

6.12 INCOBOTULINUMTOXIN A, Lyophilised powder for injection, 100 units, Xeomin[®], Merz Australia Pty Ltd.

1 Purpose of Application

- 1.1 The minor submission requested an expansion of the current Section 100 Authority Required (STREAMLINED) listing for incobotulinumtoxin A (herein known as Xeomin[®]) for the treatment of moderate to severe focal spasticity of the upper limb following a stroke to also include spasticity following acute events other than stroke.
- 1.2 An expansion of the same listing was recommended for clostridium botulinum type A toxin-haemagglutinin complex (herein known as Dysport[®]) at the March 2019 PBAC meeting and the change was made to the PBS on 1 October 2019.

2 Background

Registration status

- 2.1 Xeomin[®] was TGA registered on 21 March 2014 for post-stroke spasticity of the upper limb.
- 2.2 Xeomin[®] was granted a licensing extension that removed the restriction limiting use to the post-stroke subgroup on 15 March 2018, resulting in the current TGA-approved indication of “spasticity of the upper limb”.
- 2.3 Xeomin[®] is currently listed on the PBS as a Section 100 – Botulinum Toxin Program, Authority Required (STREAMLINED) listing for moderate to severe spasticity of the upper limb following a stroke.

Previous PBAC considerations

- 2.4 The PBAC recommended Xeomin[®] for the treatment of upper limb spasticity following a stroke in July 2014 meeting (in conjunction with application for use in cervical dystonia and blepharospasm) on a cost-minimisation basis compared with botulinum toxin type A (herein known as Botox[®]).
- 2.5 The PBAC recommended Botox[®] for the treatment of upper limb spasticity following a stroke in July 2008 on a cost-minimisation basis compared with Dysport[®].
- 2.6 The PBAC recommended an extension of the PBS listing of Dysport[®] from upper limb spasticity following a stroke to upper limb spasticity following an acute event in March 2019.
- 2.7 The PBAC also considered a minor submission to extend the listing of Botox[®] for the treatment of upper limb spasticity at its November 2019 meeting (refer to item 6.09).

For more detail on PBAC’s view, see section 6 PBAC outcome.

3 Requested listing

3.1 The submission requested the following changes to the existing listing:

- (i) Extension of the current restriction from “moderate to severe spasticity of the upper limb following a stroke” to “...following an acute event”;
- (ii) Modification of the current restriction to include “The treatment must not exceed a maximum of 4 treatment periods (with any botulinum toxin-A) per upper limb in the first year of treatment, and 2 treatment periods (with any botulinum toxin-A) per upper limb each year thereafter”. This amendment has been accepted by the PBAC in previous consideration of botulinum toxin in upper and lower limb focal spasticity;
- (iii) A Special Pricing Agreement (SPA) to match the effective price of Dysport®; and
- (iv) To enter into the same Risk Sharing Arrangement (RSA) as Dysport®, with 100% rebates beyond estimated subsidisation caps.

3.2 The PBAC noted that the amendments requested are relevant to Authority code 5220, which falls under PBS item 10983C.

3.3 Changes to the current restriction proposed by the sponsor are in bold. Suggestions and additions proposed by the Secretariat to the requested listing are in italics and deletions are in strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
INCOBOTULINUMTOXINA 100 units injection, 1 vial	4	0	Published: \$1,547.39 Effective: TBD	Xeomin® Merz Pharmaceuticals GmbH

Category/program:	Section 100 – Botulinum Toxin Program
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Severity:	Moderate to severe
Condition:	Spasticity of the upper limb following a stroke an acute event
PBS indication:	Moderate to severe spasticity of the upper limb following a stroke an acute event
Restriction level:	<input checked="" type="checkbox"/> Streamlined

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Clinical criteria:	<p>The condition must be moderate to severe spasticity of the upper limb/s following an acute event stroke, defined as a Modified Ashworth Scale rating of 3 or more, AND The treatment must not be initiated until three months post-stroke, AND The treatment must only be used as second line therapy when standard management has failed; OR The treatment must only be used as an adjunct to physical therapy, AND The treatment must not continue if the patient does not respond (defined as not having had a decrease in spasticity rating greater than 1, using the Modified Ashworth Scale [MAS], in at least one joint) after two treatment periods (with any botulinum toxin type A total Botox, Dysport, and Xeomin), AND <i>The treatment must not exceed a maximum of 4 treatment periods (with any botulinum toxin type A) per upper limb in the first year of treatment, and 2 treatment periods (with any botulinum toxin type A) per upper limb each year thereafter,</i> The treatment must not exceed 4 treatment periods (total Botox, Dysport, and Xeomin®) per upper limb per lifetime, AND Patient must not have established severe contracture in the limb to be treated</p>
Population criteria:	Patient must be aged 18 years or older.
Treatment criteria:	<p>Must be treated by a neurologist; OR Must be treated by an orthopaedic surgeon; OR Must be treated by a rehabilitation specialist physician; OR Must be treated by a plastic surgeon; OR Must be treated by a geriatrician.</p>
Prescriber instructions:	<p>The date and nature of the event of the stroke must be documented in the patient's medical records when treatment is initiated.</p> <p>Standard management includes physiotherapy and/or oral spasticity agents.</p>
Administrative Note:	<p>The units used to express the potency of botulinum toxin preparations currently available for PBS subsidy are not equivalent.</p> <p>An acute event may be a clinical or external event that leads to upper motor neuron lesions resulting in spasticity for example, these may be stroke, traumatic brain injury (TBI), spinal cord injury, infection or hypoxia.</p> <p><i>Special pricing Arrangement apply.</i></p>
Caution:	Contraindications to treatment include known sensitivity to botulinum toxin.

Category/Program:	Section 100 – Botulinum Toxin Program
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Severity:	Moderate to severe
Condition:	Spasticity of the upper limb following an acute event
PBS Indication:	Moderate to severe spasticity of the upper limb following an acute event
Treatment phase:	Grandfathered treatment
Restriction level:	<input checked="" type="checkbox"/> Streamlined

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Clinical criteria:	<p>Patient must have previously received non-PBS subsidised treatment with this drug for this condition prior to [PBS listing date] AND The condition must have been moderate to severe spasticity of the upper limb/s following an acute event, defined as a Modified Ashworth Scale rating of 3 or more prior to commencing non-PBS subsidised treatment AND The treatment must only be used as second line therapy when standard management has failed; OR The treatment must only be used as an adjunct to physical therapy, AND The treatment must not continue if the patient does not respond (defined as not having had a decrease in spasticity rating greater than 1, using the Modified Ashworth Scale, in at least one joint) after two treatment periods (with any botulinum toxin type A) AND The treatment must not exceed a maximum of 4 treatment periods (with any botulinum toxin type A) per upper limb in the first year of treatment, and 2 treatment periods (with any botulinum toxin type A) per upper limb each year thereafter. AND Patient must not have established severe contracture in the limb to be treated.</p>
Population criteria:	Patient must be aged 18 years or older.
Treatment criteria:	<p>Must be treated by a neurologist; OR Must be treated by an orthopaedic surgeon; OR Must be treated by a rehabilitation specialist; OR Must be treated by a plastic surgeon; OR Must be treated by a geriatrician.</p>
Prescriber Instructions:	Standard management includes physiotherapy and/or oral spasticity agents.
Administrative Advice:	<p>The units used to express the potency of botulinum toxin preparations currently available for PBS subsidy are not equivalent.</p> <p>An acute event may be a clinical or external event that leads to upper motor neuron lesions resulting in spasticity for example, these may be stroke, traumatic brain injury, spinal cord injury, infection or hypoxia.</p> <p>Special Pricing Arrangements apply.</p>
Cautions:	Contraindications to treatment include known sensitivity to botulinum toxin.

MBS restriction

- 3.4 The pre-PABC response stated that in the event of a positive PBAC recommendation, the sponsor would submit an application to the MSAC proposing changes to MBS item 18365 to allow Xeomin® administration.
- 3.5 The PBAC noted that a MSAC application concerning MBS item 18365 addressing the corresponding changes to PBS listing to allow administration of Xeomin® following an acute event is required and considered that changes to the PBS and MBS listing would have to be implemented on the same date.

For more detail on PBAC’s view, see section 6 PBAC outcome.

4 Comparator

4.1 The minor submission nominated Dysport® as the main comparator. This was appropriate as BOTOX® and Dysport® are used in the same place in the clinical management algorithm.

For more detail on PBAC’s view, see section 6 PBAC outcome.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

5.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

5.3 The minor submission was based on a naïve comparison between Xeomin® and Dysport® and presented data from:

- The TOWER study: a prospective, open-label, non-randomised titration study of Xeomin® conducted over three treatment cycles (N=155); and
- Study 145: a randomised controlled trial comparing Dysport® to placebo over one treatment cycle (N=243) (previously considered by the PBAC in November 2018).

5.4 Details of the studies presented in the submission are provided below.

Table 1: Studies presented in the submission

	Protocol title/ Publication title	Publication citation
Main study		
TOWER	Prospective, open-label, non-randomized, single-arm, multi-center dose titration study to investigate the safety and efficacy of NT 201 in subjects deemed to require total body doses of 800 U of NT 201 during the course of the study for the treatment of upper and lower limb spasticity of the same body side due to cerebral causes.	18 August 2015
Open-label extension study		
Kanovsky, 2011	Kanovsky P, Slawek J, Denes Z, et al. Efficacy and safety of treatment with incobotulinum toxin A (botulinum neurotoxin type A free from complexing proteins; NT 201) in post-stroke upper limb spasticity.	J Rehabil Med. 2011; 43: 486-492.

Source: Compiled during evaluation

5.5 The TOWER study investigated the safety and efficacy of Xeomin® in subjects with upper and lower limb spasticity of the same body side due to cerebral causes. The TOWER study used a dose titration approach over three injection cycles (a fixed total body dose of 400U, 600U and 800U of Xeomin® [if permitted]), with a flexible observation period after each injection of 12 to 16 weeks and a total duration of exposure of up to 48 weeks.

- 5.6 In the TOWER study 132/155 (85.2%) of patients had stroke as their primary disease, 11/155 (7.1%) had traumatic brain injury and 12/155 (7.7%) had other cerebral vascular disorders, brain tumour or cerebral palsy. In Study 145 approximately 90% of patients had post-stroke spasticity and approximately 10% had spasticity following a traumatic brain injury.
- 5.7 Treatment response in the TOWER study was a reduction in Ashworth Scale (AS) score of ≥ 1 . Treatment response in Study 145 was a reduction in Modified Ashworth Scale (MAS) score ≥ 1 .

Comparative effectiveness

- 5.8 The results of the naïve indirect comparison are presented below.

Table 2: Treatment response outcomes from TOWER and Study 145

Population (and subgroup)	Xeomin® (TOWER)#			Population (and subgroup)	Dysport® (Study 145 – results from November 2018 PSD)					
	Cycle 1	Cycle 2	Cycle 3		4 weeks			12 weeks		
	up to 400U	up to 600U	up to 800U		1000U	500U	Placebo	1000U	500U	Placebo
	Treatment response*, n/N (%)				Treatment response**, n/N (%)					
Upper limb TCP N=114	72/114 (63%)	71/108 (66%)	69/100 (69%)	Upper limb PTMG (ITT) N=238	62/79 (78.5%)	59/80 (73.8%)	18/79 (22.8%)	38/79 (48.1%)	34/80 (42.5%)	11/79 (13.9%)
Upper limb TCP (spasticity due to stroke) N=94	60/94 (64%)	63/91 (69%)	61/87 (70%)	-	-	-	-	-	-	-
Upper limb TCP (spasticity due to other causes) N=20	12/20 (60%)	8/17 (47%)	8/13 (62%)	Upper limb PTMG (TBI subgroup) N=23	4/6 (66.7%)	5/8 (62.5%)	2/9 (22.2%)	1/6 (16.7%)	4/8 (50.0%)	1/9 (11.1%)

* Reduction in AS ≥ 1 in TCP

** Reduction in MAS ≥ 1 PTMG

Each injection cycle observation period of 12 to 16 weeks in length

AS = Ashworth Scale; ITT = intention-to-treat; MAS = Modified Ashworth Scale; PSD = Public Summary Document; PTMG = primary target muscle group; TBI = traumatic brain injury; TCP = target clinical pattern

Source: Table 4, p11 of the minor submission

- 5.9 On the basis of a *post-hoc* analysis of individual patient data from the TOWER study, the benefits of Xeomin® in patients with a target clinical pattern (TCP) in the upper limb were observed in both stroke-related spasticity and non-stroke-related spasticity populations, with a response rate of 64%, 69% and 70% across the three treatment cycles for stroke-related spasticity and 60%, 47% and 62% for non-stroke-related spasticity. The submission claimed this was comparable to the results from Study 145, in which treatment with Dysport® 1,000U produced a response rate of 78.5% after 4 weeks and 48.1% after 12 weeks.

- 5.10 The minor submission acknowledged potential weaknesses in the clinical evidence from the TOWER study in terms of:
- Two of the doses examined (600U and 800U) exceeded the maximum quantity amount requested on the PBS (400U). The submission noted that treatment in TOWER was administered to both upper and lower limbs and that treatment administered to the upper limbs would have been below 400U in the first cycle;
 - As noted above, the TOWER study outcome was Ashworth Scale score, rather than Modified Ashworth Scale score. The current and proposed PBS listing for Xeomin® specifies that patients have moderate to severe spasticity, defined as a MAS score of ≥ 3 to be eligible for treatment. The submission stated that an AS score ≥ 2 could be considered as moderate to severe spasticity. All patients in the TOWER study had an AS score ≥ 2 in the joint associated with the selected TCP at baseline.
 - The sample sizes of the non-stroke causes of spasticity were small.
- 5.11 The PBAC has previously considered that despite the lack of clinical trials in aetiologies other than stroke, the request to extend the listing of botulinum toxins to include acute events was reasonable and biologically plausible (paragraph 5.2, Botox® PSD, March 2019; paragraph 7.2, Dysport® PSD, July 2019). In addition, in July 2014 when Xeomin® was recommended for upper limb spasticity on the basis of a cost-minimisation analysis with Botox®, the PBAC considered that both agents would be likely to have similar clinical effects as they are analogues of each other (paragraph 6.17, Xeomin® PSD, July 2014).
- 5.12 As it was proposed that Xeomin® enter into the same Deed of Agreement as Dysport®, including the SPA and RSA, the submission requested the removal of the four injections per lifetime limit from the restriction. The submission presented data from an open-label extension study, Kanovsky 2011, demonstrating that Xeomin® continued to have a response after at least six treatment cycles.

Comparative harms

- 5.13 The submission did not present an analysis of comparative harms.

Clinical claim

- 5.14 The submission claimed that Xeomin® was non-inferior in terms of comparative effectiveness compared to Dysport® in patients with upper limb spasticity following an acute event.
- 5.15 The PBAC considered that the claim that Xeomin® was non-inferior to Botox® in terms of comparative efficacy following an acute event was likely to be reasonable given the established interchangeability in post-stroke upper limb focal spasticity.

Economic analysis

5.16 The minor submission presented a cost-minimisation analysis of Xeomin® compared with Dysport®.

5.17 The equi-effective doses were estimated as:

$$\text{Xeomin}^{\circledR} 1\text{U} = \text{Dysport}^{\circledR} 4.3\text{U}$$

5.18 This relativity was consistent with previous PBAC recommendations for the three botulinum toxin treatments. The submission requested that the effective price of Xeomin® retain the cost-minimisation therapeutic relativity with Dysport®.

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Table 3: Equi-effective doses and dose relativities of botulinum toxins for the upper limb spasticity indication

	PBAC meeting	Equi-effective doses	Dose relativities	Source
Previously accepted by the PBAC				
Botox® vs. Dysport®	July 2008	Botox® 229U per treatment course = Dysport® 989U per treatment course	1:4.3	Botox® PSD July 2008
Botox® vs. Xeomin®	July 2014	Xeomin® 229U (over approx 87 days) = Botox 229U Botox® (over approx 87 days)	1:1	PBS Therapeutic Relativity Sheets
Proposed in this submission				
Xeomin® vs. Dysport®	November 2019	Xeomin® 1U = Dysport® 4.3U	1:4.3	Derived from the previously accepted relativities

PBAC = Pharmaceutical Benefits Committee; PBS = Pharmaceutical Benefits Scheme; PSD = Public Summary Document
Source: Table 5, p14 of the minor submission

- 5.19 However in July 2019, Dysport® for the treatment of lower limb spasticity following an acute event was recommended based on a cost minimisation analysis with Botox®, in which the PBAC considered that the equi-effective doses of Dysport® and Botox® should be based on the maximum dispensed quantities which would result in equivalent treatment costs per cycle, that is:

$$\text{Dysport}^{\circledR} 3.75\text{U} = \text{Botox}^{\circledR} 1\text{U} \text{ (i.e. Dysport}^{\circledR} 1,500\text{U} = \text{Botox}^{\circledR} 400\text{U})$$

- 5.20 In addition, the PBAC has previously considered that the extent to which the potential use of botulinum toxin in both the upper and lower limbs in the same patient would affect utilisation, cost effectiveness and the financial implications remained uncertain. The PBAC was therefore of the view that any pricing arrangement for these indications should take these uncertainties into account by implementing a single price across these conditions. (paragraphs 5.9 and 5.10, Botox® PSD, March 2019; paragraph 7.17, Dysport® PSD, July 2019).
- 5.21 The maximum doses recommended in the approved Product Information leaflets and the maximum quantities approved on the PBS for upper and lower limb spasticity are outlined below.

Table 4: Maximum doses and PBS quantities of botulinum toxin in ULFS and LLFS

	Maximum PI dose	Maximum PBS quantity	Current/recommended/requested PBS listing	PBAC consideration
Dysport®	ULFS = 1,000U	300U x 4, or 500U x 2	Current PBS listing for ULFS after an acute event	Recommended March 2019
	LLFS = 1,500U	300U x 5, or 500U x 3	Recommended PBS listing for LLFS after an acute event	Recommended July 2019
Botox®	ULFS = 360U	100U x 4	Current/requested PBS listing for ULFS after a stroke/an acute event	Requested November 2019
	LLFS = 400U	100U x 4	Current PBS listing for LLFS after an acute event	Recommended March 2019
Xeomin®	ULFS = 500U	100U x 4	Current/requested PBS listing for ULFS after a stroke/an acute event	Requested November 2019
	LLFS = NR	-	-	-

LLFS = lower limb focal spasticity; NR = not reported; PBAC = Pharmaceutical Benefits Advisory Committee; PBS = Pharmaceutical Benefits Scheme; PI = Product Information; ULFS = upper limb focal spasticity

Source: Compiled by the Secretariat

5.22 Therefore, based on the July 2014 PBAC recommendation that 1U Xeomin® = 1U Botox®, the July 2019 PBAC recommendation that Dysport® 1,500U = Botox® 400U, and the fact that the maximum PBS quantity for Botox® in both the upper and lower limb restrictions is 400U, the PBAC was asked to consider if the equi-effective doses should be Xeomin® 400U = Dysport® 1,500U (i.e. Xeomin® 1U = Dysport® 3.75U). The pre-PBAC response noted that Xeomin® is not TGA registered or PBS listed for treatment of spasticity of the lower limb meaning that Xeomin® cannot be used in both the upper and lower limbs and therefore the previously accepted relativity should be maintained.

Estimated PBS usage & financial implications

5.23 The minor submission estimated there to be no financial implications to the PBS as the submission expects Xeomin® to substitute for Dysport® and both drugs will have the same effective AEMP.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

6.1 The PBAC recommended an extension of the current section 100 (Botulinum Toxin Program), Authority Required (STREAMLINED) listing for incobotulinumtoxinA (Xeomin®) for treatment of moderate to severe focal spasticity of the upper limb following a stroke, to also include spasticity following acute events other than stroke. The PBAC was satisfied that Xeomin® was non inferior to Dysport® in terms of comparative efficacy.

6.2 The PBAC noted that the request to add additional acute aetiologies, including traumatic brain and spinal cord injuries, to the upper limb focal spasticity restriction

was supported by the Rehabilitation Medicine Society of Australia and New Zealand (RMSANZ).

- 6.3 The PBAC noted that the proposed restriction was identical to that recommended in March 2019 for Dysport® for the same indication. The PBAC recalled that it had previously considered that it would be reasonable for future botulinum toxin restrictions to be consistent in terms of initiation and continuation criteria and lifetime limits (paragraph 5.11, Dysport® PSD, March 2019).
- 6.4 The PBAC considered that a grandfather restriction, identical to the current grandfather restriction for Dysport®, would be appropriate for patients already treated with Xeomin®, if requested by the sponsor.
- 6.5 The PBAC considered that Dysport® was the appropriate comparator.
- 6.6 The PBAC noted that the basis of the minor submission was a naïve comparison between Xeomin® and Dysport®. A *post-hoc* analysis of individual patient data from the TOWER study were compared to the results from Study 145. The PBAC considered the evidence was of low quality, noting the different measuring scores and small patient numbers with aetiologies other than stroke in both trials. The PBAC noted that it had previously considered that despite lack of clinical trials in aetiologies other than stroke, the request to extend the listing of botulinum toxin to include acute events was reasonable and biologically plausible (paragraph 5.2, Botox® PSD, March 2019; paragraph 7.2, Dysport® PSD, July 2019). Therefore the PBAC considered that Xeomin® was likely to be non-inferior in terms of comparative efficacy to Dysport® in patients with focal upper limb spasticity due to an acute event.
- 6.7 The PBAC noted that no comparative safety data was presented but considered that Xeomin® was likely to be non-inferior in terms of safety compared to Dysport®.
- 6.8 The PBAC noted that the minor submission presented a cost minimisation analysis between Xeomin® and Dysport®. The PBAC noted that this analysis was based on equi-effective doses and dose relativities between Xeomin® and Botox® (i.e. Xeomin® 1U = Botox® 1U) which were accepted by the PBAC for upper limb spasticity following a stroke in July 2014.
- 6.9 The PBAC considered that the equi-effective doses nominated in the minor resubmission (Xeomin® 1U = Dysport® 4.3U) were not appropriate due to:
 - the lack of comparative data in upper limb spasticity following an acute event other than stroke;
 - its previous recommendation of a single price across the botulinum indications (paragraphs 5.9 and 5.10, Botox® PSD, March 2019; paragraph 7.17, Dysport® PSD, July 2019); and
 - the maximum dispensed quantity of Xeomin® for upper limb spasticity was 400U. This was equivalent to the maximum dispensed quantity of Botox® for upper limb

focal spasticity. In July 2019, in consideration of lower limb spasticity, the PBAC recommended that Botox[®] 400U was equivalent to Dysport[®] 1500U (i.e. Botox[®] 1U = Dysport[®] 3.75U).

6.10 Therefore, the PBAC considered that the equi-effective doses were:

Xeomin[®] 1U = Dysport[®] 3.75U

6.11 The PBAC considered that the extension of the listing for Xeomin[®] should be cost-neutral to the PBS. The PBAC noted the proposed Special Pricing Arrangement (SPA) and recommended that Xeomin[®] join the existing Dysport[®] Risk Sharing Arrangement (RSA) which consists of subsidisation caps beyond which 100% rebates are applied. The PBAC considered that the RSA helped to address the uncertain clinical benefit in patients with upper limb spasticity due to an acute event other than stroke and the lack of data pertaining to the requested changes to the restrictions (i.e. removal of the time limitation for the first injection, removal of the lifetime limit and changes to the maximum number of cycles in the first and subsequent years).

6.12 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that because the Xeomin[®] formulation of botulinum toxin is not expected to provide a substantial and clinically relevant improvement in efficacy or reduction of toxicity over the Dysport[®] formulation and not expected to address a high and urgent unmet clinical need, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.

6.13 The PBAC noted that the Early Supply Rule cannot currently be applied to items in the Botulinum Toxin Program

6.14 The PBAC reaffirmed that Xeomin[®] remained unsuitable for prescribing by nurse practitioners.

6.15 The PBAC recalled that the different formulations of botulinum toxin are not currently considered equivalent for the purposes of substitution (i.e. 'a' flagged in the Schedule) under Section 101 (4AACD) of the National Health Act and considered this remained appropriate.

6.16 The PBAC has previously advised that BOTOX[®], Dysport[®] and Xeomin[®], should be treated as interchangeable on an individual patient basis under Section 101(3BA) of the National Health Act 1953.

6.17 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Amend existing listing as follows:

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
INCOBOTULINUMTOXINA 100 units injection, 1 vial	4	0	Xeomin® Merz Pharmaceuticals

Category/program	Section 100 – Botulinum Toxin Program
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Severity:	Moderate to severe
Condition:	Spasticity of the upper limb following an acute event
PBS indication:	Moderate to severe spasticity of the upper limb following an acute event
Restriction level:	<input checked="" type="checkbox"/> Streamlined
Clinical criteria	The condition must be moderate to severe spasticity of the upper limb/s following an acute event defined as a Modified Ashworth Scale rating of 3 or more, AND The treatment must only be used as second line therapy when standard management has failed; OR The treatment must only be used as an adjunct to physical therapy, AND The treatment must not continue if the patient does not respond (defined as not having had a decrease in spasticity rating greater than 1, using the Modified Ashworth Scale, in at least one joint) after two treatment periods (with any botulinum toxin type A), AND The treatment must not exceed a maximum of 4 treatment periods (with any botulinum toxin type A) per upper limb in the first year of treatment, and 2 treatment periods (with any botulinum toxin type A) per upper limb each year thereafter, AND Patient must not have established severe contracture in the limb to be treated
Population criteria	Patient must be aged 18 years or older.
Treatment criteria	Must be treated by a neurologist; OR Must be treated by an orthopaedic surgeon; OR Must be treated by a rehabilitation specialist; OR Must be treated by a plastic surgeon; OR Must be treated by a geriatrician.
Prescriber instructions	Standard management includes physiotherapy and/or oral spasticity agents.
Administrative Advice	The units used to express the potency of botulinum toxin preparations currently available for PBS subsidy are not equivalent. An acute event may be a clinical or external event that leads to upper motor neuron lesions resulting in spasticity for example stroke, traumatic brain injury, spinal cord injury, infection or hypoxia. Special pricing Arrangement apply.
Caution:	Contraindications to treatment include known sensitivity to botulinum toxin.

Category/Program:	Section 100 – Botulinum Toxin Program
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Severity:	Moderate to severe
Condition:	Spasticity of the upper limb following an acute event
PBS Indication:	Moderate to severe spasticity of the upper limb following an acute event

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Treatment phase	Grandfathered treatment
Restriction Level	<input checked="" type="checkbox"/> Streamlined
Clinical criteria:	<p>Patient must have previously received non-PBS subsidised treatment with this drug for this condition prior to [PBS listing date]</p> <p>AND</p> <p>The condition must have been moderate to severe spasticity of the upper limb/s following an acute event, defined as a Modified Ashworth Scale rating of 3 or more prior to commencing non-PBS subsidised treatment,</p> <p>AND</p> <p>The treatment must only be used as second line therapy when standard management has failed; OR</p> <p>The treatment must only be used as an adjunct to physical therapy,</p> <p>AND</p> <p>The treatment must not continue if the patient does not respond (defined as not having had a decrease in spasticity rating greater than 1, using the Modified Ashworth Scale, in at least one joint) after two treatment periods (with any botulinum toxin type A)</p> <p>AND</p> <p>The treatment must not exceed a maximum of 4 treatment periods (with any botulinum toxin type A) per upper limb in the first year of treatment, and 2 treatment periods (with any botulinum toxin type A) per upper limb each year thereafter.</p> <p>AND</p> <p>Patient must not have established severe contracture in the limb to be treated.</p>
Population criteria:	Patient must be aged 18 years or older.
Treatment criteria:	<p>Must be treated by a neurologist; OR</p> <p>Must be treated by an orthopaedic surgeon; OR</p> <p>Must be treated by a rehabilitation specialist; OR</p> <p>Must be treated by a plastic surgeon; OR</p> <p>Must be treated by a geriatrician.</p>
Prescriber Instructions	Standard management includes physiotherapy and/or oral spasticity agents.
Administrative Advice:	<p>The units used to express the potency of botulinum toxin preparations currently available for PBS subsidy are not equivalent.</p> <p>An acute event may be a clinical or external event that leads to upper motor neuron lesions resulting in spasticity for example stroke, traumatic brain injury, spinal cord injury, infection or hypoxia.</p> <p>Special Pricing Arrangements apply.</p>
Cautions:	Contraindications to treatment include known sensitivity to botulinum toxin.

These restrictions may be subject to further review. Should there be any changes made to the restrictions the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.