Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Clostridium botulinum neurotoxin type A for treating chronic sialorrhoea

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of clostridium botulinum neurotoxin type A within its marketing authorisation for treating chronic sialorrhoea.

Background

Sialorrhoea, also known as hypersalivation 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 sialorrhoea 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]. Complications of sialorrhoea may include dehydration, reduced oral hygiene, social embarrassment and isolation, increased risk of respiratory tract infections, depression and anxiety as well as difficulty swallowing, eating and speaking.

There are an estimated 12.5 million people in the UK with a neurological condition[3]. Approximately one in two people with motor neurone disease is affected by sialorrhoea and one in five needs continuous saliva elimination[4]. In people with Parkinson's disease or cerebral palsy, approximately 63,500 and between 11,000 to 88,000 are affected by sialorrhoea, 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, then a 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, glycopyrronium bromide and other anticholinergic drugs or botulinum toxin A may be considered. Glycopyrronium bromide has a marketing authorisation for the symptomatic treatment of severe sialorrhoea (hypersalivation) but only

in children and adolescents aged 3 years and older with chronic neurological disorders.

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 sialorrhoea or chronic troublesome sialorrhoea, respectively.

Intervention(s)	Clostridium botulinum neurotoxin type A
Population(s)	Adults with chronic sialorrhoea
Comparators	• Anticholinergic drugs such as glycopyrronium bromide For people where anticholinergic drugs are unsuitable: • Established clinical management without clostridium botulinum toxin A
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.

Appendix B

Other considerations	If the evidence allows the following subgroups will be considered. These include: • adults with dysphagia (difficulty swallowing) • underlying condition causing sialorrhoea 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 (2018). NICE quality standard QS164. **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

Appendix B

References

1. Bavikatte G, Sit PL and Hassoon A. Management of drooling of saliva. British Journal of Medical Practitioners 2012;5(1):a507
2. Hockstein NG, Samadi DS, Gendron K, *et al*. Sialorrhea: A management challenge. American Family Physician 2004;69(11):2628-2635.
3. The neurological Alliance. Measuring up: improving the collection of neurological data and intelligence. London: April 2014 http://www.neural.org.uk/store/assets/files/380/original/Final_-_Measuring_up_30_April_2014_.pdf
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
5. Jongerius PH, Rotteveel JJ, Van Limbeck J, Gabreels FJM, Van Ilulst KBS, Van Den Ilogen FJA. Botulinum toxin effect on salivary flow rate in children with cerebral palsy. Neurology 2004;63:1371-5
6. Boothwell JE, Clarke K, Dooley JM, Gordon KE, Anderson R, Wood Camfied CS, Camfield PR. Botulinum toxin A as a treatment for excessive drooling in children. Paediatr Neurology 2002; 27(1):18-22