NICE advice

Hyperhidrosis: oxybutynin

Evidence summary
Published: 21 March 2017

www.nice.org.uk/guidance/es10

Key points

The content of this evidence summary was up-to-date in March 2017. See the summary of product characteristics (SPCs), British national formulary (BNF) or the MHRA or NICE websites for up-to-date information.

Regulatory status: off-label use of a licensed medicine. Oxybutynin is an antimuscarinic medicine that can be used to treat hyperhidrosis (excessive sweating); use for this indication is off-label.

Overview

This evidence summary includes 4 studies (3 randomised controlled trials [RCTs] and 1 quasi-randomised controlled trial) that investigated oxybutynin 2.5 mg to10 mg for treating hyperhidrosis in adults. All the studies compared oxybutynin with placebo and were in non-UK settings.

Three studies found that more people treated with oxybutynin reported an improvement in symptoms of hyperhidrosis compared with those treated with placebo; the difference between the groups was statistically significant in all studies. Volume of sweating was

measured in the fourth study, which found that the oxybutynin group had statistically significant reductions in sweating from baseline, whereas the placebo group did not.

Quality of life was assessed in 3 studies, which found that people treated with oxybutynin reported greater improvements compared with those treated with placebo; all differences between the groups were statistically significant.

The studies included in this evidence summary have many limitations. For example, all were small (range 32 to 140 participants), of short duration (2 to 6 weeks) and did not compare oxybutynin to other active treatments for hyperhidrosis.

Dry mouth was the most common adverse event reported across the studies. Other common adverse events were constipation, dry eyes and urinary retention.

NICE has not published a guideline on managing hyperhidrosis. However, the clinical knowledge summary on hyperhidrosis suggests systemic therapies, including oral antimuscarinics, as treatment options for people whose hyperhidrosis is not adequately managed through lifestyle modifications and antiperspirants.

A summary to inform local decision-making is shown in table 1.

Table 1 Summary of the evidence on effectiveness, safety, patient factors and resource implications

Effectiveness

- In Schollhammer et al. (2015) (n=62), 60% of people taking oxybutynin had an improvement in Hyperhidrosis Disease Severity Scale (HDSS) score of 1 or more at 6 weeks compared with 27% taking placebo (p<0.01, statistically significant). It is unclear what level of improvement on the 4-point HDSS is considered clinically important.
- In Wolosker et al. (2012) (n=50) 74% of people taking oxybutynin scored their improvement in palmar or axillary hyperhidrosis as 'moderate' or 'great' at 6 weeks compared with 27% taking placebo (p<0.001, statistically significant).
- In Ghaleiha et al. (2012) (n=140), after 2 weeks, HDSS score improved by about 1.3 points in the oxybutynin group and about 0.8 points in the placebo group (p=0.03, statistically significant).
- Costa Jr et al. (2014) (n=32) found people taking oxybutynin group had reductions in transepidermal water loss from baseline at 4 sites (all p<0.01, statistically significant), whereas people taking placebo did not.
- Quality of life also improved significantly more with oxybutynin compared with placebo in the 3 RCTs (Schollhammer et al. 2015, Wolosker et al. 2012 and Costa Jr et al. 2014), For example, in Schollhammer et al. (2015), after 6 weeks, the mean improvement in validated, 30-point Dermatology Life Quality Index (DLQI) was 6.9 points in the oxybutynin group compared with 2.3 points in the placebo group (p<0.01, statistically significant). It is unclear if this improvement is clinically important.
- The largest study by Ghaleiha et al. (2012) included people who were taking sertraline for major depressive disorder and it is unclear whether the results of this study apply to a more general population of people with hyperhidrosis.

Safety

- The SPC states that adverse effects of oxybutynin are mainly due to its anticholinergic effects, with dry mouth reported most commonly.
- The very common adverse events, occurring in 1 in 10 people or more, are constipation, nausea, dry mouth, dizziness, headache, somnolence, vision blurred and dry skin (SPC: oxybutynin).
- Apart from dry mouth, oxybutynin was generally well tolerated in the studies.

Patient factors

- The studies were small and short and it is unclear how well oxybutynin works for hyperhidrosis in the longer term. They also compared oxybutynin to placebo and we do not know how well oxybutynin works compared with other treatments for the condition.
- Oxybutynin is available in a number of different formulations and some people may prefer one over another. However, only the standard-release tablets were used in the RCTs discussed in this evidence summary.
- Adverse events, especially dry mouth, are common in people treated with oxybutynin. They may be minimised by using the lowest effective dose.
- Many patients may prefer a topical treatment to risking the systemic adverse effects of an oral treatment. However, an oral treatment may be preferable to some other options, such as surgery.

Resource implications

- The standard release tablet formulation of oxybutynin, which was used in the studies, is inexpensive (costing £1.15 to £1.49 for 56 tablets). Modified release tablets and transdermal patches are also available, but are more expensive (costing £13.77 to £27.20 per pack).
- Oxybutynin tablets, at a daily dose of 2.5 mg to10 mg, cost between £0.62 and £1.60 for 30 days treatment (all prices taken from Drug Tariff, February 2017; excluding VAT).
- The 30-day cost of other oral antimuscarinics is £5.56 to £33.33 for propantheline bromide 15 mg to 90 mg daily (Drug Tariff, February 2017; excluding VAT) and £96.00 to £768.00 for glycopyrronium bromide oral solution (Sialanar) 1 mg to 8 mg daily (MIMS, February 2017; excluding VAT).

Introduction and current guidance

Hyperhidrosis is a chronic condition in which a person sweats in excess of what is necessary to maintain normal body temperature. Hyperhidrosis can be classified by the presence or absence of an underlying cause (primary [idiopathic] or secondary) and location (localised [focal] or generalised). Primary hyperhidrosis has no recognised cause, and is generally localised to certain parts of the body, mainly the axillae (armpits), hands, feet, face or scalp. It typically begins during childhood or adolescence, but can occur at any age and is usually life-long (clinical knowledge summary on hyperhidrosis).

Secondary hyperhidrosis is caused by another condition, such as hyperthyroidism, diabetes, neuropathy, spinal disease or spinal injury, or can be an adverse effect of a drug. Secondary hyperhidrosis can be generalised, affecting the whole body, or can affect only localised areas, similar to primary hyperhidrosis.

Excessive sweating can have a profound effect on quality of life, interfering with daily activities and causing anxiety and embarrassment (NICE interventional procedures guidance on endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limb).

NICE has not published a guideline on managing hyperhidrosis.

The clinical knowledge summary on hyperhidrosis recommends that people with primary localised hyperhidrosis should receive advice on lifestyle measures, information and support on their condition and an antiperspirant (20% aluminium chloride hexahydrate). If these measures are inadequate or unacceptable a referral to a dermatologist may be required. Treatments that may be offered in secondary care include:

- topical therapies (including emollients, antiperspirants and antimuscarinic medicines)
- iontophoresis (with tap water or glycopyrronium)
- botulinum toxin type A injections
- systemic therapies (for example oral antimuscarinics [such as oxybutynin, propantheline and glycopyrronium: see the NICE evidence summary on glycopyrronium for hyperhidrosis for more information], clonidine, diltiazem, benzodiazepines)
- surgery (NICE has published interventional procedures guidance on endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limb).

The clinical knowledge summary on hyperhidrosis recommends that people with secondary localised hyperhidrosis or generalised hyperhidrosis should be investigated for an underlying cause, which should be managed appropriately.

Specialists involved in the production of this evidence summary advised that the choice of initial treatment for hyperhidrosis is usually guided by the site of excessive sweating.

Product overview

Mode of action

Oxybutynin is an antimuscarinic (anticholinergic) medicine that is licensed for the treatment of urinary incontinence, urgency and frequency in the unstable bladder, whether due to neurogenic bladder disorders (detrusor hyperreflexia) in conditions such as multiple sclerosis and spina bifida, or to idiopathic detrusor instability (motor urge incontinence; SPC: oxybutynin).

Regulatory status

Oxybutynin is not licensed for the treatment of hyperhidrosis; use of oxybutynin for this indication is off-label.

In line with the guidance from the General Medical Council (GMC) on prescribing unlicensed medicines, the prescriber should take full responsibility for determining the needs of the patient and whether using oxybutynin is suitable outside its authorised indications. Supporting information and advice is also available from the GMC.

Dosing information

Dosing information for oxybutynin for hyperhidrosis (an off-label indication) is discussed in the evidence review within this evidence summary.

For the licensed indication of urinary incontinence, urgency and frequency in the unstable bladder, the usual adult dose is 5 mg 2 or 3 times a day. This may be increased to a maximum of 5 mg 4 times a day to obtain a clinical response provided that the side effects are tolerated (SPC: oxybutynin).

Cost

Oxybutynin is available in a number of different formulations and strengths, with a considerable difference in price between the different preparations (all prices taken from the Drug Tariff, February 2017):

- oxybutynin 2.5 mg tablets cost £1.15 for 56 tablets
- oxybutynin 3 mg tablets cost £16.80 for 56 tablets
- oxybutynin 5 mg tablets cost £1.49 for 56 tablets
- oxybutynin 5 mg modified release tablets cost £13.77 for 30 tablets
- oxybutynin 2.5 mg/5 ml oral solution sugar free costs £144.50 for 150 ml
- oxybutynin 5 mg/5 ml oral solution sugar free costs £199.20 for 150 ml
- oxybutynin 3.9 mg/24 hours transdermal patches cost £27.20 for 8 patches.

Evidence review

A literature search was conducted which identified 78 references (see search strategy for full details). These references were screened using their titles and abstracts and 26 references were obtained and assessed for relevance.

Three randomised controlled trials (RCTs) identified from the search (Schollhammer et al. 2015, Wolosker et al. 2012 and Costa Jr et al. 2014) were included in this evidence summary. A quasi-randomised controlled trial is also included (Ghaleiha et al. 2012). The included studies were conducted in France, Iran and Brazil. There were no UK-based RCTs identified. A summary of the included studies is shown in table 2 (see evidence tables for full details).

The remaining 22 references were excluded. These are listed in excluded studies with reasons for their exclusion.

Table 2 Summary of included studies

Study	Population	Intervention and comparison	Main outcome
Schollhammer et al. (2015) RCT	Adults with hyperhidrosis (generalised[a] and localised) and a HDSS[b] score of 2 or more (n=62)	Oxybutynin 2.5 mg to 7.5 mg daily versus placebo	Proportion of patients with an improvement in HDSS[b] score of 1 or more at week 6
Wolosker et al. (2012) RCT	Adults with localised palmar and axillary hyperhidrosis (n=50)	Oxybutynin 2.5 mg daily to 5 mg twice daily versus placebo	Patient assessment of hyperhidrosis severity and quality of life at week 6
Costa Jr et al. (2014) RCT	Women with plantar hyperhidrosis who had previously undergone endoscopic thoracic sympathectomy (n=32)	Oxybutynin 2.5 mg to 10 mg daily versus placebo	Transepidermal water loss and quality of life at day 30

Ghaleiha et al. (2012) Quasi-RCT[c]	Adults with depression and hyperhidrosis secondary to sertraline treatment (n=140)	Oxybutynin 5 mg daily versus placebo	Change in HDSS[b] score at week 2

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale; RCT, randomised controlled trial.

[a] Generalised hyperhidrosis was defined as excessive sweating occurring at 2 or more locations (among palmar, plantar, axillary, facial or truncal).

[b] The HDSS is a 4-point measure of hyperhidrosis severity. A score of 1 or 2 indicates mild or moderate hyperhidrosis. A score of 3 or 4 indicates severe hyperhidrosis.

[c] Treatment groups were determined by participants drawing black or red chips from a ballot box.

Clinical effectiveness

An overview of the results for clinical effectiveness can be found in results tables.

Patient-reported hyperhidrosis severity

Three of the clinical trials discussed in this evidence summary used a subjective, patient-reported measure of hyperhidrosis severity as a primary or main efficacy outcome measure. Schollhammer et al. (2015) and Ghaleiha et al. (2012) used the validated Hyperhidrosis Disease Severity Scale (HDSS), and Wolosker et al. (2012) used a patient questionnaire that appears to have been developed for this individual study.

Schollhammer et al. (2015) found more people in the oxybutynin group responded to treatment (had an improvement in HDSS score of 1 or more) at 6 weeks than in the placebo group (60% compared with 27%, $p<0.01$, which is statistically significant). The mean improvement in HDSS score was approximately 1.1 points in the oxybutynin group compared with 0.3 points in the placebo group, from a baseline score of approximately 3.2 in the study population (no statistical analysis reported). It is unclear what level of improvement on the 4-point HDSS scale is considered clinically significant but, on average, the description changed from 'barely tolerable and frequently interferes with daily activities' to 'tolerable but sometimes interferes with daily activities' in the oxybutynin group.

In Wolosker et al. (2012), at 6 weeks, 74% of people treated with oxybutynin scored their

improvement in palmar or axillary hyperhidrosis as 'moderate' or 'great' compared with only 27% of people treated with placebo; the difference between the groups was statistically significant (p<0.001). Statistically significant improvements in plantar hyperhidrosis were also observed, with 92% in the oxybutynin reporting 'moderate' to 'great' improvements, compared with around 13% in the placebo group (p<0.001). However, only 27 patients were included in this analysis and it may have been statistically underpowered to detect any differences between the groups.

In Ghaleiha et al. (2012), at baseline the mean HDSS score was approximately 2.8 (barely tolerable and frequently interferes with my daily activities) across the 2 groups. After 2 weeks, the HDSS score had improved to approximately 1.5 in the oxybutynin group (never noticeable and never interferes with my daily activities) and approximately 2.0 in the placebo group (tolerable but sometimes interferes with my daily activities), and the difference between the groups was statistically significant (p=0.03).

Quality of life

Three of the included studies reported on change in quality of life associated with oxybutynin treatment, although different scales were used to measure this outcome.

Schollhammer et al. (2015) used the validated 30-point Dermatology Life Quality Index (DLQI) questionnaire to report on changes in quality of life. At baseline the mean DLQI score across the groups was approximately 11 points (out of maximum score of 30), suggesting that the condition was having a very large effect on the patient's lives. After 6 weeks' treatment, the mean improvement in DLQI score was higher in the oxybutynin group (6.9 points) compared with the placebo group (2.3 points), the difference between groups was statistically significant (p<0.01). It is unclear if this improvement is clinically important.

Wolosker et al. (2012) assessed quality of life using patient questionnaires. It is unclear whether those used for measuring change on treatment have been validated, although the authors say the questionnaire assessing the impact of hyperhidrosis on quality of life before treatment has been validated. At baseline, approximately 69% of participants considered their quality of life to be 'very poor', with the remaining participants (31%) reporting 'poor' quality of life. After 6 weeks of treatment with oxybutynin, 35% reported that their quality of life was 'much better', 39% 'a little better' and 26% 'the same'. In contrast, the majority of people in the placebo group (86%) felt that their quality of life remained 'the same' after 6 weeks, with only 14% saying that it was 'a little better' and

nobody reporting that it was 'much better'. Nobody in the study reported worsening quality of life. The difference between the groups was statistically significant ($p<0.001$).

Costa Jr et al. (2014) used a questionnaire for assessing the quality of life associated with hyperhidrosis, which the authors say has been validated. At baseline the adjusted mean quality of life score in the oxybutynin group was 40.4/100 and in the placebo group was 34.8/100; these scores correspond to a rating of 'very good' quality of life. At the end of the treatment period, the mean quality of life score in the oxybutynin group was 17.5 ('excellent', $p=0.001$ compared to baseline, statistically significant difference from baseline) and in the placebo group was 33.2 (SD 15.3, 'very good', $p=0.1$ compared to baseline, no statistically significant difference from baseline).

Transepidermal water-loss

Costa Jr et al. (2014) was the only study included in this evidence summary that used an objective measure of sweating: transepidermal water loss. After 30 days' treatment, people in the oxybutynin group had reductions in water loss from the right foot (140.3 g/m^2/h to 7.6 g/m^2/h), right hand (61.7 g/m^2/h to 28.6 g/m^2/h), back (38.2 g/m^2/h to 10.8 g/m^2/h) and abdomen (39.7 g/m^2/h to 16.5 g/m^2/h); the differences from baseline were all statistically significant (all $p<0.01$). In contrast, in the placebo group, there were no statistically significant differences in water loss from baseline to day 30 at any of these sites (all $p>0.2$, see evidence tables for more information).

Other formulations of oxybutynin

No RCTs were identified that investigated the efficacy and safety of modified-release oral oxybutynin or transdermal oxybutynin.

A non-comparative, prospective observational study involving 25 people with hyperhidrosis (mean age 28 years) who received oxybutynin patches twice a week for 10 weeks found that 15/25 (60%) of patients showed an improvement in HDSS score of 1 point or more (Bergón-Sendín et al. 2016). However, without a control arm it is not possible to draw conclusions on the effectiveness of oxybutynin patches for treating hyperhidrosis.

Long-term studies

The RCTs discussed in this evidence summary are all short in duration, although a number

of observational studies have looked at the longer-term impact of oxybutynin treatment for hyperhidrosis. Observational studies are more prone to bias and confounding compared with RCTs. Long-term RCTs are needed to confirm the findings of these lower quality studies.

In a retrospective review by Millán-Cayetano et al. (2016), 110 people with hyperhidrosis (mean age 34 years) treated with oxybutynin were evaluated using HDSS at 3 and 12 months. At 3 months, 87/110 (79%) people had partial response to treatment (defined as an improvement in HDSS score of 1 or more), with 69/110 (63%) having an excellent response (defined as an improvement in HDSS score of 2 or more or a HDSS score of 1 at the end of treatment). At 12 months, 101 people remained on treatment, of whom 63/101 (62%) responded to treatment, with 51/101 (50%) having an 'excellent' response.

Wolosker et al. (2014a) reported on 431 people attending a Brazilian dermatology clinic who received oxybutynin for axillary hyperhidrosis, of whom 181 people received oxybutynin for 6 months or more. After a median treatment duration of 17 months (range 6 to 72 months), 83% (150/181) of people reported a moderate to great improvement in axillary hyperhidrosis (defined as an improvement of 5 to10 points on a 10-point scale).

In a similar study, Wolosker et al. (2014b) reported on 570 people with palmar hyperhidrosis treated with oxybutynin. Of the 246 people treated for more than 6 months (median follow-up 16 months, range 6 to 72 months), 90% (222/246) reported moderate to great improvements in palmar hyperhidrosis (defined as an improvement of 5 to 10 points on a 10-point scale).

Studies in children

No RCTs of children treated with oxybutynin for hyperhidrosis were identified. In a retrospective observational analysis of patient records by Wolosker et al. (2014c), 45 children (aged 7 to 14 years) were treated with oxybutynin. After 6 weeks' treatment, 22/45 children (49%) reported a large improvement in symptoms (score 8 to 10 on a 10-point scale), 17/45 (38%) a moderate improvement (score 5 to 7) and 6/45 no or slight improvement (score 0 to 4). No children in the study reported a worsening of symptoms. The investigators also reported on changes in quality of life, with 80% of participants reporting an improvement following treatment.

Safety and tolerability

An overview of the results for safety and tolerability can be found in the results tables.

The SPC for oxybutynin states that the adverse effects of oxybutynin were mainly due to its anticholinergic effects, with dry mouth the most commonly reported. The very common adverse events, occurring in 1 in 10 people or more, are constipation, nausea, dry mouth, dizziness, headache, somnolence, vision blurred and dry skin.

Specialists involved in producing this evidence summary raised concerns that taking oxybutynin long-term may increase the risk of some adverse effects. Antimuscarinic medicines should be used with caution in elderly patients due to the risk of cognitive impairment. Oxybutynin may reduce salivary secretions which could result in dental caries, parodontosis (a periodontal disease) or oral candidiasis (SPC: oxybutynin).

The most common adverse event reported in Schollhammer et al. (2015) was dry mouth, reported by 13/30 people (43%) in the oxybutynin group and 3/28 people (11%) in the placebo group, with a statistically significant difference between the groups ($p<0.01$). Of the 13 people with dry mouth in the oxybutynin group, 6/13 (46%) evaluated it as being of 'slight intensity', 5/13 (38%) evaluated it as 'mild intensity' and 2/13 (15%) as 'severe intensity'. Four people in the oxybutynin group (13%) also reported blurred vision compared with no people in the placebo group. Other adverse events were reported by 1 or fewer people in each group, and included diarrhoea, headache, dizziness and urinary difficulty.

The only adverse event observed in Wolosker et al. (2012) was dry mouth, which at week 6 was reported by 35% (8/23) of those taking higher doses in the oxybutynin group compared with 9% (2/22) of the placebo group (difference between groups statistically significant, $p=0.038$). It should be noted that participants in this study were specifically asked about the presence of dry mouth.

In Costa Jr et al. (2014), 16/16 (100%) people in the oxybutynin reported dry mouth, compared with 7/16 (44%) in the placebo group ($p=0.001$). Other adverse events were constipation and drowsiness, although there were no statistically significant differences between the groups.

In Ghaleiha et al. (2012) participants were asked to report gastrointestinal complications, sedation, dry mouth and urinary complications. In the oxybutynin group, 7/66 people (11%)

reported gastrointestinal complications, compared with 6/74 (8%) in the placebo group. Dry mouth and urinary complications were both reported by 3/66 people (4%) in the oxybutynin group compared with 0/74 (0%) in the placebo group. No participants in the study reported sedation.

The studies included in this evidence summary used an oxybutynin dose between 2.5 mg and 10 mg daily. The dose of oxybutynin used for overactive bladder conditions is generally higher, ranging from 7.5 mg to 20 mg daily (SPC: oxybutynin). Since patients in the hyperhidrosis trials received a lower dose that was gradually titrated up, they may have tolerated oxybutynin better than people taking it for bladder conditions.

Evidence strengths and limitations

This evidence summary discusses the results of 3 RCTs that investigated oxybutynin for the treatment of hyperhidrosis, and included a total of 144 participants. The results of a quasi-randomised controlled trial involving 140 participants with drug-induced hyperhidrosis are also considered. There are a number of limitations with the studies.

In all studies, oxybutynin was compared to placebo; there are no RCTs comparing oxybutynin to active treatments for hyperhidrosis. In addition, all studies used immediate release oral oxybutynin; the relative efficacy and safety profile of modified release and transdermal patch formulations of oxybutynin for the treatment of hyperhidrosis is not known.

All studies were short in duration, ranging from 14 to 42 days, including the titration phase. Hyperhidrosis is a chronic condition; data supporting longer-term use of oxybutynin are limited to lower quality, observational studies, which are more subject to bias and confounding than RCTs. The 3 RCTs were small, ranging from 32 to 62 participants. Small studies may not have sufficient power to detect a treatment effect, and may not be large enough to identify less common adverse events. The quasi-randomised trial by Ghaleiha et al. (2012) was larger, involving 140 participants, although this study does not use an appropriate randomisation method, which may have introduced bias.

Although the baseline characteristics recorded were generally similar between the oxybutynin and placebo groups, none of the studies appear to have considered factors which may have affected the degree of hyperhidrosis, such as outdoor or sporting activities and local climate. The studies were conducted in France, Brazil and Iran. None of these studies considered the effect of the local climate on hyperhidrosis. There were no

UK-based RCTs.

The RCTs included in this evidence summary did not provide a detailed description of the randomisation method, or how blinding was maintained. It is not clear whether allocation was concealed. In addition to this, the anticholinergic effects of oxybutynin, most notably dry mouth, mean it is possible that participants may have known which treatment they were receiving. Participants in Costa Jr et al. (2014) were told that dry mouth was the most common side effect of anticholinergic treatment, and participants in Ghaleiha et al. (2012) were specially asked to report anticholinergic effects, including dry mouth, sedation and urinary complications. This may have further increased the chance of the participants guessing which treatment they were receiving.

Two studies (Schollhammer et al. 2015 and Ghaleiha et al. 2012) used the validated HDSS scale to assess hyperhidrosis severity. However, being only a 4-point scale the HDSS is potentially less sensitive than other, larger scales (Schollhammer et al. 2015). The scale used by Wolosker for assessing improvement in symptoms does not appear to have been validated.

Unlike the other 3 studies, Costa Jr et al. (2014) did not use a subjective measure of hyperhidrosis; the study reported on objective improvements using transepidermal water loss. There are no validated objective methods to measure the intensity of hyperhidrosis (Schollhammer et al. 2015). The authors of Schollhammer et al. (2015) justify their use of subjective outcome measures by saying that impairment of quality of life depends not only on the severity of hyperhidrosis, but also on each person's individual adaptation to their condition. Specialists involved in the development of this evidence summary suggested that subjective, person-focused measures of sweating (such as HDSS or DLQI) are more widely used in clinical practice compared with objective measures (such as water loss).

Although Costa Jr et al. (2014) used a validated questionnaire to measure quality of life, the authors acknowledge that the questionnaire was designed to assess palmar hyperhidrosis, with only 2/20 questions asking about plantar hyperhidrosis (the condition affecting people in this trial). The authors suggest that this may be the reason that people in the study reported 'very good' quality of life at baseline.

The DLQI used to assess quality of life in Schollhammer et al. (2015) has been validated. It is unclear however, whether the scale used to measure improvements in quality of life in Wolosker et al. (2012) has also been validated.

Many of the participants in the 3 RCTs had localised hyperhidrosis, for which topical treatments, including antiperspirants, are normally the first-line treatment. Systemic treatments would usually be considered only when topical treatments have not controlled the person's sweating. It is not clear from the studies whether topical treatments had been ineffective in all participants.

The participants in Ghaleiha et al. (2012) were taking sertraline for major depressive disorder and in Costa Jr et al. (2014) had previously undergone endoscopic thoracic sympathectomy. It is unclear whether the results of these studies apply to a more general population with hyperhidrosis. It is also unclear whether the antidepressant treatment used in Ghaleiha et al. (2012) may have improved hyperhidrosis as a result of improving anxiety and depression in the participants, particularly as the placebo group also improved.

An overview of the quality assessment of each included study can be found in evidence tables.

Estimated impact for the NHS

Other treatments

A number of antimuscarinics can be used to treat hyperhidrosis, although propantheline bromide is the only antimuscarinic licensed for this indication. Oral glycopyrronium bromide is sometimes used for this indication and is discussed in the NICE evidence summary on hyperhidrosis: oral glycopyrronium bromide. Other systemic treatments mentioned in the clinical knowledge summary on hyperhidrosis are clonidine, diltiazem and benzodiazepines.

Costs of other treatments

See table 3 for the cost of other systemic treatments used for hyperhidrosis.

Table 3 Costs of other antimuscarinics

Medicine	Usual dose[a]	30 day cost excluding VAT

Oxybutynin tablets[b]	2.5 mg to 10 mg daily[c]	£0.62 to £1.60[d]
Oxybutynin modified release tablets[b]	5 mg to 10 mg daily	£13.77 to £27.54[d]
Oxybutynin oral solution sugar-free[b]	2.5 mg to 10 mg daily[c]	£144.50 to £398.40[d]
Oxybutynin transdermal patch[b]	3.9 mg/24 hour patch applied twice weekly (every 3 to 4 days)	£29.14[d,e]
Propantheline bromide tablets (Pro-Banthine)[f]	15 mg to 90 mg daily[g] in divided doses	£5.56 to £33.33[d]
Glycopyrronium bromide oral solution (Sialanar)[b]	1 mg to 8 mg daily in divided doses[h]	£96.00 to £768.00[i]

[a] Doses shown do not represent the full range that can be used and do not imply therapeutic equivalence.

[b] Not licensed for the treatment of hyperhidrosis.

[c] Based on the doses used in the studies included in this evidence summary.

[d] Costs based on Drug Tariff, February 2017; excluding VAT.

[e] Based on a person applying 2 patches a week for 30 days.

[f] Licensed for the treatment of hyperhidrosis.

[g] Dose range suggested by specialists involved in the development of this evidence summary.

[h] Dose range based on the studies discussed in the NICE evidence summary on hyperhidrosis: oral glycopyrronium bromide.

[i] Costs based on MIMS, February 2017; excluding VAT.

Current or estimated usage

No information on oxybutynin for hyperhidrosis was available at the time this evidence summary was prepared. It is not possible to provide estimated usage based on the available data.

Likely place in therapy

Local decision makers need to take safety, efficacy, cost and patient factors into account when considering the likely place in therapy of oxybutynin for hyperhidrosis.

The studies found that oxybutynin (at a dosage of 2.5 mg to 10 mg daily) improved symptoms of hyperhidrosis and quality of life significantly more than placebo. The medicine appeared to be well tolerated, although dry mouth was frequently reported. The standard release formulation of oxybutynin, which was used in the studies, is inexpensive. Many people may prefer a topical treatment to risking the adverse effects of an oral treatment. However, an oral treatment may be preferable to some other options, such as surgery.

The clinical knowledge summary on hyperhidrosis suggests systemic therapies, including oral antimuscarinics, as treatment options for people whose hyperhidrosis is not adequately managed through lifestyle modifications and antiperspirants. Other treatments that may be considered include topical therapies (including topical glycopyrronium), iontophoresis, botulinum toxin injections, other systemic therapies (including clonidine, diltiazem, benzodiazepines) and surgery.

Adverse events are common with oxybutynin, with dry mouth the most frequently reported, occurring in up to 100% of participants taking oxybutynin in the studies discussed in this evidence summary. Other common adverse events include dizziness, nausea, constipation and urinary retention. Treatment with oxybutynin may be limited by a person's ability to tolerate these side effects, although anticholinergic effects are often dose-dependent and may be minimised by using the lowest effective dose.

Many of the participants involved in the studies discussed in this evidence summary had localised hyperhidrosis, which may be more appropriately managed using local treatments including antiperspirants and iontophoresis.

Information for the public about medicines

Evidence summaries provide an overview of the best evidence that is available about specific medicines. They also give general information about the condition that the medicine might be prescribed for, how the medicine is used, how it works, and what the

aim of treatment is.

Evidence summaries aim to help healthcare professionals and patients decide whether medicines are safe to use and if they are likely to work well, especially when there isn't another suitable medicine that has a licence for the condition. They don't contain recommendations from NICE on whether the medicine should be used.

Information about licensing of medicines

In the UK, medicines need to have a licence before they can be widely used. To get a licence, the manufacturer of the medicine has to provide evidence that shows that the medicine works well enough and is safe enough to be used for a specific condition and for a specific group of patients, and that they can manufacture the medicine to the required quality. Evidence summaries explain whether a medicine has a licence, and if it does what the licence covers.

There is more information about licensing of medicines on NHS Choices.

Medicines can be prescribed if they don't have a licence (unlicensed) or for 'off-label' use. Off-label means that the person prescribing the medicine wants to use it in a different way than that stated in its licence. This could mean using the medicine for a different condition or a different group of patients, or it could mean a change in the dose or that the medicine is taken in a different way. If a healthcare professional wants to prescribe an unlicensed medicine, or a licensed medicine off-label, they must follow their professional guide, for example for doctors the General Medical Council's good practice guidelines. These include giving information about the treatment and discussing the possible benefits and harms so that the person has enough information to decide whether or not to have the treatment. This is called giving informed consent.

Questions that might be useful to ask about medicines

- Why am I being offered this medicine?
- Why am I being offered a medicine that is unlicensed or is being used off-label?
- What does the treatment involve?

- What are the benefits I might get?
- How good are my chances of getting those benefits?
- Could having the treatment make me feel worse?
- Are there other treatments I could try?
- What are the risks of the treatment?
- Are the risks minor or serious? How likely are they to happen?
- What could happen if I don't have the treatment?

Relevance to other NICE programmes

The use of oxybutynin for hyperhidrosis is not appropriate for referral for a NICE technology appraisal and is not currently planned into any other work programme.

NICE has issued guidance on endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limb.

NICE has not issued any clinical guidelines on managing hyperhidrosis but has published the following advice relating to this condition:

- Hyperhidrosis: oral glycopyrronium bromide.

References

Bergón-Sendín M, Pulido-Pérez A, Sáez-Martín LC et al. (2016) Preliminary experience with transdermal oxybutynin patches for hyperhidrosis. Actas Dermosifiliogr 107(10), 845–50

Costa Jr. AS, Leão LEV, Succi JE et al. (2014) Randomized trial – oxybutynin for treatment of persistent plantar hyperhidrosis in women after sympathectomy. Clinics (Sao Paulo) 69(2), 101–5

Ghaleiha A, Jahangard L, Sherafat Z et al. (2012) Oxybutynin reduces sweating in depressed patients treated with sertraline: a double-blind, placebo-controlled, clinical

study. Neuropsychiatric Disease and Treatment 8, 407–12

Millán-Cayetano JF, del Boz J, Rivas-Ruiz F et al. (2016) Oral oxybutynin for the treatment of hyperhidrosis: outcomes after one-year follow-up. Australasian Journal of Dermatology. doi:10.1111/ajd.12473

Schollhammer M, Brenaut E, Menard-Andivot N et al. (2015) Oxybutynin as a treatment for generalized hyperhidrosis: a randomized, placebo-controlled trial. British Journal of Dermatology 173(5), 1163–8

Wolosker N, Milanez de Campos JR, Kauffman P et al. (2012) A randomized placebo-controlled trial of oxybutynin for the initial treatment of palmar and axillary hyperhidrosis. Journal of Vascular Surgery 55(6), 1696–700

Wolosker N, Teivelis MP, Krutman M et al. (2014a) Long-term results of the use of oxybutynin for the treatment of axillary hyperhidrosis. Annals of Vascular Surgery 28(5), 1106–12

Wolosker N, Teivelis MP, Krutman M et al. (2014b) Long-term results of oxybutynin treatment for palmar hyperhidrosis. Clinical Autonomic Research 24(6), 297–303

Wolosker N, Schvartsman C, Krutman M et al. (2014c) Efficacy and quality of life outcomes of oxybutynin for treating palmar hyperhidrosis in children younger than 14 years old. Pediatric Dermatology 31(1), 48–53

Evidence tables

Table 4 Schollhammer et al. 2015

Study reference	Schollhammer M, Brenaut E, Menard-Andivot N et al. (2015) Oxybutynin as a treatment for generalized hyperhidrosis: a randomized, placebo-controlled trial. British Journal of Dermatology 173(5): 1163–8
Unique identifier	NCT01855256
Study type	RCT

Aim of the study	To evaluate the efficacy and safety of oxybutynin in people with hyperhidrosis
Study dates	June 2013 to January 2014
Setting	4 centres in France
Number of participants	62 randomised (58 analysed[a])
Population	Adults (mean age approximately 35 years) with generalised[b] (83%) or localised hyperhidrosis (17%)[c]
Inclusion criteria	HDSS score of 2 or more
Exclusion criteria	Aged less than 18 years, current pregnancy, breastfeeding, hypersensitivity to oxybutynin or any of the excipients, known prostatic disorders, intestinal occlusion, toxic megacolon, intestinal atony, severe ulcerative colitis, myasthenia and closure glaucoma of the anterior chamber angle
Intervention(s)	Oxybutynin 2.5 mg daily, increased over 8 days until an effective dose was achieved. Maximum dose 7.5 mg daily, achieved by all but 1 patient (n=32)
Comparator(s)	Placebo (n=30)
Length of follow-up	6 weeks
Outcomes	Primary outcome: • Proportion of people with an improvement in HDSS score of 1 or more at week 6
	Secondary outcomes: • Change in DLQI score from baseline to week 6
	Safety outcomes: • Reported adverse effects

Source of funding	This study was partially funded by the French Society of Dermatology	
Overall risk of bias/quality assessment (CASP RCT checklist)	Did the trial address a clearly focused issue?	Yes
	Was the assignment of patients to treatments randomised?	Yes
	Were patients, health workers and study personnel blinded?	Unclear[d]
	Were the groups similar at the start of the trial?	Yes
	Aside from the experimental intervention, were the groups treated equally?	Yes
	Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes
	How large was the treatment effect?	See table 8
	How precise was the estimate of the treatment effect?	See table 8
	Can the results be applied in your context (or to the local population)?	Yes
	Were all clinically important outcomes considered?	Unclear[e]
	Are the benefits worth the harms and costs?	See key points

Study limitations	• The study had a short duration • Small study with limited statistical power to detect differences between the groups • Placebo-controlled study, no active comparator • An objective measure of hyperhidrosis was not used • Although the authors stated that they used an intention to treat analysis it does not appear that they used an appropriate method to account for people who were lost to follow-up (for example, last observation carried forward) • External factors influencing the degree of sweating were not assessed (for example, outdoor activities or vocational activities) • It is not clear whether allocation was concealed
Comments	[a] In the oxybutynin group, 2 participants withdraw from the study before receiving the allocated treatment. In the placebo group, 1 participant was lost to follow-up and 1 withdrew from the study on day 2. [b] Generalised hyperhidrosis was defined as excessive sweating occurring at 2 or more locations (among palmar, plantar, axillary, facial or truncal). [c] The authors defined localised hyperhidrosis as hyperhidrosis affecting only 1 location and generalised hyperhidrosis as hyperhidrosis affecting 2 or more locations. [d] Because of the anticholinergic adverse effects associated with oxybutynin, it is possible that participants were aware of the treatment. [e] No objective measures of treatment were reported.
Abbreviations:DLQI, Dermatology Life Quality Index; HDSS, Hyperhidrosis Disease Severity Scale; RCT, randomised controlled trial.	

Table 5 Wolosker et al. 2012

Study reference	Wolosker N, Milanez de Campos JR, Kauffman P et al. (2012) A randomized placebo-controlled trial of oxybutynin for the initial treatment of palmar and axillary hyperhidrosis. Journal of Vascular Surgery 55(6): 1696–700
Unique identifier	None identified
Study type	RCT
Aim of the study	To evaluate the efficacy and safety of oxybutynin in people with localised (palmar and axillary) hyperhidrosis
Study dates	January 2011 to June 2011
Setting	Single centre in Brazil
Number of participants	50 randomised (45 analysed[a])
Population	Adults (mean age approximately 28 years) with palmar or axillary hyperhidrosis
Inclusion criteria	Palmar or axillary hyperhidrosis with the intention of using a new medicine
Exclusion criteria	Previous glaucoma, urinary retention, gastric retention, narrow-angle glaucoma, and demonstrated hypersensitivity to the drug substance or other components of the product
Intervention(s)	Oxybutynin 2.5 mg daily, increased to 5 mg twice daily over 3 weeks (n=23)
Comparator(s)	Placebo (n=22)
Length of follow-up	6 weeks
Outcomes	Efficacy outcomes: • Patient assessment of change in hyperhidrosis severity[b] • Patient assessment of change in quality of life[c]

	Safety outcomes: • Reported adverse effects[d]	
Source of funding	Not reported	
Overall risk of bias/quality assessment (CASP RCT checklist)	Did the trial address a clearly focused issue?	Yes
	Was the assignment of patients to treatments randomised?	Unclear
	Were patients, health workers and study personnel blinded?	Unclear[e]
	Were the groups similar at the start of the trial?	Yes[f]
	Aside from the experimental intervention, were the groups treated equally?	Yes
	Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes
	How large was the treatment effect?	See table 9
	How precise was the estimate of the treatment effect?	See table 9
	Can the results be applied in your context? (or to the local population)	Yes
	Were all clinically important outcomes considered?	Unclear[g]
	Are the benefits worth the harms and costs?	See key points

Study limitations	• The study had a short duration • Placebo controlled study, no active comparator • Small study with limited statistical power to detect differences between the groups • An objective measure of hyperhidrosis was not used • External factors influencing the degree of sweating were not assessed (for example, outdoor activities or vocational activities) • It is not clear whether allocation was concealed
Comments	[a] Two people in the oxybutynin group and 3 people in the placebo group were lost to follow-up. [b] Patient-reported improvement in hyperhidrosis on a scale from 0 (no improvement) to 10 (absence of hyperhidrosis), based on their own estimates without any intervention or advice from the interviewer. [c] The negative effect of hyperhidrosis on QOL before the treatment was classified into 5 levels and calculated as the summed total score from the protocol (range, 20 to 100). Higher levels indicated greater severity and poorer QOL. When the total was >84, the QOL was considered as very poor; from 68 to 83, poor; from 52 to 67, good; from 36 to 51, very good; and from 20 to 35, excellent. Improvement of QOL after the treatment was also classified using 5 levels. When the total was >84, the QOL was considered as much worse; from 68 to 83, a little worse; from 52 to 67, the same; from 36 to 51, a little better; and from 20 to 35, much better. [d] Patients evaluated the presence of dry mouth on a scale from 0 to 3, where 0 represented absence; 1, mild; 2, moderate; and 3, severe. [e] Because of the anticholinergic adverse effects associated with oxybutynin it is possible that participants were aware of the treatment. [f] Patients were matched for age sex and site of hyperhidrosis but no other information is reported. [g] No objective measures of treatment were reported.

Abbreviations: QOL, quality of life; RCT, randomised controlled trial.

Table 6 Costa Jr. et al. 2014

Study reference	Costa Jr AS, Leão LEV, Succi JE et al. (2014) Randomized trial – oxybutynin for treatment of persistent plantar hyperhidrosis in women after sympathectomy. Clinics (Sao Paulo) 69(2): 101–5
Unique identifier	NCT01328015
Study type	RCT
Aim of the study	To evaluate the efficacy and safety of oxybutynin in women with localised plantar hyperhidrosis after endoscopic thoracic sympathectomy
Study dates	March 2010 to June 2010
Setting	Single centre in Brazil
Number of participants	32 randomised
Population	Women (mean age approximately 27 years) with plantar hyperhidrosis who had previously undergone endoscopic thoracic sympathectomy
Inclusion criteria	Women who had undergone G3 and G4 thoracic sympathectomy for palmar-plantar hyperhidrosis more than 6 months prior to the start of the study (mean 60.4 months in the oxybutynin group and 41.3 months in the placebo group), and were experiencing troublesome plantar hyperhidrosis
Exclusion criteria	Pregnancy, breastfeeding, glaucoma, use of tricyclic antidepressants, BMI more than 25 kg/m^2 and previous use of anticholinergic medicines
Intervention(s)	Oxybutynin 2.5 mg daily, increased to a maximum dose of 10 mg
Comparator(s)	Placebo (n=23)
Length of follow-up	30 days

Outcomes	Efficacy outcomes: • Patient assessment of change in quality of life[a] • Transepidermal water loss[b]	
	Safety outcomes: • Reported adverse effects	
Source of funding	Not reported	
Overall risk of bias/quality assessment (CASP RCT checklist)	Did the trial address a clearly focused issue?	Yes
	Was the assignment of patients to treatments randomised?	Unclear[c]
	Were patients, health workers and study personnel blinded?	Unclear[d]
	Were the groups similar at the start of the trial?	Yes
	Aside from the experimental intervention, were the groups treated equally?	Yes
	Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes
	How large was the treatment effect?	See table 10
	How precise was the estimate of the treatment effect?	See table 10
	Can the results be applied in your context? (or to the local population)	Yes
	Were all clinically important outcomes considered?	Yes
	Are the benefits worth the harms and costs?	See key points

Study limitations	• The study had a short duration • Small study with limited statistical power to detect differences between the groups • The quality of life questionnaire used was designed for palmar rather than plantar hyperhidrosis, with only 2/20 questions asking about foot sweating. • Placebo controlled study, no active comparator • External factors influencing the degree of sweating were not assessed (for example, outdoor activities or vocational activities) • It is not clear whether allocation was concealed
Comments	[a] Patient questionnaire assesses the negative impact of hyperhidrosis on quality of life. Scored from 20 to 100, with lower scores indicating better quality of life. Scores were adjusted to be scored from 0 to 100. [b] Evaluated at the feet, hands, back and abdomen using a portable device with a humidity sensor. [c] Participants drew lots for randomisation. [d] Because of the anticholinergic adverse effects associated with oxybutynin it is possible that participants were aware of the treatment (despite being reported as a double-blind study).
Abbreviations: RCT, randomised controlled trial.	

Table 7 Ghaleiha et al. 2012

Study reference	Ghaleiha A, Jahangard L, Sherafat Z et al. (2012) Oxybutynin reduces sweating in depressed patients treated with sertraline: a double-blind, placebo-controlled, clinical study. Neuropsychiatric Disease and Treatment 8: 407–12
Unique identifier	None identified
Study type	Quasi-randomised, placebo-controlled trial

Aim of the study	To evaluate the efficacy and safety of oxybutynin in adults with sertraline-induced hyperhidrosis
Study dates	Not reported
Setting	1 centre in Iran
Number of participants	140 participants randomised
Population	Adults (mean age approximately 38 years) with major depressive disorder and hyperhidrosis secondary to sertraline treatment
Inclusion criteria	Major depressive disorder treated with sertraline (average dosage 50 mg to100 mg daily) for at least 14 days, and sertraline-induced hyperhidrosis
Exclusion criteria	Physical co-morbidity (for example, hypertension, diabetes or other endocrine disorders), psychiatric morbidity, substance abuse, pregnancy and breastfeeding
Intervention(s)	Oxybutynin 5 mg tablets once daily (n=66)
Comparator(s)	Placebo (n=74)
Length of follow-up	2 weeks
Outcomes	Efficacy outcome: • Change in scores using HDSS questionnaire
	Safety outcomes: • Participants completed questionnaire related to side effects, for example gastrointestinal complications, sedation, dry mouth and urinary complications
Source of funding	Not reported

Overall risk of bias/quality assessment (CASP RCT checklist)	Did the trial address a clearly focused issue?	Yes
	Was the assignment of patients to treatments randomised?	Unclear[a]
	Were patients, health workers and study personnel blinded?	Unclear[b]
	Were the groups similar at the start of the trial?	Yes
	Aside from the experimental intervention, were the groups treated equally?	Yes
	Were all of the patients who entered the trial properly accounted for at its conclusion?	Yes
	How large was the treatment effect?	See table 11
	How precise was the estimate of the treatment effect?	See table 11
	Can the results be applied in your context? (or to the local population)	Yes
	Were all clinically important outcomes considered?	Unclear[c]
	Are the benefits worth the harms and costs?	See key points
Study limitations	• The study had a short duration • Placebo controlled study, no active comparator • Small study with limited statistical power to detect differences between the groups • External factors influencing the degree of sweating were not assessed (e.g. outdoor activities or vocational activities) • It is not clear whether allocation was concealed	

Comments	[a] Participants drew red or black chips from a ballot box, which is not a robust method of randomisation and means allocation was not concealed. [b] Because of the anticholinergic adverse effects associated with oxybutynin it is possible that participants were aware of the treatment (despite being reported as a double-blind study). [c] No objective measures of treatment were reported.
Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale.	

Results tables

Table 8 Schollhammer et al. 2015

	Oxybutynin	**Placebo**	**Analysis**
n	**30**	**28**[a]	
Primary outcome			
Proportion of participants with an improvement in HDSS score of 1 point or more at week 6	60% (18/30)	29% (8/28)	p<0.01
Selected secondary outcomes			
Level of improvement in HDSS score	0 points: 12/30 1 point: 5/30 2 points: 11/30 3 points: 2/30 (from a mean baseline score of 3.2)	0 points: 20/28 1 point: 6/28 2 points: 2/28 3 points: 0/28 (from a mean baseline score of 3.3)	No statistical analyses reported
Level of improvement in DLQI score from baseline to week 6	−6.9 (from a mean baseline score of 11.4)	−2.3 (from a mean baseline score of 10.8)	p<0.01
Safety and tolerability outcomes			

n	**30**	**28**	
Dry mouth	13/30 (43%) [6/13 slight intensity, 5/13 mild intensity, 2/13 severe intensity]	3/28 (11%) [intensity not reported]	p<0.01
Blurred vision	4/30 (13%)	0/28 (0%)	No statistical analysis reported
[a] The authors state that the ITT analysis included 30 people in the placebo group, although results are only provided for 28 people.			
Abbreviations:DLQI, Dermatology Life Quality Index; HDSS, Hyperhidrosis Disease Severity Scale; ITT, intention to treat.			

Table 9 Wolosker et al. 2012

	Oxybutynin	**Placebo**	**Analysis**
n	**23**	**22**	
Efficacy outcomes			
Patient assessment of improvement in palmar or axillary hyperhidrosis[a]	0–4: 6/23 5–7: 6/23 8–10: 11/23	0–4: 16/22 5–7: 6/22 8–10: 0/22	p<0.001 More people in the oxybutynin group had an improvement of 5–7 or 8–10 points compared with placebo (statistically significant difference)

Patient assessment of improvement in quality of life[b]	20–35: 8/23 36–51: 9/23 52–67: 6/23 68–83: 0/23 84–100: 0/23	20–35: 0/22 36–51: 3/22 52–67: 19/22 68–83: 0/22 84–100: 0/22	p<0.001 More people in the oxybutynin had an improvement of 36–51 or 52–67 points compared with placebo (statistically significant difference)
n	**12**	**15**	
Patient assessment of improvement in plantar hyperhidrosis[a]	0–4: 1/12 5–7: 7/12 8–10: 4/12	0–4: 13/15 5–7: 2/15 8–10: 0/15	p<0.001
Safety and tolerability outcomes			
n	**30**	**28**	
Dry mouth: moderate and severe	5 mg: 6/23 10 mg: 8/23	5 mg: 7/22 10 mg: 2/22	No statistical analysis reported
Dry mouth: absent and mild	5 mg: 17/23 10 mg: 15/23	5 mg: 15/22 10 mg: 20/22	No statistical analysis reported
[a] A score of 0–4 corresponds to a 'null or slight' improvement; 5–7 a 'moderate' improvement and 8–10 a 'great' improvement. [b] Improvements of 20–35 points correspond to the person feeling 'much better'; 36–51 'a little better'; 52–67 'the same'; 69–83'a little worse'; and 84–100 'much worse'.			

Table 10 Costa Jr et al. 2014

	Oxybutynin	Placebo	Analysis
n	**16**	**16**	
Efficacy outcomes			
Mean adjusted quality of life score (SD)[a]	Before treatment 40.4 (14.4) 'Very good'	Before treatment 34.8 (16.3) 'Very good'	Oxybutynin: p=0.001 Placebo: p=0.099 Statistically significant difference in oxybutynin group only
	After treatment 17.5 (11.9) 'Excellent'	After treatment 33.2 (15.3) 'Very good'	
Right foot – mean transepidermal water loss (SD), g/m^2/hour	Before treatment 140.3 (40.3)	Before treatment 112.6 (49.3)	Oxybutynin: p=0.008 Placebo: p=0.796 Statistically significant difference in oxybutynin group only
	After treatment 87.6 (70.2)	After treatment 102.2 (55.9)	
Right hand – mean transepidermal water loss (SD), g/m^2/hour	Before treatment 61.7 (43.9)	Before treatment 58.3 (39.3)	Oxybutynin: p=0.001 Placebo: p=0.245 Statistically significant difference in oxybutynin group only
	After treatment 28.6 (20.5)	After treatment 50.4 (37.8)	

Back – mean transepidermal water loss (SD), g/m^2/hour	Before treatment 38.2 (64.3)	Before treatment 18.2 (19.0)	Oxybutynin: p=0.004 Placebo: p=0.959 Statistically significant difference in oxybutynin group only
	After treatment 10.8 (8.7)	After treatment 19.0 (27.9)	
Abdomen – mean transepidermal water loss (SD), g/m^2/hour	Before treatment 39.7 (46.0)	Before treatment 24.0 (18.1)	Oxybutynin: p=0.004 Placebo: p=0.501 Statistically significant difference in oxybutynin group only
	After treatment 16.5 (19.2)	After treatment 26.8 (31.4)	
Safety and tolerability outcomes			
n	**16**	**16**	
Dry mouth	100.0% (16/16)	43.8% (7/16)	p=0.001
Constipation	31.0% (5/16)	6.3% (1/16)	p=0.172
Drowsiness	18.0% (3/16)	6.3% (1/16)	p=0.600
[a] Scored from 0 to 100, with lower scores indicating better quality of life. 0–20= 'excellent' ; 21–40= 'very good'; 41–60= 'good'; 61–80= 'poor'; 81–100= 'very poor'.			
Abbreviations: g, gram; m, metre; SD, standard deviation.			

Table 11 Ghaleiha et al. 2012

	Oxybutynin	**Placebo**	**Analysis**

n	**66**	**74**	
Efficacy outcomes			
HDSS score at week 2	1.546, from a baseline score of 2.864	1.961 from a baseline score of 2.648	p=0.03
Safety and tolerability outcomes			
n	**66**	**74**	
Gastrointestinal complications	7/66 (10.6%)	6/74 (8.1%)	p=0.61
Sedation	0/66 (0.0%)	0/74 (0.0%)	NA
Dry mouth	3/66 (4.4%)	0/74 (0.0%)	p=0.10
Urinary complications	3/66 (4.4%)	0/74 (0.0%)	p=0.10
Abbreviations:HDSS, Hyperhidrosis Disease Severity Scale; NA, not applicable.			

Excluded studies

Study reference	Reason for exclusion
Bergon-Sendin M, Pulido-Perez A, Saez-Martin L C et al. (2016) Preliminary experience with transdermal oxybutynin patches for hyperhidrosis. Actas Dermo-Sifiliograficas 107(10), 845–50	Study not prioritised (not the best available evidence)
Campanati A, Gregoriou S, Kontochristopoulos G, and Offidani A (2015) Oxybutynin for the Treatment of Primary Hyperhidrosis: Current State of the Art. Skin Appendage Disorders 1(1), 6–13	Study not prioritised (not the best available evidence)

Del Boz J , Millan-Cayetano JF, Blazquez-Sanchez N et al. (2016) Individualized dosing of oral oxybutynin for the treatment of primary focal hyperhidrosis in children and teenagers. Pediatric Dermatology 33(3), 327–31	Study not prioritised (not the best available evidence)
Harmsze A M, Houte Mv, Deneer V H et al. (2008) Exercise-induced sweating in healthy subjects as a model to predict a drug's sweat-reducing properties in hyperhydrosis: a prospective, placebo-controlled, double-blind study. Acta Dermato-Venereologica 88(2), 108–12	Study not prioritised (not the best available evidence)
Karlsson-Groth A, Rystedt A, and Swartling C (2015) Treatment of compensatory hyperhidrosis after sympathectomy with botulinum toxin and anticholinergics. Clinical Autonomic Research 25(3), 161–7	Study not prioritised (not the best available evidence)
Kim WO, Kil HK, Yoon KB et al. (2010) Treatment of generalized hyperhidrosis with oxybutynin in post-menopausal patients. Acta Dermato-Venereologica 90(3), 291–3	Study not prioritised (not the best available evidence)
Millan-Cayetano JF, Del Boz J , Rivas-Ruiz F, et al. (2016) Oral oxybutynin for the treatment of hyperhidrosis: outcomes after one-year follow-up. Australasian Journal of Dermatology 30, 30	Study not prioritised (not the best available evidence)
Nicholas R, Quddus A, and Baker DM (2015) Treatment of primary craniofacial hyperhidrosis: a systematic review. American Journal of Clinical Dermatology 16(5), 361–70	Study not prioritised (not the best available evidence)
Stashak AB and Brewer JD (2014) Management of hyperhidrosis. Clinical, and Cosmetic and Investigational Dermatology CCID 7, 285–99	Not a relevant study

Teivelis MP, Wolosker N, Krutman M, et al. (2014) Compensatory hyperhidrosis: Results of pharmacologic treatment with oxybutynin. Annals of Thoracic Surgery 98(5), 1797–802	Study not prioritised (not the best available evidence)
Teivelis MP, Wolosker N, Krutman M, et al. (2014) Treatment of uncommon sites of focal primary hyperhidrosis: experience with pharmacological therapy using oxybutynin. Clinics (Sao Paulo, and Brazil) 69(9), 608–14	Study not prioritised (not the best available evidence)
Wolosker N, Teivelis MP, Krutman M, et al. (2015) Long-term efficacy of oxybutynin for palmar and plantar hyperhidrosis in children younger than 14 years. Pediatric Dermatology 32(5), 663–7	Study not prioritised (not the best available evidence)
Wolosker N, Teivelis MP, Krutman M et al. (2015) Long-term results of the use of oxybutynin for the treatment of plantar hyperhidrosis. International Journal of Dermatology 54(5), 605–11	Study not prioritised (not the best available evidence)
Wolosker N, Teivelis MP, Krutman M et al. (2014) Long-term results of the use of oxybutynin for the treatment of axillary hyperhidrosis. Annals of Vascular Surgery 28(5), 1106–12	Study not prioritised (not the best available evidence)
Wolosker N, Campos JR, Kauffman P et al. (2011) The use of oxybutynin for treating facial hyperhidrosis. Anais Brasileiros de Dermatologia 86(3), 451–6	Study not prioritised (not the best available evidence)
Wolosker N, De Campos JR, Kauffman P et al. (2011) An alternative to treat palmar hyperhidrosis: Use of oxybutynin. Clinical Autonomic Research 21(6), 389–93	Study not prioritised (not the best available evidence)

Wolosker N, De Campos JR, Kauffman P et al. (2011) The use of oxybutynin for treating axillary hyperhidrosis. Annals of Vascular Surgery 25(8), 1057–62	Study not prioritised (not the best available evidence)
Wolosker N, de Campos JR, Kauffman P et al. (2013) Use of oxybutynin for treating plantar hyperhidrosis. International Journal of Dermatology 52(5), 620–3	Study not prioritised (not the best available evidence)
Wolosker N, Krutman M, Kauffman P et al. (2013) Effectiveness of oxybutynin for treatment of hyperhidrosis in overweight and obese patients. Revista Da Associacao Medica Brasileira 59(2), 143–7	Study not prioritised (not the best available evidence)
Wolosker N, Teivelis M P, Krutman M et al. (2014) Long-term results of oxybutynin use in treating facial hyperhidrosis. Anais Brasileiros de Dermatologia 89(6), 912–6	Study not prioritised (not the best available evidence)
Wolosker N, Teivelis MP, Krutman M et al. (2014) Long-term results of oxybutynin treatment for palmar hyperhidrosis. Clinical Autonomic Research 24(6), 297–303	Study not prioritised (not the best available evidence)
Wolosker N, Krutman M, Teivelis MP (2014) Quality of life before hyperhidrosis treatment as a predictive factor for oxybutynin treatment outcomes in palmar and axillary hyperhidrosis. Annals of Vascular Surgery 28(4), 970–6	Study not prioritised (not the best available evidence)

Terms used in this evidence summary

Dermatology Life Quality Index (DLQI)

The Dermatology Life Quality Index (DLQI) questionnaire is a qualitative measure of how a person's skin condition is impacting on their life. DLQI can be used for many dermatology conditions, not just hyperhidrosis. The person is asked 10 questions covering a number of factors including symptoms, embarrassment, activities and relationships. The DLQI is scored from 0 to 30, with higher scores suggesting a greater impairment in quality of life. The DLQI has been validated for assessing quality of life associated with hyperhidrosis.

Meaning of DLQI Scores

0–1 = no effect at all on patient's life

2–5 = small effect on patient's life

6–10 = moderate effect on patient's life

11–20 = very large effect on patient's life

21–30 = extremely large effect on patient's life

Hyperhidrosis Disease Severity Scale (HDSS)

The Hyperhidrosis Disease Severity Scale (HDSS) is a validated, qualitative measure of severity of hyperhidrosis based on how it affects daily activities. The patient is asked 1 question: 'How would you rate the severity of your hyperhidrosis?' with 4 possible answers, scored from 1 to 4:

1. My sweating is never noticeable and never interferes with my daily activities
2. My sweating is tolerable but sometimes interferes with my daily activities
3. My sweating is barely tolerable and frequently interferes with my daily activities
4. My sweating is intolerable and always interferes with my daily activities

A score of 3 or 4 indicates severe hyperhidrosis. A score of 1 or 2 indicates mild or moderate hyperhidrosis.

Search strategy

Database: Medline

Platform: Ovid

Version: 1946 to November wk 4 2016

Search date: 02/12/2016

Number of results retrieved: 40

Search strategy:

Database: Ovid MEDLINE(R) <1946 to November Week 4 2016>

Search Strategy:

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1 (anturol or cystonorm or cystrin or delifon or ditropan or diutropin or dridase or driptane or esoxybutynin or esoxybutynin or frenurin or gelnique or iliaden or kentera or lenditro or lyrinel or "mutum cr" or nefryl or ovitropan or oxibutinin or oxibutynin or oxybutynin or oxyban or oxytrol or oyrobin or pollakis or reteven or tropan or uricont or uroflax or urotrol or "zatur ge" or tavor).tw. (1224)

2 exp hyperhidrosis/ (3401)

3 (hyperh?drosis or sweat* or hyperperspiration or perspir*).tw. (21275)

4 2 or 3 (22122)

5 1 and 4 (44)

6 limit 5 to english language (40)

Database: Medline in-process

Platform: Ovid

Version: November 29 2016

Search date:02/12/2016

Number of results retrieved: 6

Search strategy:

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <November 29, 2016>

Search Strategy:

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1 (anturol or cystonorm or cystrin or delifon or ditropan or diutropin or dridase or driptane or esoxybutynin or esoxybutynin or frenurin or gelnique or iliaden or kentera or lenditro or lyrinel or "mutum cr" or nefryl or ovitropan or oxibutinin or oxibutynin or oxybutynin or oxyban or oxytrol or oyrobin or pollakis or reteven or tropan or uricont or uroflax or urotrol or "zatur ge" or tavor).tw. (111)

2 exp hyperhidrosis/ (0)

3 (hyperh?drosis or sweat* or hyperperspiration or perspir*).tw. (1763)

4 2 or 3 (1763)

5 1 and 4 (6)

6 limit 5 to english language (6)

Database: Medline epubs ahead of print

Platform: Ovid

Version: December 01 2016

Search date: 02/12/2016

Number of results retrieved: 2

Database: Ovid MEDLINE(R) Epub Ahead of Print <December 01, 2016>

Search Strategy:

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1 (anturol or cystonorm or cystrin or delifon or ditropan or diutropin or dridase or driptane or esoxybutynin or esoxybutynin or frenurin or gelnique or iliaden or kentera or lenditro or lyrinel or "mutum cr" or nefryl or ovitropan or oxibutinin or oxibutynin or oxybutynin or oxyban or oxytrol or oyrobin or pollakis or reteven or tropan or uricont or uroflax or urotrol or "zatur ge" or tavor).tw. (13)

2 exp hyperhidrosis/ (0)

3 (hyperh?drosis or sweat* or hyperperspiration or perspir*).tw. (273)

4 2 or 3 (273)

5 1 and 4 (3)

6 limit 5 to english language (2)

Database: Embase

Platform: Ovid

Version: 1074 to 2016 wk 48

Search date: 02/12/2016

Number of results retrieved: 68

Search strategy:

Database: Embase <1974 to 2016 Week 48>

Search Strategy:

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1 *oxybutynin/ (1436)

2 (anturol or cystonorm or cystrin or delifon or ditropan or diutropin or dridase or driptane or esoxybutynin or esoxybutynin or frenurin or gelnique or iliaden or kentera or lenditro or lyrinel or "mutum cr" or nefryl or ovitropan or oxibutinin or oxibutynin or oxybutynin or oxyban or oxytrol or oyrobin or pollakis or reteven or tropan or uricont or uroflax or urotrol or "zatur ge" or tavor).tw. (2770)

3 1 or 2 (3137)

4 hyperhidrosis/ (7298)

5 (hyperh?drosis or sweat* or hyperperspiration or perspir*).tw. (30779)

6 4 or 5 (34097)

7 3 and 6 (77)

8 limit 7 to english language (68)

Database: Cochrane Library – incorporating Cochrane Database of Systematic Reviews (CDSR); DARE; CENTRAL; HTA database; NHS EED

Platform: Ovid

Version:

CDSR –12 of 12 December 2016

DARE – 2 of 4, April 2015 (legacy database)

CENTRAL – 11 of 12 November 2016

HTA – 4 of 4 October 2016

NHS EED – 2 of 4, April 2015 (legacy database)

Search date:02/12/2016

Number of results retrieved: CDSR 0; DARE 0 ; CENTRAL 9 ; HTA 0 ; NHS EED 0

Search strategy:

Search Name:

Date Run: 02/12/16 10:43:24.646

Description:

ID Search Hits

#1 anturol or cystonorm or cystrin or delifon or ditropan or diutropin or dridase or driptane or esoxybutynin or esoxybutynin or frenurin or gelnique or iliaden or kentera or lenditro or lyrinel or "mutum cr" or nefryl or ovitropan or oxibutinin or oxibutynin or oxybutynin or oxyban or oxytrol or oyrobin or pollakis or reteven or tropan or uricont or uroflax or urotrol or "zatur ge" or tavor:ti,ab,kw (Word variations have been searched) 472

#2 MeSH descriptor: [Hyperhidrosis] explode all trees 187

#3 hyperh?drosis or sweat* or hyperperspiration or perspir*:ti,ab,kw (Word variations have been searched) 2674

#4 #2 or #3 2674

#5 #1 and #4 9

Development of this evidence summary

The evidence summary: process guide (2017) sets out the process NICE uses to select topics for evidence summaries and details how the summaries are developed, quality assured and approved for publication.

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Declarations of interest

Richard Oliver: Interests declared: Custodian and advisor for the Hyperhidrosis UK Information Site. Distributes iontophoresis machines and antiperspirants for the treatment of hyperhidrosis for STD Pharma. Educates healthcare professionals in the aetiology, diagnosis and management of hyperhidrosis.

William Perkins: No interests declared.

Jane Ravenscroft: No interests declared.

About this evidence summary

Evidence summaries provide a summary of the best available published evidence for selected new medicines, unlicensed medicines or off-label use of licensed medicines.

The summaries assess the strengths and weaknesses of the best available evidence to inform health professionals and commissioners' decision-making.

This summary is not NICE guidance.

ISBN: 978-1-4731-2384-7