Glycopyrronium bromide is an antimuscarinic drug that prevents the stimulation of sweat glands. This evidence reviews the use of oral glycopyrronium bromide for treating hyperhidrosis, or excessive sweating.

Oral preparations of glycopyrronium bromide (tablets and solution or suspension) are not licensed or available in the UK for treating hyperhidrosis. Such preparations must be either imported or prepared by ‘specials’ manufacturers. Use for this indication would be unlicensed.

Glycopyrronium bromide powder for solution (Robinul powder) is currently licensed for the iontophoretic treatment (electromotive drug administration) of primary (idiopathic) hyperhidrosis of the palms of hands and soles of feet in children and adults. As such this is excluded from this review – note iontophoresis (together with botulinum toxin and surgical procedures) for hyperhidrosis is currently included within the Surrey Collaborative list of treatments that are not routinely funded requiring individual funding applications.

Botox for Hyperhidrosis is not routinely commissioned in North Facing Sussex CCGs

- **How strong is the evidence for claimed efficacy?**
No randomised controlled trials were identified. Across a number of case series, involving around 150 adults, children and young people, hyperhidrosis ‘responded’ to oral glycopyrronium bromide tablets in 67-90% of participants. These response rates were based on absolute responses to therapy as recorded in patient records, or on patient questionnaires, which could be subjective and do not appear to be validated. Overall the 5 case series provide weak evidence of the efficacy and safety of oral glycopyrronium bromide for treating hyperhidrosis.

- **Potential advantages in terms of: efficacy, compliance, pharmacokinetics, drug interactions and adverse effects?**
There are limited treatment options for the treatment of hyperhidrosis which initially include lifestyle changes to improve symptoms, then antiperspirants (aluminium chloride). All other treatments require a referral to a dermatologist however all these options are included currently within the Treatments not Routinely Funded policy (iontophoresis, botulinum toxin and surgical procedures). This is an oral treatment but it should be noted that across the case series 29-79% of participants experienced adverse effects, most frequently dry mouth (affecting 16-63%). In 3 case series 26%, 20% and 3% of participants withdrew because of adverse effects.

- **Is there a clear place in therapy / treatment pathway?**
Not really. This would be after lifestyle changes / antiperspirants. See above

- **Is monitoring for toxicity required?** No

- **Is monitoring for efficacy required?** No, however treatment would be discontinued if no benefit obtained

- **Financial implications:**
  No cost-effectiveness studies of oral glycopyrronium bromide for use in hyperhidrosis identified. The Drug Tariff includes prices for the glycopyrronium specials oral solution / suspension in Part VIIIB (arrangements for payment for specials and imported unlicensed medicines) as follows (October 2014 Drug Tariff):

<table>
<thead>
<tr>
<th>VOLUME</th>
<th>PRICE FOR VOL LISTED (p)</th>
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<tbody>
<tr>
<td>Glycopyrronium bromide 1mg/5ml oral solution/suspension</td>
<td>100ml</td>
</tr>
<tr>
<td>Glycopyrronium bromide 2.5mg/5ml oral solution</td>
<td>100ml</td>
</tr>
<tr>
<td>Glycopyrronium bromide 2.5mg/5ml oral suspension</td>
<td>200ml</td>
</tr>
<tr>
<td>Glycopyrronium bromide 200micrograms/5ml oral solution</td>
<td>100ml</td>
</tr>
<tr>
<td>Glycopyrronium bromide 200micrograms/5ml oral suspension</td>
<td>100ml</td>
</tr>
<tr>
<td>Glycopyrronium bromide 2mg/5ml oral solution</td>
<td>100ml</td>
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<tr>
<td>Glycopyrronium bromide 2mg/5ml oral suspension</td>
<td>100ml</td>
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<tr>
<td>Glycopyrronium bromide 5mg/5ml oral solution</td>
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<tr>
<td>Glycopyrronium bromide 5mg/5ml oral suspension</td>
<td>50ml</td>
</tr>
<tr>
<td>Glycopyrronium bromide 500micrograms/5ml oral solution</td>
<td>100ml</td>
</tr>
<tr>
<td>Glycopyrronium bromide 500micrograms/5ml oral suspension</td>
<td>300ml</td>
</tr>
</tbody>
</table>

No price is listed for glycopyrronium bromide oral tablets, and the cost of these will therefore differ depending on the source. NHS Prescription Cost Analysis for England 2012 reported that the various glycopyrronium tablets cost between £268.57 and £712.34 per item (the number of tablets per item is not known).

- **National Guidance available** –
  - NICE Evidence summary: unlicensed or off-label medicines (ESUOM) 16 (July 2013) Hyperhidrosis: oral glycopyrronium bromide
  - NICE Clinical Knowledge Summaries: Hyperhidrosis (Last reviewed in July 2013) http://cks.nice.org.uk/hyperhidrosis#Itopicsummary
  - East of England Priorities Advisory Committee: Management of Hyperhidrosis (March 2014) which states: *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).*
  - Primary Care Dermatology Society http://www.pcds.org.uk/clinical-guidance/hyperhidrosis which states for Systemic anticholinergics (AC):
- Are best used for **generalised hyperhidrosis, and compensatory sweating** following endoscopic thoracic sympathectomy, as opposed to just one or two areas of hyperhidrosis

- **Propanthelene bromide** is the only licensed systemic product for primary hyperhidrosis. Start at a low dose of 15 mg once to twice a day, increasing as tolerated to 30 mg tds

- Some patients are unable to tolerate standard release formulations of systemic AC, in which case consider a **modified-release formula of oxybutynin** eg Lyrinel XL 10 mg®

**Recommendation to PCN:**

1. Oral glycopyrronium bromide (unlicensed) for the treatment of hyperhidrosis is not routinely supported and should be considered as black on the traffic light system. Oxybutynin immediate release (IR / off-label) should be the oral anticholinergic of choice to treat hyperhidrosis or propanthelene bromide (licensed but less effective).

**VERSION CONTROL SHEET**

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<td>Linda Honey</td>
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**For full information and review of available evidence please refer to:**

1. NICE Evidence summary: unlicensed or off-label medicines (ESUOM) 16 (July 2013) Hyperhidrosis: oral glycopyrronium bromide which is circulated together with this summary document.

2. East of England Priorities Advisory Committee: Management of Hyperhidrosis (March 2014) which is circulated together with this summary document.

3. NICE Clinical Knowledge Summaries: Hyperhidrosis [http://cks.nice.org.uk/hyperhidrosis#topicsummary](http://cks.nice.org.uk/hyperhidrosis#topicsummary)

Other treatments that may be used:

CKS found no good-quality RCTs of the efficacy and safety of oral antimuscarinics (propanthelene, oxybutynin, glycopyrronium bromide, benzatropine), clonidine, diltiazem, or benzodiazepines in the treatment of primary focal hyperhidrosis.

A randomized controlled trial compared oxybutynin with placebo and found a greater improvement in symptoms in the oxybutynin group. However, the study was of short duration and small (n = 50), with 10% loss to follow up, therefore it is difficult to draw firm conclusions on the place of oxybutynin in treating primary focal hyperhidrosis [Wolosker et al, 2012].
There is very limited evidence of the efficacy of oral glycopyrronium bromide from a case series, in which a third of people stopped taking it because of adverse effects [Bajaj and Langtry, 2007].

Expert opinion is divided in relation to these treatments. They are recommended by the International Hyperhidrosis Society which states' while antiperspirants are usually recommended as first-line treatment for primary axillary hyperhidrosis, there is a possible exception if the patient's excessive sweating symptoms occur during, or are exacerbated by, known anxiety-provoking situations such as presentations at work or dramatic performances. In these cases, the patient may be treated prior to such events with an anticholinergic or short course benzodiazepine' [International Hyperhidrosis Society, 2012b]. CKS questions whether performance would be improved by medications (antimuscarinics and benzodiazepines) that can cause drowsiness, dry mouth, palpitations, or dizziness [Hornberger et al, 2004; BNF 65, 2013].

Oral glycopyrronium bromide (2 mg, two to three times daily) and oxybutynin (an antimuscarinic) were recommended in feedback from two expert reviewers. However, antimuscarinic medication is not recommended in Guidelines for the primary care treatment and referral of focal hyperhidrosis [Lowe et al, 2003], or the Drug and Therapeutics Bulletin [DTB, 2005], and it is only recommended as third- or fourth-line treatment in the Canadian consensus statement [Solish et al, 2007], or as a final option before considering surgery in the US consensus statement [Hornberger et al, 2004].

Additional information:

**Current use:** ePACT data for oral glycopyrronium bromide at CCG level shows:
- NW Surrey CCG Aug 13- July 2014: 181 items £45K (average of £248/item)
- Surrey Downs CCG 13/14: 865 items £280K (average of £323/item)
- G&W CCG 13/14: 180 items £36K (average of £200/item)
- Surrey Heath CCG 13/14: 114 items £19K (average of £166/item)
- East Surrey CCG 13/14: 312 items £64K (average of £205/item)
- Crawley CCG and Horsham and Mid Sussex CCG do not have Iontophoresis on their formulary. Epact data has been requested and will be tabled on the day

**Other areas policies:** limited information available. Information available:

1. **Mid Essex CCG (Jan 2014)**
Oxybutinin IR (off-label) should be prescribed in preference to glycopyrronium bromide (unlicensed). The level of evidence for oxybutynin IR and glycopyrronium bromide are of similar strength (weak). Propantheline bromide is the only oral anticholinergic licensed for hyperhidrosis in the UK but is considered to be less effective than oxybutynin or glycopyrronium. Prescribing of (unlicensed) glycopyrronium is considered to be low priority and not routinely commissioned.

2. **Herts Valley CCG:**
Glycopyrronium Bromide is NOT recommended for the treatment of hyperhidrosis in both primary and secondary care.

Recommendations for oral anticholinergic choices to treat hyperhidrosis:

1. **Oxybutynin immediate release** (IR, off-label) should be prescribed in preference to glycopyrronium bromide (unlicensed/off-label) or propantheline bromide (less effective): Start with 2.5mg daily and gradually titrate according to response.