Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Clostridium botulinum neurotoxin type A for treating hypersalivation associated with neurological conditions

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of clostridium botulinum neurotoxin type A within its marketing authorisation for treating hypersalivation associated with neurological conditions.

Background

Hypersalivation, also known as sialorrhea or ptyalism, is a common secondary symptom of neurological conditions such as Parkinson's disease and cerebral palsy. It can be defined as the increased amount of saliva in the mouth, often leading to unintentional drooling[1]. Causes of hypersalivation could include poor oral and facial muscle control, the inability to effectively swallow or clear saliva from the mouth or as a reaction to some medications[1,2].

There are an estimated 12.5 million people in the UK with a neurological condition[3]. Approximately one in two people with the condition is affected by hypersalivation and one in five needs continuous saliva elimination[4]. In people with Parkinson's disease or cerebral palsy, approximately 88,900 and between 11,000 to 88,000 are affected by hypersalivation, respectively[5,6].

The NICE guideline on cerebral palsy in under 25s (NG62) recommends considering anticholinergic drugs (glycopyrronium bromide, transdermal hyoscine hydrobromide or trihexyphenidyl hydrochloride) to reduce the severity and frequency of drooling in children and young people with cerebral palsy. If anticholinergic drugs provide insufficient benefit or are not tolerated, the guideline recommends that specialist assessment and the use of botulinum toxin A injections to the salivary glands with ultrasound guidance may be considered. NICE's guideline on Parkinson's disease in adults (NG71) recommends the use of non-pharmacological management (for example speech and language therapy) to manage drooling in people with Parkinson's disease. If non-pharmacological management is not available or has not been effective, the guideline recommends that pharmacotherapies (glycopyrronium bromide and other anticholinergic drugs or botulinum toxin A) may be considered. Glycopyrronium bromide is has a marketing authorisation for the symptomatic treatment of severe sailorrhoea (hypersalivation) but only in children and adolescents aged 3 years and older with chronic neurological disorders.

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The technology

Clostridium botulinum neurotoxin type A (Xeomin, Merz Pharma UK) is a purified botulinum toxin type A, which acts as a neuromuscular blocking agent by inhibiting acetylcholine release and therefore slowing saliva production. It is administered by injection.

Clostridium botulinum neurotoxin type A does not currently have a marketing authorisation in the UK for treating hypersalivation. It has been studied in clinical trials compared with placebo in adults and children and young people with a neurological condition associated with sialorrhea or chronic troublesome sialorrhea, respectively. Clostridium botulinum neurotoxin type A has a marketing authorisation in the UK for the symptomatic treatment of blepharospasm, cervical dystonia of a predominantly rotational form (spasmodic torticollis) and spasticity of the upper limb in adults.

Intervention(s)	Clostridium botulinum neurotoxin type A
Population(s)	People with hypersalivation associated with neurological conditions
Comparators	Anticholinergic drugs such as: • glycopyrronium bromide • transdermal hyoscine hydrobromide • trihexyphenidyl hydrochloride
Outcomes	The outcome measures to be considered include: • unstimulated salivary flow rate • response rate • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.

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Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Guidelines:** Parkinson's disease in adults (2017). NICE clinical guideline NG71 Cerebral palsy in under 25s: assessment and management (2017). NICE guideline NG62 Spasticity in under 19s: management (2016). NICE clinical guideline CG145 **Related Evidence Summaries:** Severe sialorrhoea (drooling) in children and young people with chronic neurological disorders: oral glycopyrronium bromide (2017) NICE evidence summary ES5 Hypersalivation: oral glycopyrronium bromide (2013) NICE evidence summary ESUOM15 **Related Quality Standards:** Cerebral palsy in children and young people (2017). NICE quality standard QS162. Parkinson's disease (in development). Publication expected February 2018 **Related NICE Pathways:** Neurological conditions. NICE pathway https://pathways.nice.org.uk/pathways/neurological-conditions
Related National Policy	Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 2 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for the symptomatic treatment of hypersalivation in people with neurological conditions?
How is severity of hypersalivation defined?

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Have all relevant comparators for Clostridium botulinum neurotoxin type A been included in the scope?

Would surgery or radiotherapy be considered for this population?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom Clostridium botulinum neurotoxin type A is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider Clostridium botulinum neurotoxin type A will fit into the existing NICE pathway, Neurological conditions?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which Clostridium botulinum neurotoxin type A is licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider Clostridium botulinum neurotoxin type A to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a ‘step-change’ in the management of the condition)?

Do you consider that the use of Clostridium botulinum neurotoxin type A can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

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To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

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4. Giles R, Naummann M, Werner E, Riemann M, Beck I, Puls I, Reinners C, Toyka KV. Injection of botulinum toxin A in to salivary glands improve sialorrhoea in amyotropic lateral sclerosis. J Neurol Neurosurg Psychiatry 2000;69:121-3
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