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Health Technology Briefing
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Xeomin (Botulinum neurotoxin type A) for lower limb and/or upper limb spasticity

Company/Developer	Merz Pharma UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 27767	NICE ID: N/A	UKPS ID: 653825

Licensing and Market Availability Plans

The company received UK marketing authorisation in June 2023 for the treatment of focal spasticity of the lower limb affecting the ankle joint.[1,2]

Summary

Xeomin (Botulinum neurotoxin type A) is in clinical development for the treatment of adults with lower limb and/or upper limb spasticity. Spasticity is a long-term symptom described as a pathological increase in muscle tension (hypertonicity) resulting from damages to the brain, spinal cord, or motor nerves associated with conditions such as stroke, traumatic brain injury (TBI), cerebral palsy, multiple sclerosis, etc. The hypertonicity in muscles leads to permanent hardening and stiffening. While there are treatments available for treating upper limb spasticity, there are limited options for spasticity affecting the lower limbs. Xeomin could provide an additional treatment option for lower limb spasticity and/or upper limb spasticity.

Xeomin is a formulation of the purified botulinum neurotoxin type A (BoNT-A) which is free from complexing proteins. Xeomin works as an effective therapeutic for several neuromuscular disorders via the induction of temporary muscle paralysis. Xeomin is administered via intramuscular injection into the target limbs. If licensed, Xeomin will be an additional treatment option for lower limb spasticity and/or upper limb spasticity.

Proposed Indication

For the treatment of adults with lower limb or combined lower limb and upper limb spasticity.[3]

Technology

Description

Xeomin (Botulinum neurotoxin type A, NT 201) is a formulation of the purified botulinum neurotoxin type A (BoNT-A) free from complexing proteins, belonging to the family of botulinum neurotoxins (serotypes A – G) contained in the botulinum toxin produced by the anaerobic spore-forming bacteria called clostridium botulinum.[4,5] Botulinum neurotoxins are the most potent toxins known to mankind but types A and B are commonly used clinically.[4] Type A works as an effective therapeutic for several neuromuscular disorders via the induction of temporary muscle paralysis when used in low concentrations.[4-6] It attaches itself exclusively to nerve cells that activate the muscular system or specific glands, inhibiting acetylcholine release at the neuromuscular junction – effectively and accurately blocking an overactive muscle or gland.[5,7]

Xeomin (Botulinum neurotoxin type A) is in clinical development for the treatment of adults with lower and/or upper limb spasticity.[3] In the Phase III trial (NCT03992404), subjects receive an intramuscular injection of Xeomin (Botulinum neurotoxin type A) (400 units) into muscles of the lower limb.[3] During the open-label extension phase (4 – 5 treatment cycles), subjects receive intramuscular injections of up to 800 units of Xeomin into muscles of the lower and upper limbs if indicated.[3]

Key Innovation

It is important to treat spasticity to improve comfort, mobility, and independence. Without therapy, spasticity can result in pain, permanent joint deformity, urinary tract infection, chronic constipation, and pressure sores.[8] Available treatments include muscle relaxants and anxiolytics and physiotherapy.[9] Botulinum toxin type A is recommended as a safe and effective treatment for upper and lower limb spasticity, resulting in both passive and active functional gains.[10]

There are currently limited treatment options for spasticity affecting the lower and/or upper limb region. Xeomin (Botulinum neurotoxin type A), Botox (Botulinum toxin type A), and Dysport (Botulinum toxin type A) are all licensed for the treatment of adults with lower limb spasticity mainly targeting the ankle, and foot (Botox only) and upper limb spasticity.[11-13] If licensed, Xeomin will be an additional treatment option for lower limb spasticity and/or upper limb spasticity.

Regulatory & Development Status

Xeomin (Botulinum neurotoxin type A) is licensed in the UK for treatment of the following indications in adults and children:[13]

- blepharospasm and hemifacial spasm
- cervical dystonia of a predominantly rotational form (spasmodic torticollis),
- focal spasticity of the upper limb,
- focal spasticity of the lower limb affecting the ankle joint,
- chronic sialorrhea due to neurological / neurodevelopmental disorders.

Xeomin (Botulinum neurotoxin type A) is currently in phase II and III clinical development for several indications including:[14]

- glabellar frown lines
- essential tremor of the upper limb

- androgenetic Alopecia
- platysma prominence
- degenerative rotator cuff disease
- prevention of Atrial Fibrillation

Patient Group

Disease Area and Clinical Need

Spasticity is a long-term symptom described as a pathological increase in muscle tension (hypertonicity) resulting from damages to the brain, spinal cord, or motor nerves associated with conditions such as stroke, traumatic brain injury (TBI), cerebral palsy, multiple sclerosis, etc.[8,15] The hypertonicity in muscles leads to permanent hardening and stiffening.[15,16] Evidence reports that the prevalence of leg spasticity in patients with TBI is 13%.[17] Up to 89% of people with spasticity associated with stroke report total or partial inability to work.[9] Spasticity has a disabling effect through pain and reduced movement and mobility, which can result in difficulties with walking, sitting, standing, and other everyday activities.[9] Spasticity can affect any muscle of the body, but it is more common in the muscles of the leg.[8]

Neurological symptoms associated with spasticity include weakness, poor postural reactions, and sensory loss.[18] Others include pain, bladder, bowel, and sexual dysfunction.[18] When it worsens, spasticity will typically involve deterioration of mobility, involuntary movements, and an increase in care needs.[17] Patients with spasticity had worse HRQoL in terms of their physical functioning, role limitations, physical pain, and vitality.[19]

In 2014 in England, it was estimated that approximately 110,000 people have a stroke each year and between 19 and 38% of them (up to 41,800 people) are affected by spasticity. Of the people who have spasticity associated with stroke, 79% report spasticity in the elbow, 66% report spasticity in the wrist, 50% report spasticity in the hip, 54% report spasticity in the knee, and 66% report spasticity in the ankle. These figures suggest that up to 27,588 people have lower limb spasticity and up to 33,022 have upper limb spasticity.[9] TBI impacts the lives of 1.5 to 2 million new individuals each year; 75,000 to 100,000 of these are classified as severe and will suffer enduring severe spasticity in addition to cognitive, vestibulomotor (balance), and other motor impairments.[20] In England, 2021-22, there were 6896 diagnoses, 5,085 finished consultant episodes (FCE), and 3,064 admissions for a primary diagnosis of unspecified stroke (ICD-10 code I64) of which spasticity may affect up to 38% of all diagnoses.[21] The primary diagnosis of stroke resulted in 28,539 FCE bed days and 40 day cases.[21] There are no ICD-10 codes classifying TBI.[21]

Recommended Treatment Options

There are currently no National Institute for Health and Care Excellence (NICE) recommended treatment options for this patient population.

Clinical Trial Information

Trial	**PATTERN;** NCT03992404, 2018-001639-35; Prospective, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Investigate the Efficacy and Safety of NT 201 in the Treatment of Lower Limb Spasticity Caused by

	Stroke or Traumatic Brain Injury in Adult Subjects, Followed by an Open-Label Extension With or Without Combined Upper Limb Treatment **Trial phase** – Phase III **Location(s):** 10 EU countries, UK, USA, and other countries **Primary completion date:** August 2025
Trial Design	Randomised, Parallel Assignment, Double-Blind
Population	N = 600 (planned); adult subjects with lower limb spasticity caused by stroke or TBI, with or without upper limb spasticity.
Intervention(s)	• 1 treatment cycle of 400 units of Xeomin (Botulinum neurotoxin type A) intramuscular injection (main period) • 4 to 5 treatment cycles of 400 – 800 units of Xeomin (Botulinum neurotoxin type A) intramuscular injection (open-label extension period)
Comparator(s)	Matched placebo
Outcome(s)	Primary outcomes: • Change from baseline in derived Modified Ashworth Scale-Bohannon (MAS) ankle score (knee extended) at weeks 4 to 6 • Global Impression of Change Scale (GICS) assessed by a physician at Weeks 4 to 6 • Occurrence of treatment emergent adverse events [TEAEs] in the Main Period See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The NHS indicative price for 200 units of Xeomin (Botulinum neurotoxin type A) powder for solution for 200 injection vials is £259.80, 100 units is £129.90, and 50 units is £72.00.[22]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in the development of Botulinum toxin type A for treating upper or lower limb focal spasticity associated with stroke (ID768). Expected publication date: to be confirmed
- NICE Medtech Innovation Briefing. Mollii suit for spasticity (MIB 100). March 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. Specialized Commissioning Policy: Selective dorsal rhizotomy for treatment of spasticity in cerebral palsy. 170063P. March 2019.
- NHS England. 2013/14 NHS Standard Contract for Specialized Rehabilitation for Patients with Highly Complex Needs (All ages). D02/S/a.
- NHS England. Clinical Commissioning Policy: Cerebellar Stimulator Implants. NHSCB/D04/PS/b

Other Guidance

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- AJ Thompson et. al., Clinical management of spasticity. 2005.[23]
- Royal College of Physicians. Spasticity in adults: management using botulinum toxin. 2018.[10]
- Giovanni Morone et al. The Current State of Knowledge on the Clinical and Long-Term Spasticity Management in Post-Stroke Patients: Issues and Possible Actions—A Systematic Review with an Italian Expert Opinion. 2023.[24]
- Gavin Williams et. al. A synthesis and appraisal of clinical practice guidelines, consensus statements and Cochrane systematic reviews for the management of focal spasticity in adults and children. 2019.[25]

Additional Information

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