East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Briefing Paper for Prescribing Clinical Network on NICE Technology Appraisal TA605

NICE TA Guidance	Xeomin® (botulinum neurotoxin type A) for treating chronic sialorrhoea (TA605)
Date of issue	09 October 2019
Available at	https://www.nice.org.uk/guidance/ta605

Medicine details	
Name, brand name	Botulinum neurotoxin type A, Xeomin®
Manufacturer	Merz Pharma UK Ltd
Licensed indications	Blepharospasm, spasmodic torticollis, spasticity of the upper limb, and chronic sialorrhoea due to neurological disorders in adults.
Formulation	50, 100, 200 units powder for injection
NICE recommended dosage/schedule	A reconstituted solution at a concentration of 5 units/0.1 ml should be used. Xeomin® is injected into the parotid and submandibular glands on both sides (per treatment four injections in total). The dose is divided with a ratio of 3:2 between the parotid and submandibular glands. The injection site should be close to the centre of the gland. The recommended dose per treatment session is 100 units. This maximum dose should not be exceeded. Treatment intervals should be determined based on the actual clinical need of the individual patient. Repeat treatment more frequent than every 16 weeks is not recommended.

Disease and potential patient group	
Brief description of disease	Chronic sialorrhoea and excessive saliva accumulation can occur because of dysfunction or weakness of the muscles in the mouth and face. It is a common secondary symptom of many neurological conditions such as Parkinson's disease, cerebral palsy, stroke and traumatic brain injury and is often caused by swallowing issues and poor lip seal. Complications of sialorrhoea may include poor oral hygiene, bad breath, perioral dermatitis, dehydration, eating and speaking difficulties, sleep disturbance and fatigue. Sialorrhoea may also increase the risk of aspiration pneumonia if the saliva is inhaled. This may affect mortality and is more prevalent in older people. Sialorrhoea, and the resulting excessive drooling, also has a psychosocial effect on patients including embarrassment, decreased self-esteem and the potential for social isolation.

Potential patient numbers

Number of people eligible for treatment in England [3]

Population	Parkinson's disease related - proportion of previous row (%)	Other conditions related (%)	Number of people
Adult population			43,752,473
Prevalence of Parkinson's disease1	0.28		121,900
People with Parkinson's disease who have sialorrhoea2	22.50		27,400
People who have Parkinson's disease who require treatment2 (a)	63.5		17,400
People who have other conditions who require treatment (proportion of adult population)3 (b)		0.038	16,700
Total number of people eligible for treatment with Xeomin (a + b)			34,100
Total number of people estimated to have Xeomin each year from year 2023/24	90	90	30,700

1 Source: Prevalence of Parkinson's disease 2018.
2 Source: Company submission - based on clinical opinion.
3 Source: The data from the SIAXI trial shows 79.4% of people with chronic sialorrhoea are people who have Parkinson's disease. This has been used to derive the total population as follows: 17,400 people with Parkinson's disease requiring treatment / 79.4% = 21,900 total population. The company estimates the total population to be around 46,300 people. Mid-point taken, therefore 34,100 people who may receive treatment. People with other conditions = 34,100 minus people who have Parkinson's disease 17,400 = 16,700 or around 0.038% of the adult population in England.
4 Source: Company submission.

SUMMARY

Guidance

Xeomin® (botulinum neurotoxin type A) is recommended, within its marketing authorisation, as an option for treating chronic sialorrhoea caused by neurological conditions in adults. It is recommended only if the company provides it according to the commercial arrangement.

Cost implications

Cost:
NB: NICE TA, therefore funding is mandatory.
The list price of botulinum neurotoxin type A, Xeomin® is £129.90 per 100-unit powder for solution for injection vial (excluding VAT; BNF accessed online November 2019).

Cost per patient per annum (including OP & ultrasound) is ~ £746. This is a similar to cost per annum to atropine and hyoscine and, is cheaper than the annual cost of glycopyrronium.

NICE resource impact- 34,100 people with chronic sialorrhoea are eligible for treatment with Xeomin® each year. This includes people who have Parkinson's disease, cerebral palsy, traumatic brain injury, motor neurone disease, stroke and multiple sclerosis.[3]

Estimated number of people having Xeomin® using NICE assumptions.[3]

	Population having Xeomin each year
2019/20	1,900
2020/21	10,200
2021/22	17,100
2022/23	23,900
2023/24	30,700

Cost-effectiveness estimates (extract from NICE)
The company provided base-case incremental cost-effectiveness ratios (ICERs) and scenario analyses based on the list price of Xeomin® and based on a confidential commercial arrangement. Because the ICERs based on the commercial arrangement are confidential, only the list-price ICERs are presented in NICE.

The company's base-case deterministic ICER was £9,583 per quality-adjusted life year (QALY) gained for Xeomin® compared with standard care. Xeomin® dominated glycopyrronium bromide. The ERG's exploratory analyses provided both a deterministic ICER and a probabilistic ICER for Xeomin® compared with standard care; £47,309 and £45,423 per QALY gained respectively. Xeomin® continued to dominate glycopyrronium bromide.

The committee also agreed that standard care was the most appropriate comparator. Therefore, it concluded that the most appropriate ICER for decision making was the ERG's exploratory probabilistic ICER of £45,423 per QALY gained for Xeomin® compared with standard care.

Availability of PAS and details (if appropriate):
The company has a commercial arrangement. This makes Xeomin® available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount. It is only recommended if the company (Merz Pharma) provides it according to the commercial arrangement.

Availability of homecare service (if appropriate):
Not required.

Alternative treatments and cost per patient per year

Xeomin® is the only botulinum neurotoxin type A licensed for chronic sialorrhoea.

The treatment and management of sialorrhoea involves suction, drug treatment and invasive procedures, including injection of botulinum toxin A to the salivary gland, radiotherapy, surgical excision of the salivary glands, salivary duct rerouting or ligation of the salivary glands. Although injection of botulinum toxin A into the parotid and submandibular glands is considered safe and effective in controlling drooling, its effects are short lived, thus requiring repeat injections. Surgical intervention is the only permanent treatment currently available.[4]

In accordance with NICE, Xeomin® should be considered as:

- an alternative first-line treatment to non-pharmacological management such as bibs, speech and language therapy and occupational therapy (referred to as standard care by the company) and to anticholinergics and
- as an alternative second-line treatment to standard care (in line with the 3 NICE guidelines NG42, NG71 and NG62)

Impact to patients
An NICE approved treatment option for patients ensuring improved accessibility.
Impact to primary care
• This drug should be administered in specialist centres. • There should be no prescribing in primary care. • Primary care prescribers should be aware that their patient is receiving botulinum neurotoxin type A, Xeomin® and ensure that this is recorded in the patient's notes in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.
Impact to secondary care
• The initiation, administration and on-going treatment and monitoring is managed by secondary care in specialist centres. • The PAS scheme discounted price is only available to secondary care providers. • All prescribing is recommended to be retained by secondary care. • Repeat treatment more frequent than every 16 weeks is not recommended- Potential of three injections per annum • Any specialist starting botulinum neurotoxin type A, Xeomin® must write to the patient's GP to inform them that it is being prescribed within secondary care so that this can be recorded on the primary care clinical system. • This TA is likely to have a significant impact on capacity within existing specialist centres. Commissioning arrangements for local services will need to be explored to ensure the service can meet RTT national targets and manage on-going patient activity.
Impact to CCGs
• Cost impact to the CCGs • NICE recommended place in therapy for botulinum neurotoxin type A, Xeomin® to be reflected in Adult hypersalivation treatment pathways. • Review of locally commissioned services to meet patient population needs
Implementation
NICE TA implementation must be within 90 days from publication (9th October 2019)
Recommendation to PCN
PbRe – NHSI drug list indicates botulinum toxin as PbRe drug only for torsion dystonias and other involuntary movements. The APC to agree the local commissioning arrangements to either pay as excluded drug or within tariff. APC to consider **RED** Traffic Light Status.

References:

1. Summary of Product Characteristics: Xeomin®. Accessed 18th November 2019. www.medicines.org
2. National Institute for Health and Care Excellence. Technology Appraisal 605: Xeomin® (botulinum neurotoxin type A) for treating chronic sialorrhoea, 09 October 2019. Accessed 18th November 2019. www.nice.org.uk
3. National Institute for Health and Care Excellence. Resource impact report: Xeomin® (botulinum neurotoxin type A) for treating chronic sialorrhoea (TA605). Published: October 2019
4. Ganesh Bavikatte, Poh Lin Sit and Ali Hassoon. Management of Drooling of saliva, BJMP 2012;5(1):a507

Please provide Declarations of Interest (in last 12 months) for Author and contributors of this document. Please mark NULL if there are none.

Declaration of interest										
Date reported	Type of potential or actual conflict of interest (use a separate line for each entry if more than one)	Name of company	Drug / drug group	Your name	Your organisation (who are you representing)	Member of APC	Member of MCG	Date of interest (month)	Date of interest (year)	One off interest or on-going?
18/11/2019	None			Michelle Barnard	CHMSCCG	No	No			
21/11/2019	None			Ashleigh Bradley	CHMSCCG	Yes	Yes			
25/11/2019	None			Katherine Regan	CHMSCCG	Yes	No			
20/12/2019	None			Sarah Watkin	SDCCG (Hosted service)	Yes	Yes			

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VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
V1.1	18/11/19	Michelle Barnard	Draft	
V1.2	21/11/19	Ashleigh Bradley	Draft for review	Peer review by Ashleigh Bradley prior to consultation. Addition of the following: ➢ Exact SPC wording for sialorrhoea license ➢ NG number added
V1.3	25/11/19	Katherine Regan	Final draft for consultation	Peer review by Katherine Regan. Typo corrected.
Final	24/12/2019	Michelle Barnard	FINAL	Comments received included as appropriate

Comments

Hi Michelle,

Couple of things from me for consideration:

1) There are no costs included. I know there is a confidential PAS and taking this into account George and I have worked out that cost per pt per annum (incluing OP & ultrasound) is ~ £746. This is similar to cost per annum of atropine and hyoscine and according to NICE resource template, is cheaper than a year of glycopyronium. We are however confused about then why the NICE costing template is showing a cost in implementation rather than being neutral or saving. Any ideas why? Assumed implementation costs are due to lack of services to administer Botulinum injections for this indication- Costs included.
2) It is stated in "impact to primary care" that it is a PbRe drug however, NHSI drug list indicated PBR only for torsion dystonias and other involuntary movements. The APC will need to agree to a local commissioning agreement to pay as excluded rather than in tariff – they may agree if it is demonstrated that glycopyronium is stopped in primary care (and some saving made there) – but not sure if this is the case based on NICE template rather than our calculations! - Statement amended to reflect APC requirement to agree commissioning route.

No declarations of interest for me.

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