The East of England
Priorities Advisory Committee
A function of the PrescQIPP Programme

POLICY DOCUMENT

Management of hyperhidrosis

PAC recommendations

- **Patients with localised (focal) hyperhidrosis should initially be treated in primary care.**
- **Patient with localized hyperhidrosis Disease Severity Scale (HDSS) score or 3 or 4 who do not respond to initial treatment in primary care should be referred to secondary care (see treatment pathway).**
- **Patients with generalised hyperhidrosis should be referred to secondary care.**
- **Oxybutynin immediate release (IR, off-label) should be prescribed in preference to glycopyrronium bromide (unlicensed) or propantheline bromide (less effective). The level of evidence for oxybutynin IR and glycopyrronium bromide are of similar strength (weak).**
- **Endoscopic Thoracic Sympathectomy (ETS) should no longer be offered due to weak evidence and a significant risk of morbidity.**
- **Tap-water iontophoresis is non-invasive and should be offered for palmar, plantar and axillary hyperhidrosis. Axillary iontophoresis may be effective in practice despite lack of published evidence (expert opinion). Costs should be limited to activity costs for the initial treatment schedule.**
- **Iontophoresis with glycopyrronium bromide is not recommended as the level of evidence for adding glycopyrronium bromide solution is weak and costs in primary care are prohibitive. It is not appropriate for ongoing prescriptions to originate from secondary care as patients could be discharged from the service after a successful trial of iontophoresis.**
- **Ablation surgery of the axillae should be offered as an alternative to botulinum toxin A in specialised centres.**

Introduction

Multiple localised and systemic therapies are available for the management of hyperhidrosis. The purpose of this document is to provide an evidence based and cost-effective treatment pathway for primary and secondary care.

Hyperhidrosis is a disorder of excessive sweating beyond what is required for thermoregulation. The condition may be localised (also referred to as primary or focal hyperhidrosis) or secondary to medication or a medical condition (generalised hyperhidrosis).[1] The most important issue in directing therapy for hyperhidrosis is to differentiate between primary and secondary hyperhidrosis and between subtypes of primary hyperhidrosis (i.e. palmar, plantar, axillary, or craniofacial – the areas with a high density of eccrine sweat glands).

A complex dysfunction of the innervation of sweat glands via the sympathetic nervous system is likely to play a role in the pathophysiology of hyperhidrosis. Primary hyperhidrosis increases the risk of cutaneous infection and has a significant psychosocial burden and a negative impact on quality of life.[2]

As there is no standardised definition of 'excessive sweating', clinicians base their diagnoses in part on measures to estimate how hyperhidrosis affects a patient's quality of life. The Hyperhidrosis Disease Severity Scale (HDSS) should be used as this is easy to use and validated against other questionnaires (see appendix 1).[3]

The recommendations in this policy are broadly in line with a recent publication in the British Medical Journal[4] and the Clinical Knowledge Summary on hyperhidrosis.[5] However, the pathway is simplified by recommending GPs could initiate oral anticholinergic prior to referral into secondary care. A Cochrane review is in preparation; the contents of this review should be reconsidered following publication.[6]

Treatment pathway for focal hyperhidrosis in primary care

History and diagnosis (exclude secondary hyperhidrosis)

Offer lifestyle advice: http://cks.nice.org.uk/hyperhidrosis and http://www.hyperhidrosisuk.org/self-help.html

Assess site and HDSS score.

Refer to secondary care in case of secondary hyperhidrosis of unknown cause.

Address cause if known (e.g. hyperthyroidism, menopause, medication, amphetamines)

Primary/focal hyperhidrosis:

Topical aluminium salt + 1% hydrocortisone cream if necessary. Advise to purchase over the counter.

Successful after 1 month (see criteria below): continue and review regularly .

Not successful after 1 month

Consider oral anticholinergic* (off-label)

NOT successful after 1 month or treatment limiting side-effects:

HDSS 1-2: stop treatment.

HDSS 3-4: refer to secondary care.

Criteria for successful treatment of hyperhidrosis: reduction in HDSS from 3 or 4 to HDSS 1 or 2. Treatment failure can be defined as no change in HDSS score after 1 month of therapy or lack of tolerability for the treatment.

* First-line Oxybutynin 2.5mg IR: start with 2.5mg od and gradually titrate according to response. Alternative options could be offered if effective but not well tolerated (see NICE CG171: Management of urinary incontinence (off-label) for alternative anticholinergics), though lack evidence. Propantheline bromide is licensed for hyperhidrosis but less effective. Glycopyrronium bromide is unlicensed in the UK and costs are prohibitive; evidence base is similar as for oxybutynin.

Treatment pathway for hyperhidrosis in secondary care (HDSS 3-4 only)

Assess HDSS and hyperhidrosis area (use minor iodine).

If HDSS 1-2: refer back to primary care.

Repeat lifestyle advice and recommend use of topical aluminium chloride if not already tried in primary care before offering any alternative treatment.

Axillary	Palmar /plantar hyperhidrosis	Craniofacial
Axillary iontophoresis (initial schedule day 1, 2, 4, 7, 10, 15, 22) Assess after 1 month. Patients are expected to purchase their own machine for home treatment if successful.	Iontophoresis (initial schedule day 1, 2, 4, 7, 10, 15, 22) Assess after 1 month. Patients are expected to purchase their own machine for home treatment if successful.	
Not successful: Botulinum toxin A (Botox®) 50 units per axilla OR local surgery (laser sweat ablation or retrodermal curettage where available and commissioned.	Not successful: Consider anticholinergic (if not already tried in primary care) or Botulinum toxin A* (for palmar hyperhidrosis only, not for plantar) with adequate anaesthesia. NOTE: Associated with significant morbidity.	Consider anticholinergic (if not already tried in primary care) or Botulinum toxin A*

If successful, repeat injections with botulinum toxin A can be given when production of sweat is back to 50% of baseline, with a minimum treatment interval of 16 weeks.

NOT successful or treatment limiting side-effects: STOP treatment.

Criteria for successful treatment: reduction in HDSS from 3 or 4 to HDSS 1 or 2.

Treatment failure for secondary care options can be defined as no change in HDSS score after 4 weeks of therapy (3 months for surgery) or lack of tolerability for the treatment.

With botulinum toxin A injections, it is important to evaluate the treatment area as apparent failure may be due to a small area being missed. In this case, repeat injections of the symptomatic area (at the same or higher dose) once before concluding whether treatment with botulinum toxin A is successful or not.

*At time of publication, there was no Botulinum toxin A product available in the UK that is licensed for hyperhidrosis other than axillary hyperhidrosis. Products are not interchangeable. Centres are advised to consult the latest information available from the UK marketing authorisation holders of the different botulinum toxin A preparations.

Clinical evidence

Localised treatment

Antiperspirants with aluminium salts

If regular antiperspirants do not help, products containing aluminium chloride salts can be tried. Licensed products include Anhydrol Forte and Driclor (both roll-on) which can be purchased from a community pharmacy or online (for less than the prescription charge), but are also available on prescription. They are usually applied nightly at bedtime; when clinical efficacy is noted (in 1–2 weeks for most patients), the frequency can be reduced. Alternatives are Odaban spray or lotion (unlicensed but prescribable) and Zeasorb absorbent powder (for plantar hyperhidrosis).[5]

Local irritation is a common limitation of topical aluminium chloride, but can in many cases be controlled with occasional application of 1% hydrocortisone cream the morning after treatment (also available over the counter).[7,8] Another problem is that these products can stain clothing.

The strength of evidence for aluminium chloride for hyperhidrosis is poor and is predominantly based on a few case-series and quasi-controlled studies.

It should be used at night in a cool environment without physical or emotional stress and washed off in the morning. For the first week it should be applied for 3 to 5 consecutive nights, then once or twice a week.

Summary of evidence for aluminium chloride

	Axillary	Plantar/palmar
20% aluminium chloride in ethanol	24/38 patients achieved satisfactory results (subjective); 26% experienced treatment limiting irritation.[7] 64/65 achieved excellent control (subjective).[8]	12/12 patients (17% reduction of water loss at 1 week and 30% reduction at week 4; measured through evaporimeter); 1 patient experienced treatment-limiting irritation.[9]
25% aluminium chloride in ethanol:	30/30 patients had reduction of 25% (subjective), 26% experienced treatment-limiting irritation.[10]	12/13 patients with palmar hyperhidrosis responded after 3-4 weeks of treatment and 10/11 patients with plantar hyperhidrosis after 5-6 weeks of treatment.[11]
Aluminium chloride in 4% salicylic acid (different strengths)	Good response in axillary, palmar, plantar and groin hyperhidrosis with good tolerability in 238 patients.[12]	
Zeasorb absorbent powder	No studies identified	

Topical glycopyrrolate

As acetylcholine is the main neurotransmitter of the nerve innervating sweat glands, there is a pharmacological rationale for using anticholinergic agents to treat hyperhidrosis.

Topical glycopyrrolate in a solution or cream (0.5%-4%) is not available commercially, but can be prepared by a specials manufacturer. The evidence for topical glycopyrrolate is derived from case-series and consensus statements based on expert opinion for use in various types of gustatory sweating and craniofacial hyperhidrosis, but is also sometimes also used for axillary and palmar hyperhidrosis. The level of evidence for topical glycopyrronium is weak.[13]

Guidelines for focal hyperhidrosis based on expert opinion from British dermatologists do not mention use of glycopyrronium except when used with iontophoresis.[14] However, glycopyrrolate cream and solution are included in the British Association of Dermatologists list of preferred unlicensed dermatological preparations (specials).[15] A yet to be published study using 1% glycopyrrolate in cetomacrogol cream demonstrated only limited response for axillary hyperhidrosis: only 2 out of 35 patients (6%) treated indicated they would wish to continue treatment.[16]

Summary of evidence

	Craniofacial	Gustatory
2% glycopyrrolate	Half forehead with placebo and half with glycopyrrolate. 24/25 patients were satisfied with the effectiveness; one did not tolerate glycopyrrolate due to headache. Improvement lasted 1–2 days for most patients.[17]	Compensatory hyperhidrosis post-sympathectomy: 8/10 patients responded, 2 discontinued due to systemic anticholinergic effects.[18]
0.5%-1% glycopyrrolate	-	Frey's syndrome - gustatory sweating following parotidectomy-induced facial nerve injury: 16/16 patients found it was effective and free of adverse effects.[19]
Unspecified %	-	Diabetic patients (cross-over study):13/13 patients experienced a significant reduction in sweat response to challenge (>80% reduction) as well as a decrease in the frequency of episodes.[20]

Iontophoresis

While tap water iontophoresis is known to be highly effective, several studies have reported augmented effects by adding glycopyrrolate. The evidence to support this is weak.

There is no published evidence on axillary iontophoresis. Dermatologists have indicated this is a useful non-invasive treatment option for their patients, especially where access to Botulinum toxin A is limited.[21]

Summary of evidence

	Plantopalmar
Tap water	Left-right comparison; 15/18 patients responded.[22]
Tap water	Left-right comparison; significant reduction in sweat production. In 6 patients receiving maintenance therapy sweat production was reduced by 81%.[23]
0.05% glycopyrrolate vs. tap water	Left-right comparison with unilateral tap water, unilateral glycopyrrolate and bilateral glycopyrrolate iontophoresis. 20/20 patients reported benefit of iontophoresis. 3/20 did not achieve dryness with unilateral treatment and 2/20 did not achieve dryness with any of these options. Mean duration of dryness was significantly greater with use of glycopyrronium compared to tap water.[24]
0.05% glycopyrrolate	22/25 patients with palmar hyperhidrosis reported dryness; all reported improvement in symptoms and 81.8% reported improvement on subjective severity scores.[25]

Botulinum toxin A

Currently, the only licensed product for the treatment of axillary hyperhidrosis is Botox®. Treatment of hyperhidrosis with other botulinum toxin preparations or for other areas of the body is off-label. Injections can be painful (particularly in the hands and soles) and need to be repeated every 6 -8 months.[6]

The majority of evidence for botulinum toxin A is for axillary hyperhidrosis.[26,27] Evidence for use in palmar hyperhidrosis is based on smaller studies of lower quality. No trials were identified for plantar and craniofacial hyperhidrosis. Most studies have been conducted by the same authors, some of whom received honoraria for their work.

Axillary hyperhidrosis

	Naumann et al, 2001[26]		P value
	Botulinum toxin A 50 units (Botox) (n=242)	Placebo (n=78)	
>50% reduction in sweat production	Week 4: 94% Week 16: 82%	Week 4: 36% Week 16: 21%	P<0.001
Adverse events	11%	5%	P>0.05

In the trial by Heckmann et al, 145 patients received 200 units of botulinum toxin A in one axilla and placebo in the other, followed by 100 units after 2 weeks. There was a significant reduction in sweat production after 2 weeks (24 ± 27 mg/min vs. 144 ± 113 mg/min compared to 192 ± 136 mg/min at baseline). Injection of 100 units into the axilla that had first been treated with placebo, reduced the mean rate of sweat production in that axilla to 32 ± 39 mg per minute (P<0.001). At 26 weeks after the first injection, sweat production remained reduced compared to baseline in both axillae: at 67 ± 66 mg/min and 65 ± 64 mg/min respectively.[27]

Lowe et al[28] investigated the effect on injections of botulinum toxin A (75 units and 50 units vs. placebo) on HDSS score. A 2-point improvement on the 4-point scale was reported in 75% of patients treated with botulinum toxin A compared to 25% in the placebo group. The effect was maintained twice as long for the botulinum toxin arms of the study (197 and 205 vs. 96 days).

Several smaller trials of lower quality also support the efficacy of botulinum toxin A in axillary hyperhidrosis.[29,30]

Palmar hyperhidrosis

Nineteen patients with plantar hyperhidrosis received injections of placebo (normal saline) in one hand and 100 units of botulinum toxin A in the other (preparation not specified).[31] The mean percentage decrease in gravimetric measurement at day 28 was significantly greater with botulinum toxin A versus placebo. One hundred per cent of 17 patients rated the treatment as successful, while only 12% (2/17) rated placebo injection successful. Grip and hand strength were unchanged with either treatment. Twenty-one per cent (4/19) reported mild adverse events.

Another small study investigated the effect of botulinum toxin A in palmar hyperhidrosis in 11 patients.[32] A total dose of 120 units of botulinum A toxin (Dysport®) was injected into six different sites on one palm, whereas the other was injected with sterile saline. Three weeks after treatment, the mean reduction of sweat production in the botulinum A toxin-treated palms was 26% (P<0·001), after 8 weeks 26% (P= 0·002) and after 13 weeks 31% (P<0·001). No statistically significant reduction of sweating was seen in the placebo-treated palms. Three patients reported reversible minor weakness of powerful handgrip after injection at the toxin-treated site, lasting between 2 and 5 weeks.

Saadia et al[33] evaluated the efficacy and safety of intradermal botulinum toxin A (Botox®) in reducing hyperhidrosis, and aimed to determine the most effective dose of toxin in a prospective, single blind, randomized trial. Twenty-four patients with severe palmar hyperhidrosis received either a low (50 units) or a high dose (100 units) of botulinum toxin type A (Botox®) injected in 20 sites in each palm. A significant decrease in sweating was observed within the first month. Six months after injection, the anhidrotic effect was still evident in two thirds of the patients in both groups. Handgrip strength was not affected with either dose but finger pinch strength, 2 weeks after the injection, decreased 23 +/- 27% with 50 units ($p < 0.05$) and 40 ± 21% with 100 units ($P < 0.001$). Pinch strength improved gradually but 6 months after treatment it was still 7-11% lower than at baseline.

Comparison studies of different preparations have shown similar efficacy, but numbers are small.[4]

Systemic treatment

Anticholinergics may be considered for patients with primary generalised or craniofacial hyperhidrosis (due to anatomical limitations of local therapies), however side effects often limit treatment and these should be discussed with the patient. Systemic use of anticholinergic agents is not usually recommended in the UK for the treatment of mild focal hyperhidrosis for the same reason.[14,34]

Propantheline bromide is the only oral anticholinergic licensed for hyperhidrosis in the UK, and licensed products could be used off-label. Off-label use is preferred over the use of unlicensed medicines from a risk-perspective as per MHRA guidance on unlicensed medicines.

Glycopyrronium bromide is the most referred to anticholinergic agent in the literature. However, tablets are unlicensed in the UK and need to be imported, making it a costly intervention.

Oxybutynin immediate release (IR) appears to be equally effective with a similar (low) level of evidence, is widely available at a fraction of the costs of glycopyrronium bromide and clinicians are familiar with its use in the treatment of urinary incontinence. Based on pharmacology, other anticholinergics should offer similar effects and recommendations on choice in line with the NICE clinical guideline on the management of urinary incontinence could be followed in case first line choices (oxybutynin IR, tolterodine IR and darifenacin) are not tolerated.[35] The cognitive effects of oxybutynin are likely to be less problematic in the younger population with hyperhidrosis, compared to the elderly population with overactive bladder. Both oxybutynin and trospium are first line choices on many primary care formularies.

The only anticholinergic licensed for hyperhidrosis is propantheline bromide. However, published evidence of efficacy in hyperhidrosis is limited to a single publication[36] and it is considered to be less effective compared to oxybutynin and glycopyrronium bromide.[37]

Anticholinergics should be taken one hour before the application of aluminium chloride, preventing sweating and irritation.[38]

Clonidine for hyperhidrosis has only been reported in a limited number of case reports and series.

	Craniofacial or generalised hyperhidrosis	Palmar, plantar, axillary hyperhidrosis
Oxybutynin	11/14 patients with generalised hyperhidrosis had a good to excellent response to oxybutynin 2.5-5mg three times daily (Dermatology Life Quality Index (DLQI) score dropped from 15.9 to 3.7); adverse effects were generally mild. 8/14 pts had no or minor side effects with a good response; 3 patients stopped treatment because of adverse effects.[39]	Of 102 patients treated with an increasing dose of oxybutynin (2.5mg once daily - 5mg twice daily) >80% showed improvement, 36.3% of them presented a great improvement, and half of the patients showed improvements at all hyperhidrosis sites. Most of the patients showed improvements in quality of life (67.5%). Main adverse effect was dry mouth.[40]

Oral glycopyrronium 1-2 mg once to twice daily	15/19 responded to treatment; though 5 patients who responded had to discontinue due to adverse effects.[34]	30/45 responded; 6 did not respond and 9 discontinued due to adverse effects.[41]
Clonidine 0.1mg twice daily	6/13 patients responded to treatment; 23% did not respond and 31% had to discontinue treatment due to symptomatic decreases in blood pressure).[41]	

Surgical intervention

Several techniques have been developed to damage or remove the sweat glands, including excision, curettage, liposuction, and laser techniques. The procedures can be done under local anaesthesia. They are only used for axillary hyperhidrosis when small areas are affected, but results are variable.[42,43] These are specialised treatments and not available widely on the NHS. There do not appear to be severe side effects apart from possible unpleasant scars.[44]

Endoscopic Thoracic Sympathectomy (ETS) is very successful, particularly for palmar hyperhidrosis, but very commonly causes (severe) irreversible compensatory hyperhidrosis in other areas. In addition, as with any surgical procedure, there is a small risk of (sometimes serious) complications due to the use of anaesthesia and the procedure itself, which can damage the structure of the lung. Guidelines suggest it should only be considered as a last resort;[3,43] the Society of Thoracic Surgeons recommends excluding patients with widespread hyperhidrosis.[45] Due to the high level of morbidity it is considered to be a low priority for funding.

Comparative costs

	Dose	Cost per dose	Annual drug costs
Botox®	50 units per axilla[46]	£77.50 per axilla	£133 - £232/axilla + VAT , based on treatment every 4-7 months
	150-200 IU/ palm	£215-£278 per palm	£369-£828/palm + VAT , based on treatment every 4-7 months
Glycopyrronium 0.05% (with iontophoresis)	~500ml/month	£30*	£720* The reconstituted solution of glycopyrronium bromide has a shelf life of 14 days.
Glycopyrronium 200mcg/ml (injection to be taken orally)	2mg twice daily	£5.20 for 2mg	£3800
Oxybutynin 2.5mg tablets	2.5-5mg twice daily	£0.06 for 5mg	£41
Trospium chloride	20mg bd	£ 0.46 for 20mg	£339

*This is the approximate amount last paid in one of the Trusts in NHS Midlands & East for 500ml from one of the specials manufacturers. Costs may vary and can be significantly more in primary care where expenditure on 'specials' are less well managed.

Place in therapy of medical interventions for hyperhidrosis

Axillary hyperhidrosis

Canada[3] (consensus statement)		USA[2] (author's opinion)	Bedford & Hertfordshire Priorities Forum[47]
HDSS 2	HDSS 3-4		
Topical aluminium chloride	Topical aluminium chloride or Botulinum toxin A	Topical aluminium chloride	Topical aluminium chloride
Botulinum toxin A		Botulinum toxin A	Botulinum toxin A (only if HDSS 3-4)
		Add oral glycopyrronium	
Local surgery *		Local surgery	
-	ETS	ETS	ETS (only if HDSS 3-4)

*Laser sweat ablation or retrodermal curretage

Palmar/plantar hyperhidrosis

Canada[3] (consensus statement)		USA[2] (author's opinion)	Bedford & Hertfordshire Priorities Forum[47]	
HDSS 2	HDSS 3-4			
Topical aluminium chloride	Topical aluminium chloride or botulinum toxin A or iontophoresis	Topical aluminium chloride	Topical aluminium chloride	
Botulinum toxin A (100-150 units for palmar or 150-200 units for plantar) or iontophoresis		Add oral glycopyrronium	Iontophoresis (only if HDSS 3-4)	
		Iontophoresis	Palmar (HDSS 3-4)	Plantar (HDSS 3-4)
		Botulinum toxin A	Botulinum toxin A or ETS	Oral medication
Consider adding topical aluminium chloride to iontophoresis or botulinum	Consider oral medication or adding glycopyrollate to iontophoresis			Botulinum toxin A if palmoplantar
-	ETS (palmar only)[48,49]	Consider referral for ETS (palmar only)		

Craniofacial

Canada[3] (consensus statement)	USA[2] (author's opinion)	Bedford & Hertfordshire Priorities Forum[47]
Topical aluminium chloride or Botulinum toxin or oral medication	Oral glycopyrronium or clonidine	Topical aluminium chloride
	Topical aluminium chloride	Botulinum toxin A or oral medication (HDSS 3-4)
	Botulinum toxin A	(Botulinum toxin A for Frey's)
	Consider ETS	Consider ETS (HDSS 3-4)

Notes: doses of botulinum toxin A in the literature are:

- 1 unit/cm^2 for axillary hyperhidrosis (50-100 units/axilla)
- 1.5-2 units/cm^2 for plantar and palmar hyperhidrosis (100-150 units/palm or 150-200 units/sole) and up to 100 units for craniofacial hyperhidrosis[3]

References

1. British Association of Dermatologists website. www.bad.org.uk Accessed 11/04/2014
2. Walling HW, Swick BL. Treatment Options for Hyperhidrosis. Am J Clin Dermatol 2011; 12 (5): 1-1
3. Solish N et al. A comprehensive approach to the recognition, diagnosis, and severity-based treatment of focal hyperhidrosis: recommendations of the Canadian Hyperhidrosis Advisory Committee. Dermatol Surg 2007;33(8):908-23.. Available online: http://drypharmacistcom.ipage.com/uploads/2/9/5/9/2959076/chac_recommendations.pdf
4. Benson RA, Palin R, Holt PJE. Diagnosis and management of hyperhidrosis. BMJ 2013;347: f6800. Doi: 10.1136//bmj.f6800 [Epub]. Available online : http://www.bmj.com/content/347/bmj.f6800.pdf%2Bhtml
5. NICE Clinical Knowledge Summary - Hyperhidrosis. Last updated July 2013. Available online: http://cks.nice.org.uk
6. Shams K, Rzany BJ, Prescott LE, Musekiwa A. Interventions for excessive sweating of unknown cause (Protocol). Cochrane Database of Systematic Reviews 2011. Available at: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002953.pub2/full
7. Rayner, C.R., Ritchie, I.D. and Stark, G.P. Axillary hyperhidrosis, 20% aluminum chloride hexahydrate,and surgery. British Medical Journal; 1980; 280 (6224): 1168
8. Scholes KT. Axillary hyperhidrosis [letter]. Br Med J 1978 Sep 9; 2: 773
9. Goh CL. Aluminum chloride hexahydrate versus palmar hyperhidrosis: evaporimeter assessment. Int J Dermatol 1990; 29: 368-70.
10. Glent-Madsen L, Dahl JC. Axillary hyperhidrosis: local treatment with aluminium-chloride hexahydrate 25% in absolute ethanol with and without supplementary treatment with triethanolamine. Acta Derm Venereol 1988; 68 (1): 87-9.
11. Jensen O, Karlsmark T. Palmoplantar hyperhidrosis: treatment with alcohol solution of aluminium chloride hexahydrate: a simple method of transpiration measurement. Dermatologica 1980; 161: 133-5.
12. Benohanian A, Dansereau A, Bolduc C, Bloom E. Localized hyperhidrosis treated with aluminum chloride in a salicylic acid gel base Int J Dermatol 1998;37(9):701-3.

13. National Instittute for Health and Care Excellence. Evidence Summary unlicensed and off-label medicine (ESUOM16): Hyperhidrosis: oral glycopyrronium bromide. Available online: http://publications.nice.org.uk/esuom16-hyperhidrosis-oral-glycopyrronium-bromide-esuom16 Accessed 13/01/2014
14. Lowe, N.J., Cliff, S., Halford, J. et al. Guidelines for the primary care treatment and referral of focal hyperhidrosis. 2003;19:373-377. Available online: http://www.eguidelines.co.uk/eguidelinesmain/gip/media/pdfs/Full_hh_guideline.pdf
15. The British Association of Dermatologists. Preferred unlicensed dermatological preparations (specials) 2008. Available online via www.bad.org.uk Accessed 09/05/2013.
16. Mackenzie A, Burns C, Kavanagh G. Topical glycopyrrolate for axillary hyperhidrosis. Br J Dermatol. 2013 Mar 18. doi: 10.1111/bjd.12320. [Epub ahead of print]. Available online: http://onlinelibrary.wiley.com/doi/10.1111/bjd.12320/pdf
17. Kim WO, Kil HK, Yoon KB, et al. Topical glycopyrrolate for patients with facial hyperhidrosis. Br J Dermatol 2008; 158: 1094-7
18. Kim W, Kil H, Yoon D et al. Treatment of compensatory gustatory hyperhidrosis with topical glycopyrrolate. Yonsei Med J 2003;44:579–82.
19. May J, McGuirt W. Frey's syndrome: treatment with topical glycopyrrolate. Head Neck 1989; 11:85–9
20. Shaw J, Abbott C, Tindle K et al. A randomised controlled trial of topical glycopyrrolate, the first specific treatment for diabetic gustatory sweating. Diabetologia 1997; 40:299–301.
21. Feedback from dermatologists in NNUH and CUH. November 2013
22. Stolman LP. Treatment of excess sweating of the palms by iontophoresis. Arch Dermatol 1987;123:893–6. Available online: http://www.sweathelp.org/pdf/Treatment%20of%20palmar%20HH%20by%20ionto%20-%20Stolman.pdf
23. Dahl JC, Glent-Madsen L. Treatment of hyperhidrosis manuum by tap water iontophoresis. Acta Derm Venereol 1989;69:346–8. Available : http://www.ncbi.nlm.nih.gov/pubmed/2568061
24. Dolianitis C, Scarff CE, Kelly J, Sinclair R. Iontophoresis with glycopyrrolate for the treatment of palmoplantar hyperhidrosis. Australas J Dermatol 2004;45(4):208-12.
25. Chia HY, Tan AS, Chong WS, Tey HL. Efficacy of iontophoresis with glycopyrronium bromide for treatment of primary palmar hyperhidrosis J Eur Acad Dermatol Venereol 2012;26(9):1167-70.
26. Naumann M, Lowe NJ. Botulinum toxin type A in treatment of bilateral primary axillary hyperhidrosis: randomised, parallel group, double blind, placebo controlled trial. BMJ 2001;323:596–599.. Available online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC55572/
27. Heckmann M, Ceballos-Baumann AO, Plewig G. Botulinum toxin A for axillary hyperhidrosis (excessive sweating). N Engl J Med 2001;344:488–493.
28. Lowe NJ, Glaser DA, Eadie N, Daggett S, Kowalski JW, Lai PY, et al. Botulinum toxin type A in the treatment of primary axillary hyperhidrosis: a 52-week multicenter double-blind, randomized, placebo-controlled study of efficacy and safety. Journal of the American Academy of Dermatology 2007; 56(4):604-11.
29. Odderson IR. Long-term quantitative benefits of botulinum toxin type A in the treatment of axillary hyperhidrosis. Dermatologic surgery: official publication for American Society for Dermatologic Surgery 2002; 28(6):480-3.
30. Schnider P, Binder M, Kittler H, Birner P, Starkel D, Wolff K, et al. A randomized, double-blind, placebo-controlled trial of botulinum A toxin for severe axillary hyperhidrosis. British Journal of Dermatology 1999;140(4):677-80.

31. Lowe NJ, Yamauchi PS, Lask GP, Patnaik R, Iyer S. Efficacy and safety of botulinum toxin type a in the treatment of palmar hyperhidrosis: a double-blind, randomized, placebo-controlled study. Dermatol Surg 2002; 28:822–827.
32. Schnider P et al. Double-blind trial of botulinum A toxin for the treatment of focal hyperhidrosis of the palms. British Journal of Dermatology 1997; 136: 548-552.
33. Saadia D, Voustianiouk A, Wang AK, Kaufmann H. Botulinum toxin type A in primary palmar hyperhidrosis: randomized, single-blind, two-dose study. Neurology 2001;57(11):2095-9. Available online: http://www.ncbi.nlm.nih.gov/pubmed/11739832
34. Bajaj V, Langtry JAA. Use of oral glycopyrronium bromide in hyperhidrosis. British Journal of Dermatology 2007; 157 (1): 118–121.
35. National Institute for Health and Care Excellence. CG171 Urinary incontinence: The management of urinary incontinence in women. September 2013. Available online: http://guidance.nice.org.uk/CG171
36. Canaday BR, Stanford RH. Propantheline bromide in the management of hyperhidrosis associated with spinal cord injury. Ann Pharmacother 1995; 29: 489–92
37. Hyperhidrosis support group. Anticholinergics. Available at: www.hyperhidrosisuk.org Accessed 04/01/2014
38. Personal communication dermatologist Dr Mazzon, Lister hospital. January 2014
39. Tupker RA, Harmsze AM, Deneer VHM. Oxybutynin Therapy for Generalized Hyperhidrosis Arch Dermatol 2006;142(8):1065-1086. Available online: http://archderm.jamanetwork.com/article.aspx?articleid=406735
40. Wolosker N, de Campos JR, Kauffman P, et al. The use of oxybutynin for treating axillary hyperhidrosis Ann Vasc Surg 2011;25(8):1057-62.
41. Walling HW. Systemic therapy for primary hyperhidrosis: a retrospective study of 59 patients treated with glycopyrrolate or clonidine. J Am Acad Dermatol. 2012;66(3):387-92.
42. International Hyperhidrosis Society. http://www.sweathelp.org/en/hyperhidrosis-treatments/surgery/ets-surgery Accessed 04/07/2013
43. British Association of Dermatologists. www.bad.org.uk Accessed 04/07/2013
44. Personal communication P. Gillespie (Surgeon CUHFT) and Dr Mazzon (Dermatologist Lister Hospital). January 2014
45. Cerfolio RJ, Milanez De Campos JR, Bryant A et al. The Society of Thoracic Surgeons expert consensus for the surgical management of hyperhidrosis. Ann Thorac Surg 2011;91:1642-6.
46. Summary of Product Characteristics - Botox 50 units. Last revision of text 12 December 2012. Available at: http://www.medicines.org.uk/emc/medicine/20564/SPC/ Accessed 06/06/2013.
47. Hertfordshire and Bedfordshire Priorities Frorum. Final guidance 51: Botox for hyperhidrosis. Available at: http://www.hertfordshire.nhs.uk/resource-centre/bedfordshire-a-hertfordshire-priorities-forum/final-and-interim-guidance.html
48. http://www.hyperhidrosisuk.org/treatment-options.html Accessed 11/04/2014
49. British Association of Dermatologists. www.bad.org.uk Accessed 06/06/2013

Appendix 1

Hyperhidrosis Disease Severity Scale (HDSS)

Subjective score	Clinical interpretation
My sweating is never noticeable and never interferes with my daily activities	1 - mild
My sweating is tolerable but sometimes interferes with my daily activities	2 - moderate
My sweating is barely tolerable and frequently interferes with my daily activities	3 - severe
My sweating is intolerable and always interferes with my daily activities	4 - severe

From:

Solish N, Benohanian A, Kowalski JW, Canadian Dermatology Study Group on Health-Related Quality of Life in Primary Axillary Hyperhidrosis. Prospective open-label study of botulinum toxin type A in patients with axillary hyperhidrosis: effects on functional impairment and quality of life. Dermatol Surg 2005; 31: 405-13.

Document management

Experts consulted: Consultant Dermatologists, East of England NHS Trusts

Response received from: Norwich and Norfolk University Hospital (NNUH), Cambridge University Hospital (CUH), Luton and Dunstable and James Paget.

Document history

PAC approval date	3 March 2014	Version	1
Consultation process	Priorities Advisory Committe (PAC) members		
QA process	Katie Smith, 24 March 2014		