Botulinum Toxin A commissioning policy

Introduction

Botulinum toxin A is a powerful neurotoxin which is used medically to relax muscles and for certain conditions there are recognised clinical benefits to patients. However, due to its mechanism of action botulinum toxin A can be used for medical conditions for which the clinical benefits have not been proven or are unclear and inconsistencies have arisen before this policy existed. Therefore this document summarises the commissioning status of botulinum toxin A for specified medical conditions.

		Preparations ✓= licensed ×= unlicensed	
Indication	**Commissioning status**	**Botox®**	**Dysport®**
Blepharospasm (facial dystonia, muscles around the eyes can cause uncontrolled blinking, lid spasms)	Indication routinely funded	✓	✓
Hemifacial spasm (movement disorder causing muscles on the side of the face to contract uncontrollably)	Indication routinely funded	✓	✓
Spasmodic torticollis (Cervical dystonia) (muscles of the neck contract involuntarily)	Indication routinely funded	✓	✓
Prophylaxis of headaches in adults with chronic migraine (In line with NICE TA 260 - headaches on at least 15 days per month of which at least 8 days are with migraine)	Indication routinely funded	✓	×
Focal spasticity, treatment of dynamic equinus foot deformity due to spasticity in paediatric cerebral palsy patients	Indication routinely funded	✓	✓
Focal spasticity in upper body. (see specific SPCs for exact licensing)	Indication routinely funded	✓	✓
Severe hyperhidrosis of the axillae	Commissioned within defined criteria – see Northamptonshire Planned Care Policy via link below	✓	×
Chronic pain	Not routinely commissioned. Existing patients who commenced treatment prior to June 2014 may continue their treatment but should have this reviewed where possible	×	×
Gastroparesis	Not routinely commissioned	×	×
Temporary improvement in the appearance of moderate to severe vertical	Not routinely commissioned	✓	×

Indication	Commissioning status	Preparations ✓= licensed ×= unlicensed Botox®	Dysport®
lines between the eyebrows seen at frown (glabellar lines), in adults <65 years old, when the severity of these lines has an important psychological impact for the patient.			

Note:
Please check SPCs (Summary of Product Characteristics) of the specific botulinum toxin preparation for exact licencing details.
Botulinum toxin units are not interchangeable from one product to another.
Botulinum toxin type A is a high cost medicine which is excluded from Payment By Results (PbR).
Botulinum toxin is a single red drug to be prescribed in hospitals only.

Botulinum toxin A is commissioned for the following indications provided the relevant caveats are met for the stated indication:

Indication	Commissioning status	Preparations ✓= licensed ×= unlicensed Botox®	Dysport®
Achalasia	Commission botulinum toxin A for patients at high risk (e.g. elderly patients) of oesophageal perforation from pneumatic dilation treatment	×	×
Management of bladder dysfunction in adults not adequately managed with anticholinergics in line with NICE CG 171: • **Overactive bladder with urinary incontinence, urgency and frequency** • **Neurogenic detrusor overactivity with urinary incontinence due to subcervical spinal cord injury or MS**	Indications routinely funded provided prior approval is sought and agreed with Prescribing and Medicines Management at the CCG.	✓	×
Anal fissure	Commission botulinum toxin A injections as third line treatment for patients who have failed to gain benefit from GTN 0.4% ointment first line and diltiazem 2% cream/ointment second line.	×	×

MHRA Drug Safety Update Botulinum toxin products: rare but serious risk

Products that contain botulinum toxin are associated with the risk of serious adverse reactions due to distant spread of toxin. Recommendations include:

- Only physicians with appropriate experience (including use of the required equipment) should administer products that contain botulinum toxin
- 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

References

1. Summary of Product Characteristics Botox 100units (Allergan) Text revised Dec 2013 http://www.medicines.org.uk/emc/medicine/112/SPC/BOTOX+100+Units/
2. Summary of Product Characteristics Dysport 300units, 500units (Ipsen) Text revised 11th Dec 2013 http://www.medicines.org.uk/emc/medicine/870/SPC/Dysport+300+units%2c+Dysport+500+units/
3. MHRA Drug Safety Update October 2007; Vol 1, Issue 3: 10. http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON079276

Appendix 1. Evidence/Guidance summary for botulinum toxin A indications which are not routinely commissioned

Indication	Commissioning status	Evidence/Guidance	Comments
Temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows seen at frown (glabellar lines), in adults <65 years old, when the severity of these lines has an important psychological impact for the patient.	Not routinely commissioned	Scottish Medicines Consortium (SMC) do not recommend the following botulinum toxin A preparations for this indication: Bocouture http://www.scottishmedicines.org.uk/SMC_Advice/Advice/695_11_botulinum_toxin_type_a_Bocouture/botulinum_toxin_type_a_Bocouture Azzalure http://www.scottishmedicines.org.uk/SMC_Advice/Advice/679_11_botulinum_toxin_Type_a_Azzalure/botulinum_toxin_Type_A_Azzalure Vistabel http://www.scottishmedicines.org.uk/SMC_Advice/Advice/680_11_botulinum_toxin_Vistabel/botulinum_toxin_Vistabel British Association of Plastic Reconstructive and Aesthetic Surgeons – Guidelines for commissioners of plastic surgery services. Botulinum toxin is not available for the treatment of facial ageing or excessive wrinkles. http://www.bapras.org.uk/downloaddoc.asp?id=425	SMC noted that this indication was cosmetic in nature. Guidance from the British Association of Plastic Reconstructive and Aesthetic Surgeons indicate botulinum toxin is not available on the NHS for the treatment of facial ageing or excessive wrinkles.
Chronic pain	Not routinely commissioned	**Myofascial pain syndrome. Cochrane review April 2012.** http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007533.pub2/full Implications for practice The limited available evidence, involving a total of 233 participants from four studies, suggests that there was some improvement in pain intensity, duration of daily pain and more side effects in the botulinum toxin A (BTXA) group. There is currently only limited evidence to support the use of botulinum toxin in the treatment of myofascial pain syndrome (MPS). Authors' conclusions There is inconclusive evidence to support the use of botulinum toxin in the treatment of	The evidence for using botulinum toxin for the indications of chronic pain do not provide enough information on which to formulate recommendations.

Indication	Commissioning status	Evidence/Guidance	Comments
		MPS based on data from four studies with a total of 233 participants, which we considered adequate to be included in this review. Meta-analyses were not possible due to the heterogeneity between studies. We suggest that in future studies the same methodology to assess pain, a standardised dose of treatment, follow-up of at least four months (to observe the maximum/minimum curve of the drug effect) and appropriate data presentation should be used. More high-quality RCTs of botulinum toxin for treating MPS need to be conducted before firm conclusions on its effectiveness and safety can be drawn. **Botulinum toxin for subacute/chronic neck pain. Cochrane review July 2011.** http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008626.pub2/full Implications for practice Based on the current evidence, there is high quality evidence that BoNT-A alone is not better than saline for patients with subacute or chronic neck pain, based on the lack of the short-term benefit. The available evidence does not support the clinical use of BoNT-A for patients with subacute or chronic neck pain, used either alone or in combination with any other therapy. **Medicinal and injection therapies for mechanical neck disorders. Cochrane review July 2007.** http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000319.pub4/full#CD000319-sec1-0006 Implications for practice The major limitation of this review is the lack of replication in the findings of the included studies. There is moderate evidence for the benefit of intravenous methylprednisolone given within eight hours of acute whiplash, from a single trial. Lidocaine injection into myofascial trigger points appears effective in two trials. There is moderate evidence that Botulinum toxin A is not superior to saline injection for chronic MND. There is limited evidence for epidural methylprednisolone and lidocaine in chronic neck disorder with	

Indication	Commissioning status	Evidence/Guidance	Comments
		radicular findings. There is unclear evidence for oral psychotropic agents. Based on a limited number of studies providing advice on NSAIDs and analgesics it is not possible to draw conclusions. **Botulinum toxin injections for low-back pain and sciatica. Cochrane review January 2011.** http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008257.pub2/full Implications for practice There is a lack of high quality studies evaluating BoNT injections for patients with standard LBP. Among the studies that exist, there is significant heterogeneity in trial design and outcome parameters. The current body of evidence does not support the use of BoNT injections to improve pain or function in patients with LBP. There is only low quality evidence that BoNT injections are more effective than saline or corticosteroid injections or acupuncture for reducing low-back pain. Therefore, future research is very likely to change the results and our confidence in them. The present literature has yet to address the long term benefits of BoNT injections or the cost-benefits of this therapy. Finally, published studies have not addressed how pain relief from BoNT injections translates into clinically relevant outcomes for patients with LBP. Conlin A, Bhogal S, Sequeira K, Teasell R. **Treatment of whiplash-associated disorders - part II: medical and surgical interventions.** Pain Research and Management 2005; 10(1): 33-40 http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?View=Full&ID=12005000022 Centre for Review and Dissemination, University of York. CRD Summary This review evaluated medical and surgical interventions for whiplash-associated disorder following vehicle collision. It concluded that there was moderate evidence that radiofrequency neurotomy could reduce pain and psychological distress, but conflicting evidence for other surgery, steroid injections and botulinum treatment. Despite some	

Indication	Commissioning status	Evidence/Guidance	Comments
		methodological aspects being unclear, most of the conclusions were justified although the evidence for neurotomy came from one small randomised controlled trial. Practice: The authors stated that recommendations for clinical practice for medically based or surgical interventions cannot be made from the evidence in this review. Teasell RW, McClure JA, Walton D, Pretty J, Salter K, Meyer M, Sequeira K, Death B. **A research synthesis of therapeutic interventions for whiplash-associated disorder (WAD). Part 5: Surgical and injection-based interventions for chronic WAD** Pain Research and Management 2010; 15(5): 323-334 http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?LinkFrom=OAI&ID=12010008088 Centre for Review and Dissemination, University of York. CRD summary The authors concluded that it was not possible to draw firm conclusions for the effectiveness of any surgical or injection-based intervention for patients with chronic whiplash-associated disorder. Despite the risk that relevant studies were missed and the review was prone to language and publication biases, the authors' cautious conclusions reflected the limited evidence presented and are probably reliable.	
Gastroparesis	Not routinely commissioned	**The role of endoscopy in gastroduodenal obstruction and gastroparesis. American Society for Gastrointestinal Endoscopy** http://www.asge.org/uploadedFiles/Publications_and_Products/Practice_Guidelines/The%20role%20of%20Endoscopy%20in%20gastroduodenal%20obstruction%20and%20gastroparesis.pdf **Recommendations** There are insufficient data to make a recommendation regarding the role of botulinum toxin in the treatment of gastroparesis.	There is conflicting outcomes from clinical trials and the effectiveness of botulinum toxin in this indication is not clear.

Appendix 2.. Evidence/Guidance summary for botulinum toxin A indications which are commissioned/commissioned with caveats

Indication	Commissioning status	Evidence/Guidance	Comments
Blepharospasm (facial dystonia, muscles around the eyes can cause uncontrolled blinking, lid spasms)	Indication routinely funded	**Cochrane review Botulinum Toxin A therapy for blepharospasm. April 2004**. Cochrane comment: Bt therapy is probably the second most important discovery in movement disorder therapy after levodopa. Few drugs have such an obvious benefit as Bt has in some dystonias. The strength of this effect in blepharospasm has probably been responsible for the paucity of RCTs comparing BtA with placebo. Even though we do not have high quality, randomised, controlled data, indications are that BtA is indeed effective and safe in blepharospasm. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004900.pub2/abstract **Cost effectiveness review by University of York, National Institute for Health Research. January 2011.** In the treatment of blepharospasm, Xeomin increased costs by £668.92 and improved the QALYs by 0.1791, compared with placebo, resulting in an incremental cost per QALY gained of £3,734.40. The key drivers of the model were the utility values and the price of the Xeomin, but Xeomin remained cost-effective in all scenarios at the standard threshold of £30,000 per QALY. http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?LinkFrom=OAI&ID=22010001336	Evidence supports efficacy and it is cost effective from the review.
Hemifacial spasm (movement disorder causing muscles on the side of the face to contract uncontrollably)	Indication routinely funded	**Cochrane review Botulinum Toxin A therapy for hemifacial spasm. January 2005.** Author conclusions (implications for practice): All studies available strongly suggest that BtA is effective and safe for treating hemifacial spasm. Despite the absence of large RCTs, the efficacy of BtA for HFS is not in doubt. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004899.pub2/abstract **MTRAC review Botulinum Toxin A summary sheet. October 1995.** Conclusion: Botulinum toxin is effective in the treatment of both blepharospasm and hemifacial spasm. Administration should be performed by those with a thorough knowledge of the	Evidence supports efficacy, but no information on cost effectiveness was found.

Indication	Commissioning status	Evidence/Guidance	Comments
		anatomy and pathophysiology of the condition being treated, with experience of selecting and administering the appropriate dose and managing potential adverse effects. It is not therefore suitable for general prescribing in general practice. http://www.keele.ac.uk/media/keeleuniversity/fachealth/fachealthsop/mtrac/documents/summary/BOTULINUMs.pdf	
Spasmodic torticollis (Cervical dystonia) (muscles of the neck contract involuntarily)	Indication routinely funded	**Cochrane review Botulinum Toxin A therapy for cervical dystonia. January 2005.** Cochrane conclusion (Implications for practice): Despite the variety of trial formats, virtually all the trials individually, and each outcome measure separately, suggested that a single injection cycle of BtA is effective and safe for treating cervical dystonia. Enriched trials (using patients previously treated with BtA), suggest that further injection cycles continue to work for most patients. Appropriate injections of BtA into cervical muscles at therapeutic doses are well tolerated, and although adverse effects occur they are transient and rarely severe. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003633.pub2/abstract **NHS England Deep Brain Stimulation (DBS) commissioning policy. April 2013.** Before using DBS patients need to have tried and failed botulinum toxin treatment. http://www.england.nhs.uk/wp-content/uploads/2013/04/d03-p-b.pdf Page 8 **Cost effectiveness review by University of York, National Institute for Health Research. January 2011.** In the treatment of cervical dystonia (rotational), Xeomin increased the costs by £2.558.88 and improved the QALYs by 0.3973, compared with placebo, resulting in an incremental cost per QALY gained of £6,441.39. The key drivers of the model were the utility values and the price of the Xeomin, but Xeomin remained cost-effective in all scenarios at the standard threshold of £30,000 per QALY. http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?LinkFrom=OAI&ID=22010001336	Evidence supports use of botulinium toxin for cervical dystonia. NHS England have a commissioning policy that includes the use of botulinum toxin before deep brain stimulation is funded.

Indication	Commissioning status	Evidence/Guidance	Comments
Prophylaxis of headaches in adults with chronic migraine (headaches on at least 15 days per month of which at least 8 days are with migraine)	Indication routinely funded	**NICE TA 260 Botulinum toxin type A for the prevention of headaches in adults with chronic migraine. June 2012.** Botulinum toxin type A is recommended as an option for the prophylaxis of headaches in adults with chronic migraine: • that has not responded to at least three prior pharmacological prophylaxis therapies **and** • whose condition is appropriately managed for medication overuse. http://publications.nice.org.uk/botulinum-toxin-type-a-for-the-prevention-of-headaches-in-adults-with-chronic-migraine-ta260	NHS organisations have a statutory obligation to fund NICE Technology Appraisals.
Management of bladder dysfunction in adults not adequately managed with anticholinergics: • **Overactive bladder with urinary incontinence, urgency and frequency** • **Neurogenic detrusor overactivity with urinary incontinence due to**	Indications routinely funded	**NICE CG 171 Urinary incontinence: The management of urinary incontinence in women. September 2013.** After an MDT review, offer bladder wall injection with botulinum toxin A[7] to women with OAB caused by proven detrusor overactivity that has not responded to conservative management (including OAB drug therapy). Start treatment with botulinum toxin A[7] only if women: • have been trained in clean intermittent catheterisation and have performed the technique successfully, **and** • are able and willing to perform clean intermittent catheterisation on a regular basis for as long as needed. http://publications.nice.org.uk/urinary-incontinence-cg171/recommendations#pharmacological-treatment **SMC guidance September 2013.** **Botulinum toxin type A (Botox)** is accepted for use within NHS Scotland. **Indication under review:** management of urinary incontinence with neurogenic detrusor overactivity due to subcervical spinal cord injury (traumatic or not traumatic) or multiple sclerosis, who are not adequately managed with anticholinergics. Patients should	Clinical guidelines are recommendations by NICE on the appropriate treatment and care of people with specific diseases and conditions within the NHS. They are based on the best available evidence. NHS organisations are entitled to take decisions which do not follow Guidance (other than NICE TAs) if they have a good reason to do

Indication	Commissioning status	Evidence/Guidance	Comments
subcervical spinal cord injury or MS		already be catheterising with or willing and able to catheterise if required. http://www.scottishmedicines.org.uk/files/advice/botulinum_toxin_Type_A_Botox_FINAL_September_2013_website.pdf **NICE CG 148 Urinary incontinence in neurological disease: Management of lower urinary tract dysfunction in neurological disease. August 2012** Where dysfunction of the urinary bladder during the storage phase of micturition cycle can take the form of involuntary contractions of the bladder (neurogenic detrusor overactivity) botulinum toxin A should be offered to adults: • With spinal cord disease AND • With symptoms of an overactive bladder / with urodynamic investigations showing impaired bladder storage AND • In whom anti-muscarinic drugs have been ineffective or poorly tolerated. http://publications.nice.org.uk/urinary-incontinence-in-neurological-disease-cg148/guidance **NICE CG 97 Lower urinary tract symptoms: The management of lower urinary tract symptoms in men. May 2010.** 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. Consider offering bladder wall injection with botulinum toxin to men with detrusor overactivity only if their symptoms have not responded to conservative management and drug treatments and the man is willing and able to self-catheterise. http://publications.nice.org.uk/lower-urinary-tract-symptoms-cg97/guidance#drug-treatment	so. The availability of resources and competing priorities can be a good reason.
Focal spasticity, treatment of dynamic equinus	Indication routinely funded	**NICE CG 145 Spasticity in children and young people with non-progressive brain disorders: Management of spasticity and co-existing motor disorders and their early musculoskeletal complications. July 2012.**	Evidence supports efficacy but no cost effectiveness review

Indication	Commissioning status	Evidence/Guidance	Comments
foot deformity due to spasticity in paediatric cerebral palsy patients		Consider botulinum toxin type A[5] treatment in children and young people in whom focal spasticity of the upper limb is: • impeding fine motor function • compromising care and hygiene • causing pain • impeding tolerance of other treatments, such as orthoses • causing cosmetic concerns to the child or young person. Consider botulinum toxin type A[5] treatment where focal spasticity of the lower limb is: • impeding gross motor function • compromising care and hygiene • causing pain • disturbing sleep • impeding tolerance of other treatments, such as orthoses and use of equipment to support posture • causing cosmetic concerns to the child or young person. Key Point for implementation • Following treatment with botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy, provide an adapted physical therapy programme as an essential component of management. See clinical guideline 145 for more details. http://publications.nice.org.uk/spasticity-in-children-and-young-people-with-non-progressive-brain-disorders-cg145/guidance#botulinum-toxin-type-a-2 **Cochrane review. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy (UPDATE). January 2010.** Author conclusions: This systematic review found high level evidence supporting the use	was found.

Indication	Commissioning status	Evidence/Guidance	Comments
		of Botulinum toxin A as an adjunct to managing the upper limb in children with spastic Cerebral Palsy. Botulinum toxin A should not be used in isolation but should be accompanied by planned occupational therapy. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003469.pub4/abstract;jsessionid=C9C64D3DE7122321B9470473FE53C9F5.f03t04	
Focal spasticity, treatment of wrist and hand disability due to upper limb spasticity associated with stroke in adults	Indication routinely funded	**BoTULS: a multicentre randomised controlled trial to evaluate the clinical effectiveness and cost-effectiveness of treating upper limb spasticity due to stroke with botulinum toxin type A. *Health Technol Assess* 2010;14(26):1–142** The base-case incremental cost-effectiveness ratio was £93,500 per QALY gained and estimation of the cost-effectiveness acceptability curve for botulinum toxin type A plus the upper limb therapy programme indicated that there was only a 0.36 probability of its being cost-effective at a threshold ceiling ratio of £20,000 per QALY. Conclusion – implications for healthcare Management of spasticity should focus upon realistic goals for treatment. These results will help to inform clinicians which outcomes may be improved by the addition of botulinum toxin type A to an upper limb therapy programme to treat upper limb spasticity due to stroke. Most patients will not achieve an enhanced improvement in active upper limb function by the addition of botulinum toxin to an upper limb therapy programme. However, botulinum toxin type A may have a role to play in improving the ability of some patients to undertake some basic upper limb functional tasks and may reduce pain at 12 months. Despite some clinical benefits, the addition of botulinum toxin type A to an upper limb therapy programme does not appear to be a cost-effective treatment for the patients included in this study. http://www.hta.ac.uk/execsumm/summ1426.htm **Botulinum toxin type A (Botox®)** is accepted for use within NHS Scotland. **Indication under review:** focal spasticity, including the treatment of wrist and hand disability due to upper limb spasticity associated with stroke in adults. In a placebo-controlled study, botulinum toxin type A was significantly superior to placebo	NICE clinical guidance does not include a recommendation for using botulinum toxin for spasticity post stroke, although it is research recommendation. However, the Royal College of Physicians reviewed the evidence and recommend it as a treatment option in specific circumstances. SMC has accepted botulinum toxin for use in focal spasticity, including treatment of wrist and hand disability due to upper limb

Indication	Commissioning status	Evidence/Guidance	Comments
		in terms of the disability assessment scale and efficacy was maintain. http://www.scottishmedicines.org.uk/files/advice/botulinum_type_A_Botox_2nd_Resub_FINAL_Feb_2011.doc_for_website.pdf **NICE CG168 Stroke Rehabilitation. June 2013.** Mention of botulinum toxin that is used in clinical practice for shoulder pain post stroke that may have a role in spasticity post stroke. No evidence was reviewed in NICE guidance for this use. http://guidance.nice.org.uk/CG162 http://www.nice.org.uk/nicemedia/live/14182/64094/64094.pdf **Spasticity in adults: management using botulinum toxin National Guidelines. Royal College of Physicians January 2009** Local intramuscular injection of botulinum toxin (BT) is an established, well-tolerated treatment in the pharmacological management of focal spasticity. There is a strong body of Level I evidence for its effectiveness in the management of upper and lower limb spasticity. http://www.rcplondon.ac.uk/sites/default/files/documents/spasticity-in-adults-management-botulinum-toxin.pdf	spasticity associated with stroke in adults.
Hyperhidrosis of the axillae in adults	Commissioned within defined criteria – see link to Planned Care Policy (which is aligned to East Midlands Cosmetic Policy)	**Northamptonshire Planned Care Policy (aligned to East Midlands Cosmetic Policy)** http://www.nhsmknorthants.co.uk/resources/uploads/files/Botox%20treatment%20for%20Axillary%20Hyperhidrosis%20v1_1.pdf **NICE CG 159 Social Anxiety disorder. May 2013** Do not offer botulinum toxin to treat hyperhidrosis (excessive sweating) in people with social anxiety disorder. This is because there is no good-quality evidence showing benefit from botulinum toxin in the treatment of social anxiety disorder and it may be harmful. http://guidance.nice.org.uk/CG159	Evidence indicates that botulinum toxin is safe and effective in hyperhidrosis of the axillae, but the exact place in therapy is not as clear.

Indication	Commissioning status	Evidence/Guidance	Comments
		Clinical Knowledge Summaries – Hyperhidrosis revised July 2013 http://cks.nice.org.uk/hyperhidrosis#!supportingevidence1:1 The quality of trial evidence for the listed secondary care treatments varies depending on the individual treatment, and is often based on expert opinion. Whilst there is evidence of the efficacy and safety (when performed by trained healthcare professionals) of botulinum toxin in the treatment of primary axillary hyperhidrosis from four randomized, controlled trials (RCTs), including nearly 1000 people, the evidence for most other treatments or botulinum toxin at other sites (beside the axillae) is either from small or non-randomized, controlled trials, case series, or expert opinion. **Bandolier review** – Four randomised, double blind trials review The results are interesting but should be interpreted with caution. The main caveat is that there are limited data at present. With one exception, the studies were small and used within patient comparisons. That doses and outcomes differed also muddies the waters, and it is difficult to say whether the effects of the toxin are greater with increased dose. It does appear, though, that botulinum toxin reduces symptoms in this rare condition. The report of increased palmer sweating in patients with axillary hyperhidrosis should be noted, and it was not reported in the trial whether this subsided as the effects of treatment wore off. http://www.medicine.ox.ac.uk/bandolier/booth/neurol/hyperhid.html **NGH formulary** Use for hyperhidrosis is not funded by Nene Commissioning. Prior written approval from Nene Commissioning is required on a case by case basis for this indication. Please attach proof of approval when sending prescription to Pharmacy. http://www.northamptonformulary.nhs.uk/chaptersSubDetails.asp?FormularySectionID=4&SubSectionRef=04.09.03&SubSectionID=B100#1626 **Botulinum toxin treatment of axillary and palmar hyperhidrosis**	

Indication	Commissioning status	Evidence/Guidance	Comments
		Botulinum toxin increases quality of life and reduces sweat production in comparison to both placebo and aluminum chloride in patients with primary axillary hyperhidrosis. The quality of evidence is stronger with regard to placebo than it is with regard to aluminium chloride. Also patients with primary palmar hyperhidrosis experience an increased quality of life and a reduced sweat production of similar magnitudes when BTX treatment is compared to placebo. However, the quality of evidence is not as high as it is for axillary hyperhidrosis. The duration of the treatment effect is three to seven months. http://www.crd.york.ac.uk/crdweb/ShowRecord.asp?LinkFrom=OAI&ID=32013000130 http://www.sahlgrenska.se/upload/SU/HTA-centrum/HTA-rapporter/HTA-report%20BTX%202012-03-27%20%20publiceras.pdf	
Achalasia	Commission botulinum toxin A for patients at high risk (e.g. elderly patients) of oesophageal perforation from pneumatic dilation treatment	**Cochrane review. Endoscopic pneumatic dilation versus botulinum toxin injection in the management of primary achalasia (Review). Oct 2006 (updated Dec 2008).** Achalasia is an oesophageal motility disorder which results in increased lower oesophageal sphincter (LOS) tone and symptoms of difficulty swallowing. Treatments are aimed at reducing the tone of the LOS and include the endoscopic options of pneumatic dilation (PD) or botulinum toxin (BTX) injection. We set out to undertake a systematic review comparing randomised controlled trials that examined the efficacy and safety of PD and BTX injection in patients with achalasia. Six randomised controlled trials were reviewed, and four were suitable for meta-analysis. Meta-analysis suggested that, although both interventions have similar initial response rates, the remission rates at 6 and 12 months were significantly greater with PD. No serious adverse outcomes occurred in participants receiving BTX, whilst PD was complicated by perforation in three cases. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005046.pub2/abstract;jsessionid=5CFC34E0A0D82ED3B2522E7E3C4830D1.f03t02	Evidence showed pneumatic dilation was complicated by oesophageal perforation. Although the evidence shows botulinum toxin was not as effective as pneumatic dilation for achalasia over 6 to 12 months, it is useful treatment option and other commissioning organisations support this.
Anal fissure	Commission botulinum toxin A injections as third	**NICE Evidence Summary Unlicensed Off label Medicine 14: Chronic anal fissure: botulinum toxin type A injection** Evidence from 2 systematic reviews and 4 further randomised controlled trials (RCTs)	Evidence suggests botulinum toxin is no better or worse than

Indication	Commissioning status	Evidence/Guidance	Comments
	line treatment for patients who have failed to gain benefit from GTN 0.4% ointment first line and diltiazem 2% cream/ointment second line.	suggests that botulinum toxin type A injection is less effective than surgery, no better or worse than topical glyceryl trinitrate (GTN; mostly 0.2% ointment) or isosorbide dinitrate, and no better than placebo or lidocaine at healing anal fissure. The Medicines and Healthcare products Regulatory Agency (MHRA) has warned healthcare professionals about the rare but serious risk of toxin spread when using all types of botulinum toxin. • Importantly, no studies were identified that compared botulinum toxin type A with 0.4% GTN ointment, the only licensed treatment for chronic anal fissure. Most studies in the 2 systematic reviews used unlicensed 0.2% GTN ointment or surgery as the main comparator. • The only currently licensed non-surgical treatment for chronic anal fissure in the UK is topical 0.4% glyceryl trinitrate (GTN) ointment (brand name Rectogesic 4 mg/g rectal ointment). This is licensed for the relief of pain associated with chronic anal fissure in adults for a maximum of 8 weeks. It is not indicated for the healing of chronic anal fissure. It is not recommended for use in children and young people aged under 18 years because of a lack of data on safety and efficacy. • 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. 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. http://publications.nice.org.uk/esuom14-chronic-anal-fissure-botulinum-toxin-type-a-injection-esuom14	topical GTN.