

# **MSAC Application 1808**

**IncobotulinumtoxinA (XEOMIN)  
injection codes for cerebral palsy  
spasticity of the lower and/or upper  
limbs**

**PICO Set**

## Population

**Describe the population in which the proposed health technology is intended to be used:**

Patients with cerebral palsy aged 2 years and older with:

- Moderate to severe spasticity of the upper limb.
- Dynamic equinus foot deformity due to spasticity.

**Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian healthcare system in the lead up to being considered eligible for the technology:**

Cerebral palsy (CP) refers to a group of neurological disorders that appear in infancy or early childhood and permanently affect body movement and muscle coordination. Spasticity, where muscles stiffen or tighten, affects approximately 70–90% of children with the disorder (1, 2). The increased muscle tone due to spasticity results in a limited range of passive and active motion in joints and contributes to development of joint contractures, poor muscular control, and hyperactive reflexes.

### Upper limb

Upper limb spasticity is characterised by muscle stiffness and movement difficulties in the arms and hands. Over 80% of children with CP have upper limb spasticity (3), typically with flexors exhibiting increased tone over extensors, leading to abnormal limb position and function.

### Lower limb

Spasticity in the lower limb most often presents as dynamic pes equinus (4) which affects as many as 83% of children with bilateral spastic CP (5). Pes equinus is a deformity associated with insufficient dorsiflexion of the ankle that prevents the heel from contacting the ground, which may mean that walking is done on the toes, however, knee flexion and hip flexion or adduction are also common (6).

The diagnosis of spasticity in children with CP requires a complete physical examination with ancillary testing as needed, including an assessment of motor power, muscle tone, active and passive range of motion of joints, sensation, deep tendon reflexes, station (pelvic and leg alignment), limb deformity and spinal alignment.

The Ashworth scale is the most universally accepted clinical tool used to measure an increase in muscle tone, and is used in CP (7). Table 1 shows the five point grading scale with scores 2 and greater considered as indicating moderate to severe spasticity (8).

**Table 1 Ashworth Scale of Muscle Tone**

Ashworth Scale	Degree of muscle tone
0	No increase in muscle tone
1	Slight increase in muscle tone, with a catch and release or minimal resistance at the end of the range of motion when an affected part(s) is moved in flexion or extension.
1+	Slight increase in muscle tone, manifested as a catch, followed by minimal resistance through the remainder (less than half) of the range of motion.
2	A marked increase in muscle tone throughout most of the range of motion, but affected part(s) are still easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part(s) rigid in flexion or extension

A score of 2 or more is required for patients with spasticity of the upper limb to initiate treatment with incobotulinumtoxinA. Patients with dynamic equinus foot deformity must be ambulant to initiate treatment with incobotulinumtoxinA.

**Provide a rationale for the specifics of the eligible population:**

Spasticity has been associated with reduced health-related quality of life (9, 10), which may be attributed in part to factors such as reduced mobility (11), inability to self-care (12), and pain (13-15). Goals of spasticity treatments include reducing muscle spasms, facilitating mobility and dexterity, improving patient ease of care as well as hygiene/selfcare, facilitating brace use, improving posture, minimizing contractures and deformity as well as reducing pain.

The evidence base for the safety and efficacy of incobotulinumtoxinA has been established in paediatric populations with CP, however, CP does not stop at adulthood. Knowing this, the PBAC has previously shown pragmatism by recommending Botox and Dysport for treatment in adult CP patients as well, despite their respective trials being conducted exclusively in paediatric populations.

**Are there any prerequisite tests?**

No

**Are the prerequisite tests MBS funded?**

N/A

**Provide details to fund the prerequisite tests:**

N/A

## Intervention

### Name of the proposed health technology:

IncobotulinumtoxinA (brand name: Xeomin®)

### Describe the key components and clinical steps involved in delivering the proposed health technology:

XEOMIN® consists of a white to off-white powder for solution for injection. Each vial of Xeomin powder for solution for injection contains 50 or 100 units of incobotulinumtoxinA. Xeomin is reconstituted prior to use with sodium chloride 9 mg/mL (0.9%) solution for injection. A suitable sterile needle should be used for administration.

For the treatment of spasticity of the upper and lower limbs in children and adolescents aged 2-17 years reconstituted Xeomin at a concentration between 1.25 units/0.1 mL and 5 units/0.1 mL is recommended. The exact dosage, frequency and number of injection sites should be tailored to the individual patient based on size, number and localisation of involved muscles, the severity of spasticity, and the presence of local muscle weakness.

For children and adolescents with a body weight of less than 25 kg, dose ranges for muscles and injection site numbers per clinical pattern are subject to body weight-adjusted ranges and need to be calculated. A maximum dose of 25 units and a maximum volume of 0.5 mL per injection site should not be exceeded.

For children and adolescents with a body weight equal to or greater than 25 kg, a maximum dose of 50 units and a maximum volume of 1 mL per injection site should not be exceeded.

Maximum effect is usually reached within 4 weeks. The duration of effect is usually up to 14 weeks. Repeat treatment should generally be no more frequent than every 12 weeks. Treatment intervals should be determined based on the actual clinical need of the individual patient.

#### Upper limb

For uni- or bilateral treatment in patients not previously treated with a botulinum toxin the recommended initial dose is 2 units per kg body weight (BW) with a maximum dose of 50 units per single upper limb. With repeated treatments, doses for uni- or bilateral treatment may be increased if required by the individual needs of the patient. Doses of 2-8 units per kg BW up to a maximum dose of 200 units should be injected per single upper limb at repeat treatment sessions. Dosing recommendations per clinical pattern (muscle) are detailed in Table 2.

**Table 2 Initial and Repeat Dosing by Muscle for Treatment of Upper Limb Spasticity (children/adolescents)**

Clinical Pattern <i>Muscle</i>	Units per kg BW		Maximum Dose (Units)		Number of Injection Sites per Muscle
	Initial	Repeat	Initial	Repeat	
Total Dose for Upper Limb	4	4-16	100	400	
Total Dose per Single Upper Limb	2	2-8	50	200	

Clinical Pattern <i>Muscle</i>	Units per kg BW		Maximum Dose (Units)		Number of Injection Sites per Muscle
	Initial	Repeat	Initial	Repeat	
<b>Flexed Elbow:</b>					
<i>Brachioradialis</i>	0.3-0.5	0.3-2	12.5	50	1-2
<i>Biceps</i>	0.5-0.8	0.5-3	20.0	75	1-3
<i>Brachialis</i>	0.3-0.5	0.3-2	12.5	50	1-2
<b>Flexed Wrist:</b>					
<i>Flexor carpi radialis</i>	0.3	0.3-1	7.5	25	1
<i>Flexor carpi ulnaris</i>	0.3	0.3-1	7.5	25	1
<b>Pronated Forearm:</b>					
<i>Pronator quadratus</i>	0.1	0.1-0.5	2.5	12.5	1
<i>Pronator teres</i>	0.3-0.5	0.3-2	12.5	50	1-2
<b>Clenched Fist:</b>					
<i>Flexor digitorum superficialis</i>	0.3	0.3-1	7.5	25	1
<i>Flexor digitorum profundus</i>	0.3	0.3-1	7.5	25	1
<b>Thumb-in-Palm:</b>					
<i>Flexor pollicis longus</i>	0.3	0.3-1	7.5	25	1
<i>Adductor pollicis/flexor pollicis brevis/opponens</i>	0.1	0.1-0.5	2.5	12.5	1

### Lower limb

For uni- or bilateral treatment in patients not previously treated with a botulinum toxin the recommended initial dose is 2 units per kg body weight with a maximum of 50 units per clinical pattern. In clinical studies up to two clinical patterns have been treated simultaneously in the lower limbs. With repeated treatments, doses for uni- or bilateral treatment may be increased if required by the individual needs of the patient. Doses of 2-8 units per kg BW and a maximum dose of 200 units should be injected per lower limb clinical pattern at repeat treatment sessions. Dosing recommendations per clinical pattern (muscle) are detailed in Table 3.

**Table 3 Initial and Repeat Dosing by Muscle for Treatment of Lower Limb Spasticity (children/adolescents)**

Clinical Pattern <i>Muscle</i>	Units per kg BW		Maximum Dose (Units)		Number of Injection Sites per Muscle
	Initial	Repeat	Initial	Repeat	
Total Dose for Lower Limb	4	4-16	100	400	
<b>Pes Equinus:</b>	2	2-8	50	200	
<i>Gastrocnemius (medial and lateral)</i>	0.75-1.5	0.75-6	37.5	150	2-6
<i>Soleus</i>	0.5-1	0.5-4	25	100	1-4
<i>Tibialis posterior</i>	0.5-0.75	0.5-3	18.75	75	1-3
<i>Flexor digitorum longus/flexor hallucis longus</i>	0.25-0.75	0.25-3	18.75	75	1-3
<b>Flexed Knee:</b>	2	2-8	50	200	

Clinical Pattern <i>Muscle</i>	Units per kg BW		Maximum Dose (Units)		Number of Injection Sites per Muscle
	Initial	Repeat	Initial	Repeat	
<i>Semitendinosus</i>	0.5-1	0.5-4	25	100	1-4
<i>Semimembranosus</i>	0.5-1	0.5-4	25	100	1-4
<i>Biceps femoris</i>	0.5-1	0.5-4	25	100	1-4
<i>Gracilis</i>	0.5-0.75	0.5-3	18.75	75	1-3
<b>Adducted Thigh:</b>	2	2-8	50	200	
<i>Gracilis</i>	0.5-0.75	0.5-3	18.75	75	1-3
<i>Adductor longus/brevis</i>	1-1.5	1-6	37.5	150	2-6
<i>Adductor magnus</i>	0.5-1	0.5-4	25	100	1-4

### Combined spasticity of the lower and upper limb

Multi-pattern/multi-level spasticity treatment of the lower in combination with the upper limb should be performed based on the above doses and recommendations for initial and repeated treatment.

The recommended total dose for the initial combined treatment in patients not previously treated with a botulinum toxin of the lower and upper limb is 8 units per kg BW (maximum total dose of 200 units). This initial total dose is to be divided between lower limb (4 units per kg BW, maximum 100 units) and upper limb (4 units per kg BW, maximum 100 units).

If required by the individual needs of the patient maximum total doses can be increased at repeated sessions for combined treatment of the lower and upper limb:

- In case of ambulatory patients with Gross Motor Function Classification System (GMFCS) levels I-III, doses of 8-20 units per kg BW up to a maximum dose of 500 units should be administered. No more than 16 units per kg BW (maximum 400 units) should be applied for lower limb or upper limb spasticity treatment.
- In cases of non-ambulatory patients with GMFCS levels IV-V, doses of 8-16 units per kg BW up to a maximum dose of 400 units should be given.

### **Identify how the proposed technology achieves the intended patient outcomes:**

XEOMIN® blocks cholinergic transmission at the neuromuscular junction by inhibiting the release of acetylcholine from peripheral cholinergic nerve terminals. This inhibition occurs according to the following sequence:

- Heavy chain of toxin binding to cholinergic nerve terminals
- Internalization of the toxin within vesicles into the nerve terminal
- Translocation of the light-chain of the toxin molecule into the cytosol of the nerve terminal
- Enzymatic cleavage of SNAP25, the presynaptic target protein essential for the release of acetylcholine.

Complete recovery of endplate function/impulse transmission after intramuscular injection normally occurs within 3-4 months as nerve terminals sprout and reconnect with the muscle endplate and the presynaptic neurotransmitter release mechanism becomes functional again.

**Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?**

No – in this indication Xeomin can be used interchangeably with Botox.

**Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:**

N/A.

**Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):**

Yes – the service can only be delivered once every 12 weeks.

**Provide details and explain:**

N/A

**If applicable, advise which health professionals will be needed to provide the proposed health technology:**

Neurologists, orthopaedic surgeons, paediatricians and rehabilitation specialists can provide the service to patients with either upper or lower limb spasticity, in addition to plastic surgeons in patients with upper limb spasticity.

**If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:**

N/A

**If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:**

The service providers will be the service referrers.

**Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?**

Yes

**Provide details and explain:**

Merz Australia provide training workshops throughout the year in injections and ultrasound use with the aid of a sonographer.

**Indicate the proposed setting(s) in which the proposed health technology will be delivered:**

- ☒ Consulting rooms
- ☐ Day surgery centre
- ☐ Emergency Department
- ☒ Inpatient private hospital
- ☒ Inpatient public hospital
- ☐ Laboratory
- ☒ Outpatient clinic
- ☒ Patient's home
- ☐ Point of care testing
- ☐ Residential aged care facility
- ☐ Other (please specify)

**Is the proposed health technology intended to be entirely rendered inside Australia?**

Yes.

**Provide additional details on the proposed health technology to be rendered outside of Australia:**

N/A

## Comparator

**Nominate the appropriate comparator(s) for the proposed medical service (i.e., how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian healthcare system). This includes identifying healthcare resources that are needed to be delivered at the same time as the comparator service:**

Botulinum toxin type A (BOTOX®)

**List any existing MBS item numbers that are relevant for the nominated comparators:**

18354 & 18361

**Provide a rationale for why this is a comparator:**

Botox is the nominated comparator as it is the market leading injectable toxin for the indication/s sought and has a 1:1 dose equivalence with incobotulinumtoxinA (XEOMIN®).

**Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator?**

- ☐ None (used with the comparator)
- ☐ Displaced (comparator will likely be used following the proposed technology in some patients)
- ☒ Partial (in some cases, the proposed technology will replace the use of the comparator, but not all)
- ☐ Full (subjects who receive the proposed intervention will not receive the comparator)



**Outline and explain the extent to which the current comparator is expected to be substituted:**

The comparator will be substituted at the uptake rate for Xeomin, which is 2.5% in year 1, 5% in year 2, and 10% in years 3 and 4. The vast majority of the substitution will be of Botox, but a small fraction of Dysport may also be substituted.

## Outcomes

**List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):**

- ☒ Health benefits
- ☒ Health harms
- ☐ Resources
- ☐ Value of knowing

**Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:**

Treatment with incobotulinumtoxinA (Xeomin) results in non-inferior health outcomes when compared to Botox.

Health benefits evaluated in the clinical trial evidence for upper and lower limb spasticity include:

- Qualitative measure of spasticity using the Ashworth scale
- Global impression of change scale (GICS)
- Other measures of motor function including modified Tardieu Scale (MTS) and Gross Motor Function Measure (GMFM)
- Questionnaire on pain caused by spasticity (QPS)

Health harms evaluated include:

- Incidence of adverse events
- Evidence of toxin spread

## Proposed MBS items

**How is the technology/service funded at present? (e.g., research funding; State-based funding; self-funded by patients; no funding or payments):**

Self-funded by patients.

**Provide at least one proposed item with their descriptor and associated costs, for each Population/Intervention:**

MBS item number (where used as a template for the proposed item)	18354
Category number	Category 3
Category description	Therapeutic Procedures
Proposed item descriptor	<p>Botulinum Toxin Type A Purified Neurotoxin Complex (Botox), Clostridium Botulinum Type A Toxin-Haemagglutinin Complex (Dysport) <b>or IncobotulinumtoxinA (Xeomin)</b>, injection of, for the treatment of dynamic equinus foot deformity (including equinovarus and equinovalgus) due to spasticity in an ambulant cerebral palsy patient, if:</p> <p>(a) the patient is at least 2 years of age; and</p> <p>(b) the treatment is for all or any of the muscles subserving one functional activity and supplied by one motor nerve, with a maximum of 4 sets of injections for the patient on any one day (with a maximum of 2 sets of injections for each lower limb), including all injections per set</p> <p>(Anaes.)</p>
Proposed MBS fee	\$142.25 Benefit: 75% = \$106.70 85% = \$120.95
Indicate the overall cost per patient of providing the proposed health technology	\$142.25
Please specify any anticipated out of pocket expenses	N/A
Provide any further details and explain	N/A

MBS item number (where used as a template for the proposed item)	18361
Category number	Category 3
Category description	Therapeutic Procedures
Proposed item descriptor	<p>Botulinum Toxin Type A Purified Neurotoxin Complex (Botox), Clostridium Botulinum Type A Toxin-Haemagglutinin Complex (Dysport) <b>or IncobotulinumtoxinA (Xeomin)</b>, injection of, for the treatment of moderate to severe upper limb spasticity due to cerebral palsy if:</p> <p>(a) the patient is at least 2 years of age; and</p> <p>(b) the treatment is for all or any of the muscles subserving one functional activity and supplied by one motor nerve, with a maximum of 4 sets of injections for the patient on any one day (with a maximum of 2 sets of injections for each upper limb), including all injections per set</p> <p>(Anaes.)</p>
Proposed MBS fee	\$142.25 Benefit: 75% = \$106.70 85% = \$120.95
Indicate the overall cost per patient of providing the proposed health technology	\$142.25
Please specify any anticipated out of pocket expenses	N/A
Provide any further details and explain	N/A

# Algorithms

## **PREPARATION FOR USING THE HEALTH TECHNOLOGY**

**Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:**

According to the Australian therapeutic guidelines<sup>1</sup> the objectives of interventions (i.e., therapy, orthotics, splints, surgery) for individuals with cerebral palsy and associated musculoskeletal conditions including spasticity are as follows:

- optimise and maintain independence and participation (i.e., communication, mobility, education, employment, recreation)
- optimise and maintain safe eating, drinking and nutrition
- optimise and maintain muscle strength and flexibility
- prevent, control or treat dynamic tightness or fixed contractures
- reduce muscle fatigue and pain.

In clinical practice, clinicians would complete a physical examination including an assessment of motor function, muscle tone, range of motion, reflexes, limb deformity and anatomical alignment.

For prescribing purposes, as recommended by the PBAC, a diagnosis of moderate to severe spasticity (an Ashworth scale score of more than 2) is required for patients to access botulinum toxin treatment for upper limb spasticity.

To access botulinum toxin treatment for dynamic equinus foot deformity, patients are required to be ambulant.

**Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?**

No.

**Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:**

The listing of Xeomin will not change the current clinical management of patients with upper limb or lower limb spasticity due to cerebral palsy.

Xeomin would displace the use of Botox with a 1:1 equi-effective dose.

## **USE OF THE HEALTH TECHNOLOGY**

**Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:**

N/A

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<sup>1</sup> Australian Therapeutic Guidelines. Melbourne: Therapeutic Guidelines Limited; accessed April 2024. <https://www.tg.org.au>

**Explain what other healthcare resources are used in conjunction with the comparator health technology:**

N/A

**Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:**

N/A

#### **CLINICAL MANAGEMENT AFTER THE USE OF HEALTH TECHNOLOGY**

**Define and summarise the clinical management algorithm, including any required tests or healthcare resources, *after* the use of the proposed health technology:**

The sponsor does not propose any changes to the current clinical management algorithm for the treatment of upper limb or lower limb spasticity in children and adolescents with cerebral palsy. Xeomin would provide an alternate option, in addition to current botulinum toxin treatments (Botox or Dysport), for clinicians and patients.

The current clinical management algorithm for children and adolescents with moderate to severe upper limb spasticity due to cerebral palsy is outlined in Figure 1 and reflects the diagnostic/prescribing criteria as previously accepted for Botox and Dysport, as well as current Australian clinical guidelines.

The current clinical management algorithm for children and adolescents with dynamic equinus foot deformity is outlined in Figure 2 and reflects the diagnostic/prescribing criteria as previously accepted for Botox and Dysport, as well as current Australian clinical guidelines.

**Define and summarise the clinical management algorithm, including any required tests or healthcare resources, *after* the use of the comparator health technology:**

As described above.

**Describe and explain any differences in the healthcare resources used *after* the proposed health technology vs. the comparator health technology:**

The listing of Xeomin will not change the current clinical management of patients with upper limb or lower limb spasticity due to cerebral palsy.

Xeomin would displace the use of Botox with a 1:1 equi-effective dose.

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

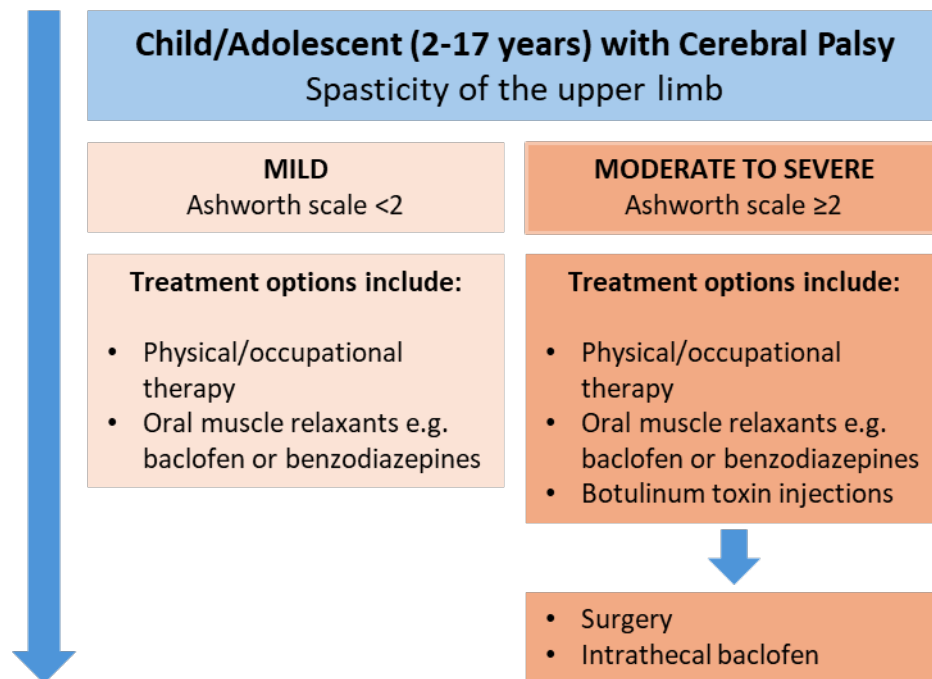


Figure 1 Clinical management algorithm - upper limb

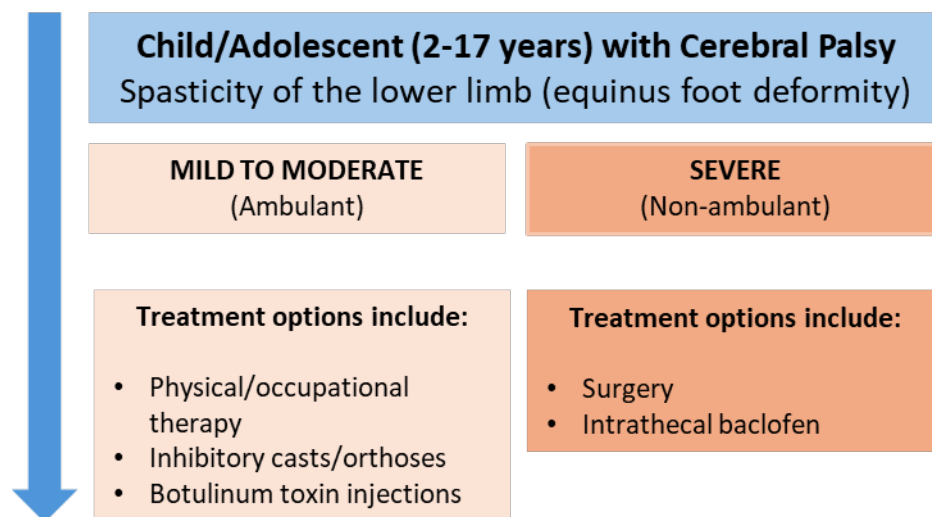


Figure 2 Clinical management algorithm - lower limb

## Claims

**In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?**

- ☐ Superior  
☒ Non-inferior  
☐ Inferior

**Please state what the overall claim is, and provide a rationale:**

Treatment of upper or lower limb spasticity with incobotulinumtoxinA (Xeomin) is non-inferior to Botox with regards to efficacy and safety, in patients with cerebral palsy aged 2 years or older. This was demonstrated in two randomised controlled trials – TIM and XARA, with supporting evidence from two other randomised studies – TIMO and Study R-201212.

Trial details are tabulated in the Summary of Evidence.

The non-inferiority of Xeomin and Botox has been well-established and accepted by the PBAC, with the products considered equivalent and interchangeable on a patient-level basis. In the public summary document for the most recent consideration of Xeomin in 2019, the PBAC declared 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." (6.12 INCOBOTULINUMTOXINA, Public Summary Document, Paragraph 6.16, November 2019 PBAC Meeting). The PBS therapeutic relativity sheets list Xeomin and Botox as having a 1:1 dose equivalence.

**Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?**

IncobotulinumtoxinA, is the only botulinum toxin formulation that is a pure botulinumtoxinA formulation, free of accessory proteins.

**Identify how the proposed technology achieves the intended patient outcomes:**

Xeomin blocks cholinergic transmission at the neuromuscular junction by inhibiting the release of acetylcholine from peripheral cholinergic nerve terminals. This inhibition occurs according to the following sequence:

- heavy chain of toxin binding to cholinergic nerve terminals
- internalization of the toxin within vesicles into the nerve terminal
- translocation of the light-chain of the toxin molecule into the cytosol of the nerve terminal
- enzymatic cleavage of SNAP25, the presynaptic target protein essential for the release of acetylcholine.

Complete recovery of endplate function/impulse transmission after intramuscular injection normally occurs within 3-4 months as nerve terminals sprout and reconnect with the muscle endplate and the presynaptic neurotransmitter release mechanism becomes functional again.

**For some people, compared with the comparator(s), does the test information result in:**

**A change in clinical management?** No

**A change in health outcome?** No

**Other benefits?** No

**Please provide a rationale, and information on other benefits if relevant:**

N/A

**In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?**

☐ More costly

☒ Same cost

☐ Less costly

**Provide a brief rationale for the claim:**

The requested PBS listing of Xeomin for the symptomatic treatment of paediatric spasticity will not change the current clinical management algorithm for treatment of upper limb or lower limb spasticity in children and adolescents with cerebral palsy. Xeomin is not expected to impact the prevalence of the disease, so the market is not expected to grow after listing. Xeomin will provide an alternate option for clinicians and patients to the currently listed botulinum toxin treatments. Therefore, Xeomin will not increase the MBS utilisation of items 18354 and 18361, as these items will still be claimed regardless of the prescribed PBS treatment.

In terms of dose relativities, Xeomin is expected to replace Botox in practice at a 1:1 equi-effective dose, resulting in total cost and utilisation neutrality for both the PBS and MBS. However, using previous TGA and PBAC determinations, the equi-effective dose for Xeomin and Dysport is expected to be 1:2.5. This means that for every patient switching from Dysport to Xeomin, the total PBS services will reduce by a ratio of 2.5 to 1. As a result of this, there will be a reduction of the overall utilisation of MBS items 18354 and 18361 if patients switch to Xeomin from Dysport, reducing the cost to the MBS. Dysport, however, only accounts for 7% of the total market for these indications, so the number of patients switching to Xeomin would be low and the resultant cost reduction to the MBS would also be minimal.

Therefore, since most patients expected to be treated with Xeomin will switch from Botox, the utilisation of MBS item numbers 18354 and 18361 will remain largely unchanged and will not generate any further costs to the MBS.



**If your application is in relation to a specific radiopharmaceutical(s) or a set of radiopharmaceuticals, identify whether your clinical claim is dependent on the evidence base of the radiopharmaceutical(s) for which MBS funding is being requested. If your clinical claim is dependent on the evidence base of another radiopharmaceutical product(s), a claim of clinical noninferiority between the radiopharmaceutical products is also required.**

N/A

## Summary of Evidence

**Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology.**

	Type of study design*	Title of journal article or research project	Short description of research	Website link to journal article or research	Date of publication
1.	Phase III, randomised, double-blind, parallel-group, dose-response trial	TIM (Treatment with IncobotulinumtoxinA in Movement)	Children and adolescents (n=311) with lower-limb spasticity due to cerebral palsy randomised 1:1:2 to three parallel Xeomin dose groups (low, mid or high).  Health outcomes and safety evaluated.	<a href="https://pubmed.ncbi.nlm.nih.gov/34092664/">https://pubmed.ncbi.nlm.nih.gov/34092664/</a>	June 2021
2.	Phase III, randomised, double-blind, parallel-group, dose-response trial	XARA (IncobotulinumtoxinA in Arm Treatment in Cerebral Palsy)	Children and adolescents (n=351) with upper and/or lower limb spasticity due to cerebral palsy randomised 1:1:2 to three parallel Xeomin dose groups (low, mid or high).  Health outcomes and safety evaluated.	<a href="https://pubmed.ncbi.nlm.nih.gov/34339951/">https://pubmed.ncbi.nlm.nih.gov/34339951/</a>	May 2021
3.	Open-label, non-controlled, long-term study	TIMO (Treatment with IncobotulinumtoxinA in Movement Open-Label)	The study included children and adolescents with lower limb spasticity from the TIM pivotal trial (n = 124) as well as new recruits with upper and/or lower limb spasticity due to cerebral palsy (n = 246).  Long-term health outcomes and safety evaluated.	<a href="https://pubmed.ncbi.nlm.nih.gov/34957963/">https://pubmed.ncbi.nlm.nih.gov/34957963/</a>	March 2022 (Follow up to TIM)
4.	Open-label, randomised, comparative study	MRZ-R-201212_01001_N_2 (Study R-201212)	Children (n=64) with spastic equinus and equinovarus foot deformity due to cerebral palsy randomised 1:1 to Xeomin or Botox.  Health outcomes and safety evaluated.	<a href="https://pubmed.ncbi.nlm.nih.gov/29265085/">https://pubmed.ncbi.nlm.nih.gov/29265085/</a> (Publication in Russian)	2017

## References

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