7.17 CLOSTRIDIUM BOTULINUM TYPE A TOXIN-HAEMAGGLUTININ COMPLEX, Lyophilised powder for I.M. injection, 300 units, 500 units, Dysport®, Ipsen Pty Ltd.

1 Purpose of Application

1.1 The minor resubmission requested an extension to the current Section 100 (Botulinum Toxin Program), Authority Required (Streamlined) listing for clostridium botulinum type A toxin-haemagglutinin complex (herein known as Dysport®) for treatment of moderate to severe focal spasticity of the upper limb following a stroke, to include spasticity following an acute event. An acute event was defined by the submission as an event that leads to an upper motor neuron lesion resulting in spasticity such as stroke, traumatic brain injury (TBI), spinal cord injury (SCI), infection or hypoxia.

1.2 A major submission to extend the upper limb listing was rejected by the PBAC in November 2018 on the basis of uncertain clinical benefit, uncertain cost-effectiveness, and high and uncertain financial impact.

1.3 Consistent with the November 2018 major submission, the current resubmission also requested the removal of the current maximum of four treatment periods per upper limb per lifetime restriction for Dysport® in upper limb focal spasticity.

1.4 The current resubmission proposed a special pricing arrangement (SPA) and a risk share arrangement (RSA) to facilitate removal of the four treatment lifetime limit. The basis for the requested listing was unchanged from the previous submission, which was a cost-effectiveness (via a cost per responder analysis) of Dysport® compared with placebo.

2 Requested listing

2.1 The resubmission requested a modified restriction to incorporate the suggested additions and deletions proposed by the Secretariat during evaluation of the previous major submission (Dysport Public Summary Document (PSD), November 2018).

2.2 The resubmission proposed a SPA in order to reduce the cost per responder, as recommended previously by the PBAC (paragraph 7.11, 6.03 Dysport PSD, November 2018). The proposed effective DPMQ of the 500U vial was $[redacted] (AEMP for one vial = $[redacted]). The proposed DPMQ of the 300U vial was $[redacted] (AEMP for one vial = $[redacted]).

Name, Restriction, Manner of administration and form	Max. Qty. (units)	№. of Rpts	DPMQ	Proprietary Name and Manufacturer	
CLOSTRIDIUM BOTULINUM TYPE A TOXIN-HAEMAGGLUTININ COMPLEX					
300 units injection, 1 vial	4	0	Published: $1,221.85 * Effective: $[redacted]	Dysport®	Ipsen Pty Ltd
500 units injection, 1 vial	2	0	Published: $1,094.79 * Effective: $[redacted]	Dysport®	Ipsen Pty Ltd

Category / Program :	Section 100 – Botulinum Toxin Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐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 / Method:	☐Restricted benefit ☐Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required – Emergency ☐Authority Required - Electronic ☒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** 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.
Prescribing instructions	The date and nature of the event must be documented in the patient's medical records when treatment is initiated. Standard management includes physiotherapy and/or oral spasticity agents.
Administrative Note	The units used to express the potency of botulinum toxin preparations currently available for PBS subsidy are not equivalent.
Administrative Advice	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, TBI, infection or hypoxia.
Caution	Contraindications to treatment include known sensitivity to botulinum toxin.

*Published DPMQ as currently listed for treatment of spasticity of the upper limbs following stroke (correct as of February 2019).

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Background

3.1 The PBAC recommended Dysport® for the treatment of upper limb spasticity following a stroke in November 2007.

3.2 At its November 2018 meeting the PBAC considered and rejected a major submission seeking extension of the current Dysport® listing. The major submission was rejected on the basis of uncertain clinical benefit, uncertain cost-effectiveness, and high and uncertain financial impact.

3.3 In its consideration of the submission in November 2018, the PBAC provided the following advice (Dysport PSD, November 2018):

- The PBAC concluded there was a clinical need for treatments of upper limb focal spasticity following an acute event (para 7.2).
- The PBAC considered that there was a lack of comparative evidence beyond the first injection, and insufficient evidence to inform the benefit of treatment, particularly beyond the first year of treatment. The PBAC also noted that there was limited data and, accordingly, a high level of uncertainty surrounding the treatment effect, for the treatment of spasticity resulting from events other than stroke (para 7.4).
- The PBAC considered that standard of care/placebo was the appropriate comparator (para 7.5).
- The PBAC considered that the benefit of Dysport® compared to placebo in the treatment of focal spasticity of the upper limb following an acute event other than stroke could not be assessed as these patients were poorly represented in the key trial. The PBAC considered that the subgroups of patients with spasticity following a traumatic brain injury were very small and analyses were post-hoc and not powered to detect statistical significance. The PBAC noted that no evidence was presented for upper limb spasticity due to other aetiologies such as spinal cord injury, hypoxia or infection (para 7.7).
- The PBAC, noting that the submission did not make a claim regarding the safety of Dysport®, considered that Dysport® was inferior compared to standard of care/placebo (para 7.8).
- The PBAC recalled that it accepted a cost per responder analysis of less than $15,000 when considering Dysport® in 2007 for the treatment of upper limb focal spasticity following a stroke (Dysport PSD, November 2007). The PBAC noted that the cost per responder, when response was defined as a MAS improvement of greater than one, was considerably higher in the November 2018 submission. The PBAC also noted that the estimated cost per responder was driven by response in stroke patients and the applicability of the results to patients with upper limb spasticity following an acute event other than stroke was uncertain (para 7.9).

- The PBAC accepted the mixed approach used to estimate the financial implications of the proposed extension to listing, but agreed with the DUSC that the financial estimates may have been under-estimated given the number of TBI patients were obtained from conflicting data sources and lower estimates were used in the base case analysis. The PBAC considered that the estimated $30 - $60 million additional cost to government over the first six years of extending the current listing was uncertain. Given the uncertainty, the PBAC considered that any future submission for upper limb focal spasticity following an acute event should consider proposing an utilisation cap (para 7.10).
- The PBAC considered that the uncertainty surrounding the treatment effect of Dysport® in patients with spasticity due to aetiologies other than stroke was unlikely to be substantially reduced by future high quality data and that such high quality data were not likely to become available. These uncertainty issues could be mitigated through adjustment of the requested price to deliver a lower incremental cost-effectiveness ratio (para 7.11)

4 Consideration of the evidence

Sponsor hearing

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

Consumer comments

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

Clinical trials

4.3 No new clinical trials or clinical information were presented in the minor resubmission.

Clinical claim

4.4 The minor resubmission did not present any new information regarding the clinical claim.

Economic analysis

4.5 The November 2018 submission presented an incremental cost per responder analysis, in which response was defined as a change in MAS of greater than 1 using the 'derived MAS' coding convention. This minor resubmission provided re-estimated cost-effectiveness calculations based on the published price and the new effective price and a change in MAS of greater than 1 using the historical MAS coding convention at Week 12. This was consistent with the coding convention used in the November 2007 submission and November 2018 Pre-Sub-Committee response.

4.6 The responder rate at Week 12 was 13.1% (95% CI: 3.5, 22.7). The responder rate at Week 4 (29.1%; 95% CI: 17.9, 40.3) was used in a sensitivity analysis.

4.7 The Department validated the respecified effective price in the economic model during the evaluation (see Table 1).

Table 1: Cost per responder analyses – base case

	November 2018 submission	Current resubmission	
		Published price	Effective price
Average number of 500U vials per treatment period	1.9978		
Corrected number of cycles with stopping rule (base case at 12 weeks)	2.54		
Average cost per treatment	$1,218.44 (+ MBS costs)	$1,093.59 (- MBS costs)	$[redacted]
Overall cost of treatment	$3,096.36 (+ MBS costs)	$2,777.71 (- MBS costs)	$[redacted]
Incremental benefit, RD (95% CI)	0.131 (0.035, 0.227)		
Cost per responder (95% CI)	$23,636 ($13,640, $88,467)	$21,204 ($12,237, $79,363)	$[redacted] ($[redacted], $[redacted])

CI = confidence interval; MBS = Medicare Benefits Schedule; RD = risk difference
Source: p.10-11 March 2019 resubmission and p.21 November 2018 ratified minutes.

4.8 In 2007 the PBAC accepted a cost per responder of less than $15,000 when considering Dysport® for the treatment of upper limb focal spasticity following a stroke (Dysport PSD, November 2007). The November 2018 pre-PBAC Response updated the 2007 cost per responder analysis to reflect the 2018 PBS costs for Dysport® and included analogous MBS costs. This resulted in an incremental cost per responder of less than $15,000 (95% CI: $[redacted], $[redacted]).

4.9 The current resubmission did not include MBS costs in order to enable direct comparison to the November 2007 accepted analyses. Using the effective price proposed by the resubmission, resulted in a cost per responder of $[redacted] at Week 12.

4.10 A sensitivity analysis using the responder rate at Week 4 is presented below.

Table 2: Cost per responder sensitivity analysis

	Published price	Effective price
Average number of 500U vials per treatment period	1.9978	
Corrected number of cycles with stopping rule (4 weeks)	3.86	
Average cost per treatment	$1,093.59	[redacted]
Overall cost of treatment	$4,220.74	[redacted]
Incremental benefit, RD (95% CI)	0.291* (0.179, 0.403)	
Cost per responder (95% CI)	$14,504 ($10,473, $23,580)	[redacted]

Ci = confidence interval; RD = risk difference
Source: p.10-11 March 2019 resubmission.
* Corrected during evaluation. The resubmission incorrectly used an incremental benefit of 0.292

4.11 The Pre-PBAC Response acknowledged the cost per responder at Week 4 sensitivity analysis corrected during the evaluation.

4.12 The Pre-PBAC Response stated that the SPA offered in the submission resulted in a cost per responder which was consistent with that previously accepted by the PBAC in its 2007 recommendation of Dysport, and a level of uncertainty well within the 95% confidence interval range previously accepted.

Drug cost/patient/cycle (1000U): Published = $1,094.79; Effective = $[redacted]

4.13 The drug cost per patient per treatment cycle was estimated assuming a Dysport® dose of 1000U per treatment cycle and using the requested published AEMP ($523.75) and effective AEMP ($[redacted]) for the 500U vial.

4.14 The DUSC considered that, on average, patients would receive three to four treatment cycles of botulinum toxin per lifetime (DUSC advice to PBAC on botulinum toxin, July 2018). The ESC previously considered that the number of treatment cycles per patient per lifetime for the proposed population was uncertain (paragraph 6.48, Dysport PSD, November 2018).

Estimated PBS usage & financial implications

4.15 In the November 2018 major submission, the net cost to government over the first six years of listing was estimated to be approximately $30 - $60 million. The key drivers of the results were uptake rates and prevalence of spasticity. DUSC considered the estimates may be under-estimated for the following reasons (paragraph 6.51, Dysport PSD, November 2018):

- the number of prevalent TBI patients with spasticity may be under-estimated; a number of conflicting sources informed this input and the lower estimate was used in the base case analysis;
- relatively low uptake rates for Dysport® were assumed in the financial estimates and utilisation could be higher in clinical practice; and
- the post-stroke population in the requested restriction has expanded relative to the current listing (MAS score of 3 or more), by including patients with a MAS score of 2 or more. These extra patients were not included in the estimates.

4.16 The resubmission addressed some uncertainty surrounding the eligible population by aligning the severity of spasticity for the initiation of treatment in the requested restriction to the current listing (MAS score of 3 or more).

4.17 The resubmission noted that the low estimated uptake rates used in the November 2018 submission financial implications for Dysport® were obtained from an advisory board meeting, which considered that there were a number of barriers to access for botulinum toxin due to treatment capacity constraints, particularly within rehabilitation centres and the multi-disciplinary team structure used to treat patients. The resubmission did not amend the proposed uptake rates from the November 2018 submission; however, these utilisation assumptions were included in the calculation of an annual sales cap (see Financial Management Section). With respect to the number of prevalent TBI patients with spasticity, the base case assumption in the November 2018 submission applied a value of 30% to this input, with a sensitivity of 75% based on the Royal College of Physicians (2018) guidelines. A rate of 75% was used in the resubmission.

4.18 Updated patient number and treatment cycle estimates are presented in Table 3.

Table 3: Estimated extent of use

	2019	2020	2021	2022	2023	2024
NOVEMBER 2018 – original submission						
New patients with non-stroke spasticity						
Number of incident patients	[redacted]					
Number of prevalent patients	[redacted]					
Number of treatment cycles	[redacted]					
Effect of removal of 4 cycle lifetime limit						
Additional number of treatment cycles (non-stroke)	[redacted]					
Increased number of treatment cycles (current stroke)	[redacted]					
Total number of treatment cycles	[redacted]					
MARCH 2019 – current resubmission						
New patients with non-stroke spasticity						
Number of incident patients	[redacted]					
Number of prevalent patients	[redacted]					
Total number of treatment cycles	[redacted]					
Effect of removal of 4 cycle lifetime limit						
Additional number of treatment cycles (non-stroke)	[redacted]					
Increased number of treatment cycles (current stroke)	[redacted]					
Total number of treatment cycles	[redacted]					

Source: Utilisation and cost model workbook supplied with submissions (November 2018 and March 2019)

4.19 The resubmission stated that the proposed SPA and RSA would extend to patients currently eligible for treatment under the existing listing, i.e. those currently receiving Dysport® for moderate to severe spasticity of the upper limb following a stroke. It was assumed in the resubmission that, if approved, the removal of the four injection lifetime limit would also apply to these patients.

4.20 The resubmission presented revised estimated financial implications for the requested extension to listing. As the resubmission requested a SPA, financial impact estimates were presented for both the requested published price (Table 4) and effective price (Table 5).

Table 4: Estimated financial implications for extension to Dysport upper limb listing (published price).

	2019	2020	2021	2022	2023	2024
Projected net cost of change to listing						
To PBS	$27,503,410	$14,003,718	$7,707,019	$7,828,296	$7,950,995	$8,076,529
To RPBS	$240,608	$122,509	$67,423	$68,484	$69,558	$70,656
Less co-payments	-$398,730	-$203,018	-$111,732	-$113,490	-$115,269	-$117,089
Net cost to PBS/RPBS	**$27,345,288**	**$13,923,209**	**$7,662,710**	**$7,783,290**	**$7,905,283**	**$8,030,096**

Source: p.13 March 2019 resubmission.

Table 5: Estimated financial implications for extension to Dysport upper limb listing (effective price).

	2019	2020	2021	2022	2023	2024
Projected net cost of change to listing						
To PBS	[redacted]					
To RPBS						
Less co-payments						
Total cost to PBS/RPBS						
Projected net costs of displaced medicines						
To PBS						
To RPBS						
Less co-payments						
Total cost to PBS/RPBS						
Overall net cost to the PBS/RPBS						
Net cost to PBS/RPBS						
November 2018						

Source: p.14 March 2019 resubmission.

4.21 The resubmission claimed a net saving for displaced medicines in the effective price calculations as the SPA proposed for the extension to listing will also apply to patients eligible for treatment under the current listing.

4.22 The net cost to the PBS over the first six years of listing was estimated to be approximately $30- $60million, based on the revised utilisation estimates and the effective price. This represents an approximate less than $10 million increase in expenditure to the PBS/RPBS compared to the financial implications considered at the November 2018 meeting.

4.23 MBS item costs were estimated to be approximately less than $10 million over the first six years of listing. In November 2018 the MBS costs were estimated to be approximately less than $10 million over the first six years of listing (Table 15, p23, Dysport PSD, November 2018).

Financial Management – Risk Sharing Arrangements

4.24 In November 2018 the PBAC considered that the financial estimates in the major submission may have been underestimated, and any future submission for upper limb focal spasticity following an acute event should consider proposing an utilisation cap (paragraph 7.10, Dysport PSD, November 2018).

4.25 The resubmission proposed a RSA with 100% rebate beyond estimated utilisation caps, which were based the PBAC proposed limits of four treatments in Year 1 and two treatments per year from Year 2 onwards (see Table 6).

4.26 The resubmission stated that the annual utilisation caps were estimated based on all Commonwealth expenditure across all brands of botulinum (Dysport®, Botox® and Xeomin®) for patients treated for moderate to severe spasticity of the upper limb following a stroke.

4.27 The resubmission requested that extension to listings for the other brands of botulinum not be cascaded down (including the removal of the four-injection limit,

and 3 month waiting period), until the sponsors of these brands enter into the same Deed of Agreement through a cost-minimisation submission to the PBS.

Table 6: Calculation of proposed annual caps.

	2019	2020	2021	2022	2023	2024
Estimated patient numbers						
Stroke – new patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Stroke – existing patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
TBI/SCI/Other – new patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
TBI/SCI/Other – existing patients	-	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Capped number of treatments per patient per year						
Capped treatments in Year 1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Capped treatments from Year 2+	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Estimation of Commonwealth expenditure per treatment						
DPMQ per treatment	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Less Co-payment – PBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Less Co-payment - RPBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Net Commonwealth cost per treatment	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proposed annual caps						
Annual Cap	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

TBI: Traumatic brain injury; SCI: spinal cord injury
Source: p.15 March 2019 resubmission

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

5.1 The PBAC recommended an extension of the current Section 100 (Botulinum Toxin Program), Authority Required (STREAMLINED) listing for clostridium botulinum type A toxin-haemagglutinin complex (Dysport®) 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 Dysport® provides, for some patients, a modest improvement in efficacy compared with standard of care. The PBAC's recommendation for listing was primarily based on its assessment that the cost-effectiveness of Dysport® would be acceptable at the price proposed in the resubmission.

5.2 The PBAC acknowledged the clinical need for treatments of upper limb focal spasticity following an acute event other than stroke and the support of the Rehabilitation Medicine Society of Australia and New Zealand (RMSANZ) for the November 2018 major submission.

5.3 The PBAC considered the restriction as proposed by the sponsor in the resubmission was reasonable and incorporated the recommendations made in November 2018 relating to condition eligibility and initiation and stopping rule clinical criteria. The PBAC recalled that in consideration of botulinum use in the lower limb at the November 2018 PBAC meeting, that the lifetime treatment limit of four treatment cycles did not account for continuing responders and recommended a limit of four treatment periods per lower limb in the first year and two treatment periods per lower

limb per year from Year 2 onwards would be reasonable. The PBAC recommended this criteria be added to the restriction.

5.4 The PBAC considered that a grandfather restriction may be appropriate for patients already treated with Dysport® who meet the response criteria, if requested by the sponsor.

5.5 The PBAC noted that no new clinical data were submitted to address the uncertain clinical benefit, uncertain cost-effectiveness and high and uncertain financial implications of the proposed extension to listing.

5.6 The PBAC noted that the proposed Special Pricing Arrangement (SPA) and associated effective price reduction and considered that this helped to address the uncertain clinical benefit in patients with upper limb spasticity due to an acute event other than stroke and in the data pertaining to the changed restriction (including removal of the lifetime limit and changes to the maximum number of cycles in the first and subsequent years).

5.7 The PBAC noted that SPAs are given effect through a deed made under Section 85E of the *National Health Act 1953* (Act) between the Minister (or his delegate) and the responsible person. The PBAC further noted that the Minister (or his delegate) has requested advice under section 101(3) of the Act as to whether Dysport® meets criteria 1 and 2(a) of the Special Pricing Arrangement criteria when used for the treatment of moderate to severe focal spasticity of the upper limb following an acute event. In regards to criteria 1, the PBAC considered that Dysport® generates a benefit for people with focal spasticity of the upper limb, and for criteria 2(a), that Dysport® has been shown to have unique characteristics compared to standard of care/placebo in improving limb function.

5.8 The reduced effective price resulted in an incremental cost-effectiveness ratio (ICER) of less than $15,000 per QALY. This was within the range the PBAC considered appropriate at the November 2018 meeting.

5.9 The PBAC recalled it had previously considered the utilisation and financial estimates, as advised by the Drug Utilisation Sub-Committee (DUSC), were likely to be underestimated. The PBAC noted the resubmission addressed a number of areas of uncertainty surrounding the eligible population including aligning the population with the initiating criteria (i.e. Modified Ashworth Scale (MAS) score of ≥ 3); and increasing the proportion of traumatic brain injury patients who have spasticity from 30% to 75%. These changes resulted in an approximately 35% increase in the total number of treatment cycles compared to the November 2018 submission. The PBAC considered that although there were uncertainties in the estimates, particularly concerning aetiologies other than stroke, the estimates were reasonable.

5.10 The PBAC noted that the resubmission proposed a Risk Sharing Arrangement (RSA), in the form of 100% rebates beyond estimated utilisation caps. The PBAC accepted that the application of the RSA to include any patients receiving treatment for spasticity of

the upper limb would address some of the uncertainties surrounding the financial implications of extending the current listing to include non-stroke aetiologies and removal of the lifetime limit of four treatment cycles. The Committee was of the view that the RSA cap should be based on the expected use of Dysport in the financial estimates and that the rebate of 100% over that Cap would be appropriate.

5.11 The PBAC considered it would be reasonable to ensure any future PBS restrictions for botulinum toxin for upper or lower limb focal spasticity are consistent in terms of initiation and continuation criteria and lifetime limits. Although the PBAC considered that there was no biologically plausible reason for response criteria (as defined by reduction in MAS score) to differ between upper and lower limb listings, it noted correspondence from the RMSANZ that suggested that there were no major concerns with these not being the same.

5.12 The PBAC recalled and noted that the Early Supply Rule cannot currently be applied to items in the Botulinum Toxin Program.

5.13 The PBAC reaffirmed that Dysport® remained unsuitable for prescribing by nurse practitioners.

5.14 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.

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

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

Outcome:

Recommended

6 Recommended listing

6.1 Amend existing listing as follows:

Item codes 10982B, 10988H

Name, Restriction, Manner of administration and form	Max. Qty. (units)	№. of Rpts	Proprietary Name and Manufacturer	
CLOSTRIDIUM BOTULINUM TYPE A TOXIN-HAEMAGGLUTININ COMPLEX				
300 units injection, 1 vial	4	0	Dysport®	Ipsen Pty Ltd
500 units injection, 1 vial	2	0		

Category/Program:	Section 100 – Botulinum Toxin Program
Prescriber type:	☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ 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/Method:	☐ Restricted benefit ☐ Authority Required - In Writing ☐ Authority Required - Telephone ☐ Authority Required - Emergency ☐ Authority Required - Electronic ☒ Streamlined
Clinical criteria:	The condition must be moderate to severe spasticity of the upper limb/s following ~~stroke~~ *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 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, 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.*
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~~ *physician*; OR Must be treated by a plastic surgeon; OR Must be treated by a geriatrician.
Prescribing instructions	~~The date of the stroke must be documented in the patient's medical records when treatment is initiated.~~ Standard management includes physiotherapy and/or oral spasticity agents.
Administrative note	The units used to express the potency of botulinum toxin preparations currently available for PBS subsidy are not equivalent. *Special Pricing Arrangements apply.*
Administrative advice	*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.*
Caution	Contraindications to treatment include known sensitivity to botulinum toxin.

Category/Program:	*Section 100 – Botulinum Toxin Program*
Prescriber type:	☐ *Dental* ☒ *Medical Practitioners* ☐ *Nurse practitioners* ☐ *Optometrists* ☐ *Midwives*
Severity	*Moderate to severe*
Condition:	*Spasticity of the upper limb following an acute event*
Treatment phase:	*Continuing treatment – grandfathered patients*
PBS Indication:	*Moderate to severe spasticity of the upper limb following an acute event*
Restriction Level/Method:	☐ *Restricted benefit* ☐ *Authority Required - In Writing* ☐ *Authority Required - Telephone*

	☐ *Authority Required - Emergency* ☐ *Authority Required - Electronic* ☒ *Streamlined*
Clinical criteria:	*Patient must have previously received non-PBS subsidised treatment with this drug for this condition prior to <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 did 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* *Patient must not have established severe contracture in the limb to be treated,* *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.*
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 physician; OR* *Must be treated by a plastic surgeon; OR* *Must be treated by a geriatrician.*
Prescribing instructions	*Standard management includes physiotherapy and/or oral spasticity agents.*
Administrative note	*The units used to express the potency of botulinum toxin preparations currently available for PBS subsidy are not equivalent.* *Special Pricing Arrangements apply.*
Administrative advice	*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.*
Caution	*Contraindications to treatment include known sensitivity to botulinum toxin.*

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

8 Sponsor's Comment

Ipsen welcomes the PBAC's recommendation to extend the restriction and remove the four injection limit per lifetime, for patients with focal spasticity of the upper limb following an acute event.

Ipsen will continue to work with the Department of Health to ensure that a PBS listing is realised at the earliest possible date.