BEDFORDSHIRE, LUTON AND MILTON KEYNES AREA PRESCRIBING COMMITTEE (BLMK APC)

GUIDANCE ON THE USE OF BOTULINUM TOXIN TYPE A

(Updated March 2023)

The Bedfordshire, Luton and Milton Keynes APC has agreed to support a modified version of the East of England Priorities Advisory Committee (EoE PAC) Guidance on Botulinum Toxin A (BTA)*.

See the document below for the locally modified version of the EoE PAC revised guidance. This version includes a Summary of BLMK agreed modifications, followed by the EoEPAC revised Guidance Statement.

*EoEPAC revised guidance statement issued Sept 2022

Approved by the BLMK Area Prescribing Committee (APC): March 2023
Review date: March 2026
(Original document, approved by the Bedfordshire and Luton Joint Prescribing committee (JPC) September 2013, revised and updated June 2017, October 2018, December 2018 and March 2021).

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Integrated Care Board; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

Summary of Locally agreed BLMK APC modifications to the EoE PAC recommendations (for specified indications outlined below):-

Indication	BLMK APC recommendations
Chronic anal fissure in adults	Recommended: Approved only for use after topical Glyceryl trinitrate or diltiazem have been unsuccessful (or are inappropriate) in healing chronic anal fissures and when surgery would be the next treatment option.
Hyperhidrosis	BTA should be considered in the management pathway for hyperhidrosis as per the BLMK ICB Pathway (December 2022)
Focal Limb Dystonia (Upper and lower limb) **JPC Bulletin 234, approved April 2016)**	Recommended as follows:- To support the use of Botulinum Toxin A for the treatment of Focal Limb Dystonia for both upper and lower limb dystonia.
Botulinum Toxin A to induce Ptosis (temporary and long term) **(JPC Bulletin 244, approved February 2017)**	Recommended as follows:- • To support use in the acute setting i.e. in corneal patients to induce temporary ptosis to prevent corneal perforations. • To support use in the chronic setting i.e. in ectropion patients who are not suitable for surgery due to other co-morbidities and who fit the following patient selection criteria:- ○ Patients with reduced mental capacity e.g dementia,learning difficulties. ○ Patients taking NOACS or other anticoagulants which cannot be stopped temporarily for surgery, for whom there would be an increased risk of retrobulbar haemorrhage (and subsequent visual loss) with surgery. ○ Patients with physical constraints e.g spinal/ back problems, who cannot lie in one position for the duration of surgery. The above recommendations are subject to administration of the Botulinum toxin using the following tariffs: • The Luton & Dunstable Hospital – Outpatient Procedure tariff • All other Trusts – Outpatient Appointment tariff
Idiopathic Toe Walking	This indication was not listed in the previous EoE PAC document, however it was listed as a JPC approved local amendment. This indication is not included in the newly updated EoE PAC guidelines however, it was agreed to retain the previous local agreement that states: “A review of the literature suggests that this treatment can be effective, although randomised controlled trials specifically in the idiopathic toe walking area are lacking. The evidence comes mainly from case reports/series’ and review articles. Some of the evidence is old and some is restricted to conference abstracts (trials not fully published). There is insufficient evidence available to agree a policy position on the use of botulinum toxin A for the treatment of idiopathic toe walking.

Indication	BLMK APC recommendations
	Requests for treatment for this indication should continue to be considered on an individual basis via the ICB Individual Funding Request Team."
Spasticity treatment in paediatric cerebral palsy	**Local agreement** To amend the wording in the 'Indications commissioned by NHS England prior to 1st April 2022' (P10 EoE PAC Guidance September 2022) with respect to this indication. EoE PAC wording: "Commissioned by NHSE at specialist centres only (including outreach when delivered as part of a provider network". Replace by: "**NHSE commission use when used by a Specialist Centre. BLMK ICB commission use when used by a non-specialist centre". (NB in Tariff from 1st April 2022)**

GUIDANCE STATEMENT

Botulinum toxin type A (BTA)

Background

Botulinum toxins cause neuromuscular blockade by inhibiting the calcium-ion mediated release of acetylcholine at the motor nerve terminals, resulting in a diminished endplate potential and subsequent flaccid paralysis of the affected muscles. The paralysis persists until new nerve terminals form, usually within two to four months. Botulinum Toxin A (BTA) is given by local injection for a range of uses including several unlicensed indications. Table 1 includes the current licensed medical indications for the various brands of botulinum toxin.

Table 1: BTA product licensed indications (does not include cosmetic uses)[1-3]

Licensed indication	Botox®	Dysport®	Xeomin®
Focal spasticity	✓	✓	✓ (Upper limb only)
Idiopathic cervical dystonia (spasmodic torticollis)	✓	✓	✓
Blepharospasm	✓	✓	✓
Hemifacial spasm	✓	✓	✓
Hyperhidrosis of axillae	✓	✓	x
Chronic migraine	✓	x	x
Bladder disorders (as specified in the Summary of Product Characteristics)	✓	✓	x
Chronic sialorrhea in adults due to neurological conditions	x	x	✓

The EoE PAC have evaluated the evidence and made recommendations on the use of BTA for several unlicensed indications. See table in appendix 1 for further information. Each recommendation also has a separate evidence review.

Safety

Botulinum toxin type A and B products have rare but serious risks of adverse effects. In March 2013, the Medicines and Healthcare products Regulatory Agency advised that all patients receiving any product containing botulinum toxin should be warned of the signs and symptoms of toxin spread, such as muscle weakness and breathing difficulties.[4] They should be advised to seek medical attention immediately if they experience breathing difficulties, choking, or any new or worsening swallowing difficulties, as such side effects may be life-threatening.[4,5]

Botulinum toxins prevent the release of acetylcholine at neuromuscular or other cholinergic junctions and reversibly denervate muscles or eccrine glands. The following safety information and advice needs to be considered when using botulinum in all clinical settings:

- Spread reactions including muscle weakness, dysphagia, and aspiration have been reported rarely with all products that contain botulinum toxin.
- Extreme caution is needed on administration of products that contain botulinum toxin to patients who have neurological disorders, or a history of dysphagia or aspiration.
- Only physicians with appropriate experience (including use of the required equipment) should administer products that contain botulinum toxin.[5]

Patients or caregivers should be informed about the risk of spread of toxin and should be advised to seek immediate medical care if problems with swallowing or speech develop, or if respiratory symptoms arise.

- Units of botulinum toxin are not interchangeable from one product to another.
- Recommended administration techniques and specific dosing guidance (including the recommendation to use the minimum effective dose and titrate according to individual need) should be followed.[5]

Tariff status and commissioning responsibility

From April 1st 2022, BTA was removed completely from the excluded high cost drug list and all the costs associated with its use are now included in the National Tariff unit costs.[6]

Prior to April 2022, NHS England were the responsible commissioner for the following indications: • Focal spasticity in children (including spasticity treatment in paediatric cerebral palsy)

• Intravesical use in spinal cord injury.
The Health and Social Care Act 2022, enabled NHS England to delegate to an Integrated Care System (ICS) any or all of its statutory functions for directly commissioning health care services and paying providers for them.[7]

In May 2022, NHS England issued preliminary guidance in relation to the transfer of certain specialised services and indications to the ICBs by April 2023.[8,9]

The evidence reviews and recommendations are intended to support the clinically appropriate use of BTA, and inform best practice within ICSs.

PAC recommendations
• PAC recommendations on the use of BTA are summarised in appendix 1, page 4.

Author: Victoria Gibson on behalf of PAC

Document history

PAC approval date	12th September 2022	**Version**	v4.1
Document history	v4.0 updated June 2022 Changes to tariff status and recommendations on: • Masseteric hypertrophy and temporomandibular disorders • New Indication: Frey's syndrome • Reynauld's disease, correction of squint in paediatrics and Hidradenitis suppurativa • v3 revised and updated June 2020; now a master summary document, with links to stand alone evidence reviews.		
Consultation process	PAC members East of England clinicians via PAC members.		
QA process	Vicky Gibson, Senior Pharmacist, Clinical Quality, PrescQIPP. 18th July 2022.		

References

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2. Summary of Product Characteristics - Dysport 300 units powder for solution for injection. Ipsen Ltd. Last updated July 2022. https://www.medicines.org.uk/emc/product/964/smpc
3. Summary of Product Characteristics - Xeomin 100 units powder for solution for injection. Merz Pharma UK Ltd. Last updated June 2022. https://www.medicines.org.uk/emc/product/6202/smpc
4. Botulinum toxin type B (Neurobloc): serious known risks. Drug Safety Update March 2013; 6 (8): A3 https://www.gov.uk/drug-safety-update/botulinum-toxin-type-b-neurobloc-serious-knownrisks#contents
5. Botulinum toxin products: rare but serious risk. Drug Safety Update 2007; 1 (3): 10 https://www.gov.uk/drug-safety-update/botulinum-toxin-products-rare-but-serious-risks
6. 2022/23 National Tariff Payment System: Annex A - National tariff workbook https://www.england.nhs.uk/pay-syst/national-tariff/national-tariff-payment-system/
7. HM Government. Health and Care Act 2022. March 2022.

https://www.legislation.gov.uk/ukpga/2022/31/contents/enacted

8. NHS England. Road map for integrating specialised services within Integrated Care Systems. May 2022. https://www.england.nhs.uk/wp-content/uploads/2022/05/PAR1440-specialisedcommissioning-roadmap-addendum-may-2022.pdf?dm_i=21A8,7VVXR,QZXL6D,W7GK7,1

9. NHS England. Delegation of NHS England's direct commissioning functions to integrated care boards (letter). 31st May 2022. https://www.england.nhs.uk/wp-content/uploads/2022/05/PAR1440-letter-roadmap-for-all-direct-commissioning-functions-may-2022.pdf

Appendix 1: Botulinum toxin A (BTA) PAC recommendations

Commissioning recommended

PAC reviewed indication – Recommended		
Indication	**Recommendation/criteria by**	**Date of last PAC review**
Focal spasticity in adults, including focal spasticity associated with stroke	**Recommended** BTA should be considered for all patients, including those with stroke, with focal or multifocal spasticity where there is a dynamic spastic component (as opposed to contracture) and there are anticipated functional gains in line with Royal College of Physician guidance.	June 2015
Chronic anal fissure in adults	**Recommended**	June 2015
Blepharospasm: Severe blepharospasm in adults	**Recommended**	June 2015
Hemi-facial spasm in adults	**Recommended**	June 2015
Cervical dystonia of a predominantly rotational form (spasmodic torticollis) in adults	**Recommended**	June 2015
Hyperhidrosis	BTA should be considered in the management pathway for hyperhidrosis as per PAC pathway.	June 2015

Dysphagia (including dysphagia caused by achalasia)	**Recommended** For use in patients with achalasia at high risk of aspiration or complications from pneumatic dilatation treatment, who may not be suitable candidates for surgery. Repeat injection of BTA can be administered when the clinical effect of a previous injection diminishes and the treating physician in consultation with the patient deems it necessary. Re-treatment can occur every 3-4 months and some patients may delay retreatment up to 6 months. **Not recommended for dysphagia resulting from any other condition.**	June 2015

PAC reviewed indication – Recommended		
Indication	**Recommendation/criteria by**	**Date of last PAC review**
Hirschsprung's disease	**Recommended** **Criteria for initiating therapy:** Ongoing constipation and recurrent enterocolitis despite continuing medical treatment of constipation. The effect of botulinum is transient and may wear off, and treatment may need to be repeated every 3-6 months. **Criteria for stopping therapy:** Effectiveness of this treatment to be monitored regularly on an outpatient basis, if partially successful or not successful after first injection, a repeated dose may be considered. If repeated dose is unsuccessful then treatment is to be discontinued.	June 2015
Overactive bladder	**Recommended**	June 2015
Frey's syndrome	**Recommended**	May 2021
Masseteric hypertrophy and temporomandibular disorders in adults aged 18 and over	**Recommended** In line with criteria specified in evidence review.	July 2020

Recommended in line with NICE Technology Appraisal (TA)		
Indication	**Recommendation**	**Date of last PAC review**
Migraine	Recommended in line with NICE TA260 Botulinum toxin type A for the prevention of headaches in adults with chronic migraine. June 2012	June 2015
Chronic sialorrhoea caused by neurological conditions in adults	Recommended in line with NICE TA605 Xeomin (botulinum neurotoxin type A) for treating chronic sialorrhoea. October 2019	June 2020

Commissioning not recommended

PAC reviewed indication – Not recommended	
Indication	**Date of last PAC review**
Cosmetic indications	June 2015
Laryngeal dystonia (spasmodic dystonia)	June 2015
Hidradenitis suppurativa	May 2021
Mechanical neck disorders	June 2015
Correction of squint (strabismus) in paediatrics	Nov 2021
Raynaud's disease	March 2022

Not recommended in line with NICE guidelines		
Indication	**Recommendation**	**Date of last PAC review**
Voiding Lower Urinary Tract Symptoms (LUTS) in men presumed secondary to Benign Prostatic Enlargement (BPE)	Routine use not recommended in line with NICE CG97 Lower urinary tract symptoms (LUTS) in men. If offering surgery for managing voiding LUTS presumed secondary to BPE, only consider offering botulinum toxin injection into the prostate as part of a randomised controlled trial.	June 2015

Indications commissioned by NHS England prior to 1st April 2022	
Indication	**NHSE commissioning position prior to 1st April 2022**
Focal spasticity in children (including spasticity treatment in paediatric cerebral palsy)	Commissioned by NHSE at specialist centres only (including outreach when delivered as part of a provider network)
Intravesical use in spinal cord injury	Commissioned by NHSE only when prescribed in an adult specialist centre.