

## Proposed MBS listing

In accordance with the fee proposed in the MSAC submission for the injection of BOTOX® for urinary incontinence due to NDO (Application 1221), MSAC has advised a fee of \$229.85. The rationale for this is that the duration and complexity of the injection for NDO and IDO (or IOAB) are comparable. The injection of BOTOX® is currently reimbursed on the MBS for a range of TGA-

approved indications, as listed in Appendix 1. The MBS fees for these items range from \$45.05 to \$267.05; the MBS fees for the two existing items for transurethral injection (items 36851 and 37339) are within this range (\$229.85 and \$239.85, respectively).

Table 1: Proposed MBS item descriptor for intravesical injection of BOTOX® (botulinum toxin) for the treatment of urinary incontinence due to IDO.

MBS [item number to be assigned by the Department if listed on the MBS]\*

BOTULINUM TOXIN (Botox), intravesical injection of, for the treatment of urinary incontinence due to idiopathic detrusor overactivity (or idiopathic overactive bladder), including cystoscopy and all injections in one day, in patients aged 18 years or older who have failed or are contraindicated for first-line conservative therapy, including anti-cholinergic medications, with injections only performed on patients with prior confirmation of detrusor involvement (demonstrated by urodynamic studies), and who are willing and able to self-catheterise.

(Anaes.)

(See para T11.1 of explanatory notes to this Category)<sup>8</sup>

MBS Fee: \$229.85                      Benefit: 75% = \$172.40

\*Age restrictions will be inserted into the descriptor if PBAC limits the drug for this indication to adults

This item will be located within Group T11 of the MBS, which lists all of the BOTOX® item numbers. The supply of BOTOX® for these items is made under section 100 of the *National Health Act 1953*.

At the present time, it is not possible to comment on the consistency of the proposed MBS descriptor with the approved TGA indication, as this indication currently lacks TGA approval. The applicant has notified MSAC that an application was submitted to TGA in early July 2012.

## Clinical place for proposed intervention

A wide range of conservative therapies are currently available for patients with urinary incontinence due to IDO (and IOAB). These include: drug therapies, behavioural therapies and interventional therapies. Drug therapies may involve anticholinergics and/or smooth muscle relaxants, as described previously. Behavioural therapies can involve diet modifications, bladder training and/or rehabilitation of pelvic muscle. Interventional therapies can include external electrical stimulation (MSAC, 2008), as well as Trans-cutaneous Electrical Nerve Stimulation (TENS) and Posterior Tibial Nerve Stimulation/SANS therapy (clinical expert advice).

However, between 25-40% of patients with detrusor overactivity (both idiopathic and neurogenic) fail to improve or insufficiently improve with conservative treatment options (Nitti, 2006). Among Australian female IDO patients, at baseline, only half were categorised as having responded to anti-cholinergics; at follow-up of 8 years, the response rate was 35% (Morris et al, 2007). After the patients have exhausted conservative treatment options they may therefore become candidates for sacral nerve stimulation or best supportive care.

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<sup>8</sup> Please see Appendix 1 for Paragraph T11.1

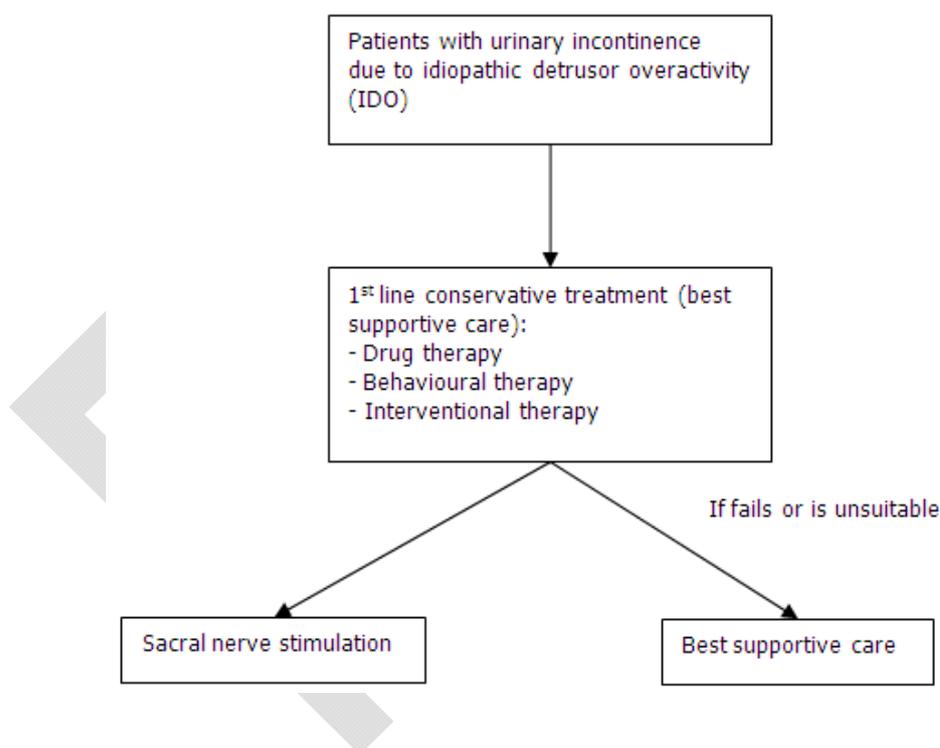
Sacral nerve stimulation involves the application of electrical stimulation to the sacral nerve via a fully implantable system. The procedure is carried out in two phases, allowing for a minimally invasive screening test before proceeding to permanent generator implant if the screening test indicates the viability of the treatment in the individual patient (MSAC, 2008). PASC considered SNS to be more invasive because a device has to be surgically implanted. This is consistent with previous considerations of both MSAC (Application 1115, November 2008) and PBAC (Application 1221, July 2012).

Best supportive care includes drug therapies, behavioural therapies and interventional therapies, as described above.

#### Current clinical management algorithm

The treatment pathway presented here is based on the one developed in MSAC's review of Sacral Nerve Stimulation for urinary indications (MSAC Application 1115, 2008).<sup>9</sup>

**Figure 1: Clinical management algorithm without the proposed intervention:**



#### Clinical management algorithm with the proposed intervention

As noted above, the first line conservative therapies for patients with urinary incontinence due to IDO have high failure rates. BOTOX<sup>®</sup> therapy is therefore proposed as a second-line approach, as BOTOX<sup>®</sup> is thought to be more invasive than the first-line conservative approaches, but less invasive than SNS (which requires implantation of a system that delivers the electrical stimulation to the sacral

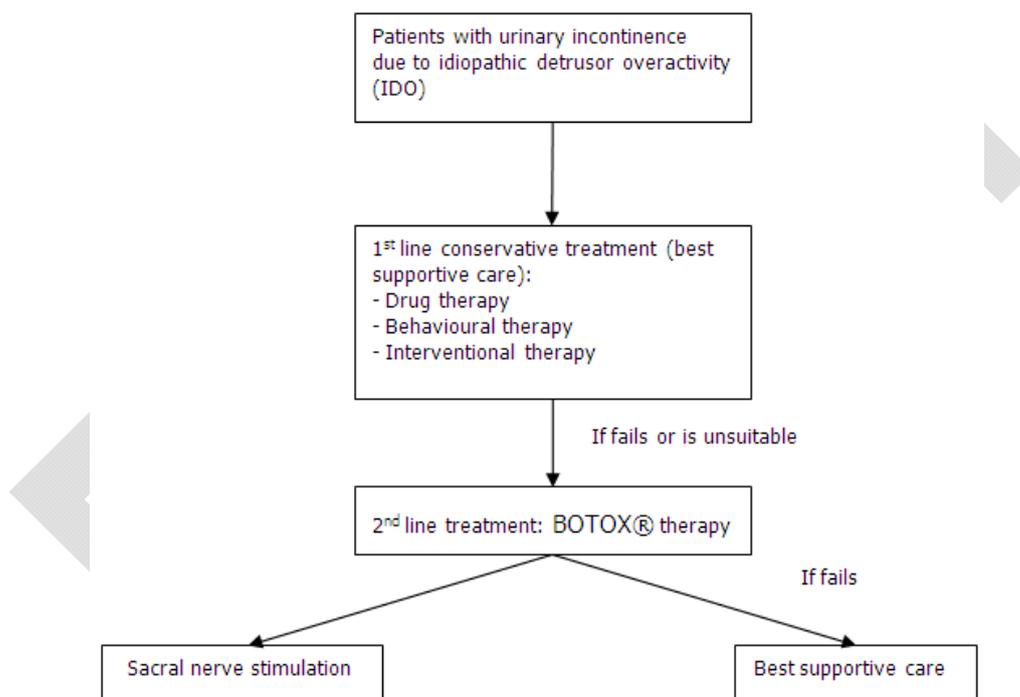
<sup>9</sup> References to major surgery have been omitted, as (according to expert clinical opinion) it has now been replaced by Sacral Nerve Stimulation.

nerve). Clinical experts advise that, in IDO patients for whom BOTOX® injections are effective, the use of anti-cholinergics is generally stopped once the BOTOX® begins to work (7-10 days after the procedure); as BOTOX®'s effectiveness wanes, the use of anti-cholinergics may be reviewed.

BOTOX® is 'reversible' in the sense that the patient may elect not to undergo a reinjection at the end of the effectiveness period. The requirement for re-injections will have cost-effectiveness implications. The applicant notes that this issue will be assessed in the economic evaluation section of the PBAC submission. However, insofar as the *re-injections themselves* fall under MSAC's remit, the issue of repeat injections would be considered by MSAC, as well.

If the BOTOX® therapy fails, the previously described Sacral Nerve Stimulation or (return to) best supportive care are possible treatment options.

**Figure 2: Clinical management algorithm with the proposed intervention:**



## Comparator

The applicant (Allergan) proposed that best supportive care (BSC) may be the appropriate comparator for the purpose of this application. PASC agreed that BSC should be the comparator. PASC agreed that existing MBS item 36851 was the most appropriate benchmark to help MSAC set the MBS fee for the treatment of urinary incontinence due to IDO (or IOAB if PBAC agrees PBS funding for this indication).

## Clinical claim

Allergan requested that the comparative safety and effectiveness of BOTOX® treatment for urinary incontinence for this application be assessed by PBAC. Allergan also requested that economic

evaluation be carried out by PBAC. In November 2012, MSAC provided advice on costs associated with similar Application 1221 (NDO) to enable PBAC to consider PBS funding for the treatment of urinary incontinence due to NDO.

PASC agreed that the submission to PBAC should consider the overall comparative safety, effectiveness and cost-effectiveness of the proposed service, whilst the MSAC assessment will be limited to the wording of the MBS item descriptor (to align with PBS restrictions), the MBS fee and the financial implications for the MBS for listing the proposed service.

As the economic evaluation of BOTOX® treatment will be carried out by PBAC, Table 2 ('Classification of an intervention for determination of economic evaluation to be presented') was not completed for this application.

## Outcomes and health care resources affected by introduction of proposed intervention

### Outcomes

This assessment will consider:

- Wording of the MBS item descriptor (which will align with PBS restrictions) and associated MBS fee; and
- Financial impact to the MBS and patients: Consequences of adding the MBS item (any potential changes in utilisation rates resulting from this addition; the billing of anaesthetic items on the same occasion of service; professional attendance items to assess, reassess and treat urinary tract infections and urinary retention – not on the same occasion of service; Extended Medicare Safety Net risk and patient out-of-pocket costs).

### Health care resources

Table 2: List of resources to be considered in the economic analysis

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS rebate	Safety nets*	Other govt budget	Private health insurer	Patient	Total cost
<b>Resources provided to identify eligible population</b>										
MBS item 104 (initial consult)	Specialist (urologist or urogynaecologist)				\$72.75					\$129.98
MBS item 11919 (urodynamic studies)	Specialist (urologist or urogynaecologist)				\$364.10					
<b>Resources provided to deliver proposed intervention</b>										
MBS item 20910 (initiation of anaesthesia) and MBS item 23010 to 24136 (provision of	Anaesthetist				\$110.71					\$267.78

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS rebate	Safety nets*	Other govt budget	Private health insurer	Patient	Total cost
anaesthesia - actual item billed depends on duration of procedure)										
Provision of drug (Botox) - PBS										
New MBS item to inject the drug					\$172.40					\$302
Other hospital costs associated with injection										
<u>Resources provided in association with proposed intervention (e.g. pre-treatments, co-administered interventions, resources used to monitor or in follow-up, resources used in management of adverse events, resources used for treatment of down-stream conditions)</u>										
MBS item 17610 to 17625 (pre-anaesthesia consult – actual item billed depends on time spent with patient)	Anaesthetist				\$32.49					\$77.45
MBS item 105 (subsequent consult to assess response and to manage re-injections)	Specialist (urologist or urogynaecologist)				\$36.55					\$66.48
MBS item 23 or 36 (to treat urinary tract infections or urinary retention)					\$36.30 (standard consult) or \$70.30 (prolonged consult)					\$41.34 \$74.97
MBS item 11900 (urine flow study – billed on separate occasion of service, to check post-injection urinary retention)	Specialist (urologist or urogynaecologist)				\$23.45					-

## Proposed structure of economic evaluation (decision-analytic)

Table 3: Summary of extended PICO to define research question that assessment will investigate

Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Patients with urinary incontinence due to idiopathic detrusor overactivity (IDO) – (or idiopathic overactive bladder (IOAB) if PBAC agrees PBS funding for this indication) – in patients who have failed or are unsuitable for first-line conservative therapy	Intravesical injection of BOTOX®, including cystoscopy and all injections in one day, and associated anaesthetic costs	Best supportive care	For PBAC	Consequences of adding the MBS item number (and any potential changes in utilisation rates resulting from this addition)

## Appendix 1: BOTOX uses currently reimbursed by the MBS

### **MBS 18350**

BOTULINUM TOXIN (Botox), injection of, for hemifacial spasm in a patient 12 years of age or older, including all injections on any one day

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$124.85

### **MBS 18352**

BOTULINUM TOXIN (Botox or Dysport), injection of, for cervical dystonia (spasmodic torticollis), including all injections on any one day

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$249.75

### **MBS 18354**

BOTULINUM TOXIN (Botox or Dysport), injection of, for dynamic equinus foot deformity due to spasticity in an ambulant cerebral palsy patient, aged two years or older, in accordance with the supply of the drug under instrument PB 122 of 2008 (Arrangements — Botulinum Toxin Program) made under Section 100 (1) (b) of the *National Health Act 1953*, including all such injections on any one day for all or any of the muscles subserving one functional activity and supplied by one motor nerve - applicable only to the first two treatments of each limb of the patient on any one day

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$124.85

### **MBS 18356**

BOTULINUM TOXIN (Botox or Dysport), injection of, for dynamic equinovarus foot deformity due to spasticity in an ambulant cerebral palsy patient, aged two years or older, in accordance with the supply of the drug under instrument PB 122 of 2008 (Arrangements — Botulinum Toxin Program) made under Section 100 (1) (b) of the *National Health Act 1953*, including all such injections on any one day for all or any of the muscles subserving one functional activity and supplied by one motor nerve - applicable only to the first two treatments of each limb of the patient on any one day

(Anaes.)

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$124.85

### **MBS 18358**

BOTULINUM TOXIN (Botox or Dysport), injection of, for dynamic equinovalgus foot deformity due to spasticity in an ambulant cerebral palsy patient, aged two years or older, in accordance with the supply of the drug under instrument PB 122 of 2008 (Arrangements — Botulinum Toxin Program) made under Section 100 (1) (b) of the *National Health Act 1953*, including all such injections on any one day for all or any of the muscles subserving one functional activity and supplied by one motor nerve - applicable only to the first two treatments of each limb of the patient on any one day

(Anaes.)

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$124.85

### **MBS 18360**

BOTULINUM TOXIN (Botox), injection of, for the treatment of focal spasticity in adults, including all injections for all or any of the muscles subserving one functional activity, supplied by one motor nerve, with a maximum of 4 treatments per patient on any one day (2 per limb)

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$124.85

**MBS 18361**

Botulinum toxin (Botox), injection of, for the treatment of moderate to severe upper limb spasticity due to cerebral palsy, in a patient who is at least 2 years but less than 18 years, in association with either: (a) physiotherapy or occupational therapy or both; or (b) electrical stimulation or ultrasound for muscle localisation; including all injections for any or all of the muscles sub-serving one functional activity supplied by one motor nerve - with a maximum of four treatments per patient on any one day, and with a maximum of two treatments per limb

(Anaes.)

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$124.85

**MBS 18362**

BOTULINUM TOXIN (Botox), injection of, for the treatment of severe primary hyperhidrosis of the axillae, including all such injections on any one day

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$246.70

**MBS 18366**

BOTULINUM TOXIN (Botox), injection of, for the treatment of strabismus in children and adults, including all such injections on any one day and associated electromyography

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$156.40

**MBS 18368**

BOTULINUM TOXIN (Botox), injection of, for the treatment of spasmodic dysphonia, including all such injections on any one day

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$267.05

**MBS 18370**

BOTULINUM TOXIN (Botox), injection of, for the treatment of blepharospasm in a patient 12 years of age or older, including all such injections on any one day.

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$45.05

**MBS 18372**

BOTULINUM TOXIN (Botox), injection of, for the treatment of bilateral blepharospasm in a patient 12 years of age or older, including all such injections on any one day

*(See para T11.1 of explanatory notes to this Category)*

**Fee:** \$124.85

**T.11.1. BOTULINUM TOXIN - (ITEMS 18350 TO 18373)**

The Therapeutic Goods Administration (TGA) assesses each indication for the therapeutic use of botulinum toxin on an individual basis. There are currently two botulinum toxin agents with TGA registration (Botox and Dysport). Each has undergone a separate evaluation of its safety and efficacy by the TGA as they are neither bioequivalent, nor dose equivalent. When claiming under an item for the injection of botulinum toxin, only the botulinum toxin agent specified in the item can be used. Benefits are not payable where an agent other than that specified in the item is used.

The TGA assesses each indication for the therapeutic use of botulinum toxin by assessment of clinical evidence for its use in paediatric or adult patients. Where an indication has been assessed for adult use, data has generally been assessed using patients over 12 years of age. Paediatric indications have been assessed using data from patients under 18 years of age. Botulinum toxin should only be administered to patients under the age

of 18 where an item is for a paediatric indication, and patients over 12 years of age where the item is for an adult indication, unless otherwise specified.

Items for the administration of botulinum toxin can only be claimed by a medical practitioner who is registered by Medicare Australia to participate in the arrangements under Section 100 of the *National Health Act 1953* relating to the use and supply of Botulinum Toxin.

Items 18354, 18356 and 18358 for the treatment of equinus, equinovarus or equinovalgus are limited to a maximum of 4 injections per patient on any one day (2 per limb). Accounts should be annotated with the limb which has been treated.

Item 18292 may not be claimed for the injection of botulinum toxin, but may be claimed where a neurolytic agent (such as phenol) is used, in addition to botulinum toxin injection(s), to treat the obturator nerve in patients with a dynamic foot deformity.

Items 18354 to 18358 have been extended to patients 18 years of age and older who have commenced on the PBS subsidised treatment as a paediatric patient. This is in line with the extension of the PBS listing for the supply of the drug for this indication under Section 100(1)(b) of the *National Health Act 1953*.

Botulinum Toxin, which is not supplied and administered in accordance with the arrangements under Section 100 of the *National Health Act 1953*, is not free of charge to patients. Where a charge is made for the Botulinum Toxin administered, it must be separately listed on the account and not billed to Medicare.

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