Hyperhidrosis treatment with Botulinum Toxin for Axillary Hyperhidrosis

Policy:
In accordance with the licensing, treatment with Botulinum Toxin A will only be funded for the management of severe (HDSS score of 3 or 4) axillary hyperhidrosis, provided first-line treatment (topical therapy) and/or iontophoresis have failed or are contraindicated.

These polices have been approved by the eight Clinical Commissioning Groups in North West London (NHS Brent CCG, NHS Central London CCG, NHS Ealing CCG, NHS Hammersmith and Fulham CCG, NHS Harrow CCG, NHS Hillingdon CCG, NHS Hounslow CCG and NHS West London CCG).

Background:
Hyperhidrosis (ICD-10 Code: R61) refers to excessive/enhanced sweating beyond that which is required to return body temperature to normal. It can be generalised or focal, primary or secondary. Primary focal hyperhidrosis is the most common type, is idiopathic, and develops in previously healthy people. It typically affects the axillae, palms, soles of feet (plantar) and face (craniofacial), areas principally involved in emotional sweating. It is thought to affect >2.5% of the population. It usually has its onset in childhood or adolescence, but can occur at any age. Palmar and plantar hyperhidrosis may be present at birth.

Secondary generalised hyperhidrosis involves the entire body, and is due to an underlying condition, most often an infectious, endocrine or neurological disorder; or may be simply drug-induced. It develops due to dysfunction of the central or peripheral nervous system. Secondary focal hyperhidrosis involves specific areas of the body, but is also caused by an underlying condition (e.g. neurological disorders, intrathoracic neoplasms, or compensatory hyperhidrosis).

The Hyperhidrosis Disease Severity Scale (HDSS) (http://www.sweathelp.org/pdf/HDSS.pdf) provides a qualitative measure of the severity of the patient’s condition, and allows tailoring of treatment. A score of 1 or 2 indicate mild or moderate hyperhidrosis. A score of 3 or 4 indicates severe hyperhidrosis. A one-point improvement in HDSS score post-treatment has been associated with a 50% reduction in sweat production and a 2-point improvement with an 80% reduction.
### Recommended treatment approaches:

<table>
<thead>
<tr>
<th>Type of hyperhidrosis</th>
<th>First-line therapy</th>
<th>Second-line therapy (options)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild axillary, palmar, and plantar hyperhidrosis (HDSS score of 2)</td>
<td>- Topical treatments - aluminium chloride-based (AC) &amp; other</td>
<td>- Iontophoresis</td>
<td>**unlicensed indication</td>
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<tr>
<td></td>
<td>- Consider treating any underlying anxiety, which may be an exacerbating factor</td>
<td>- Botulinum toxin A (ETX-A)**</td>
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<tr>
<td>Severe axillary, palmar, and plantar hyperhidrosis (HDSS score of 3 or 4)</td>
<td>- Topical treatments – AC &amp; other</td>
<td>- Iontophoresis^</td>
<td>* licensed indication only for severe axillary hyperhidrosis, but evidence exists for benefit of treatment for palmar and plantar hyperhidrosis</td>
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<td></td>
<td>- Consider treating any underlying anxiety, which may be an exacerbating factor</td>
<td>- BTX-A ^^</td>
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<td>- Local surgery (axillary) and ETS should only be considered after failure of all other treatment options</td>
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<tr>
<td>Craniofacial hyperhidrosis</td>
<td>- Topical treatments – AC &amp; other</td>
<td>- Oral anti-cholinergic medications^</td>
<td>**unlicensed indication</td>
</tr>
<tr>
<td></td>
<td>- Consider treating any underlying anxiety, which may be an exacerbating factor</td>
<td>- ETX-A^</td>
<td></td>
</tr>
<tr>
<td>Generalised hyperhidrosis</td>
<td>- Treatment of underlying condition</td>
<td>- Oral anti-cholinergic medications</td>
<td>BTX-A not indicated</td>
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</tbody>
</table>

§ based on Guidelines for the primary care treatment and referral of focal hyperhidrosis (9), an evidence-based review (22), US and Canadian expert consensus statements (6, 6).
Background continued:

Evidence base for treatment

Secondary hyperhidrosis
Management of secondary generalised or focal hyperhidrosis should be directed at looking for an underlying cause, and managing that appropriately. Oral anti-cholinergics may also be used.

Primary focal hyperhidrosis
Various medical, surgical and electrical therapies exist for primary focal hyperhidrosis. However, for many, the efficacy is short-term or they are associated with unacceptable side effects. A step-by-step approach is recommended for treatment. Local treatment options with few and minor side effects should be tried first.

First-line treatment (primary care)
- 20% aluminium chloride (AC) hexahydrate in alcohol solution e.g. Aluminium salts in OTC anti-perspirants
- Consider treating any underlying anxiety, which may be an exacerbating factor
- If that fails – refer to dermatologist/ secondary care

Secondary care treatment options

Modified topical therapy:
- emollients, topical corticosteroids, different strengths of aluminium salts (up to 50%), and topical glutaraldehyde or formaldehyde
- topical glycopyrrolate (an antimuscarinic agent) can be prepared by special order manufacturers, and may be useful for primary craniofacial hyperhidrosis
- efficacy and tolerability vary widely

Iontophoresis
- The sites of hyperhidrosis (hands, feet) are immersed in warm water (or a wet contact pad may be applied e.g. for the axillae) through which a weak electric current is passed
- In more severe cases of hyperhidrosis affecting plantar and palmar areas, glycopyrronium bromide (an antimuscarinic agent) as a 0.05% solution can be added to the water, but adverse effects are common
- Some people seem to gain considerable symptom relief. Most report an improvement after 6-10 sessions. Maintenance treatment is usually required at 1-4-week intervals.

Surgery
- Local surgery (axillary; resection of sweat glands) and endoscopic thoracic sympathectomy (ETS) should only be considered if other treatment options have failed or have not been tolerated complications may be permanent and significant
- ETS involves video-assisted laparoscopic division of the sympathetic chain over the neck of the ribs under general anaesthesia, usually by a vascular surgeon. It is mainly indicated as a last resort for severe palmar, axillary and sometimes craniofacial hyperhidrosis. Lumbar sympathectomy is not used for plantar hyperhidrosis because of the risk of sexual dysfunction.

Oral medication
- Oral anti-muscarinics, such as glycopyrronium bromide and oxybutinin, may be used, but their use is limited by adverse effects; other options include: clonidine, diltiazem, benzodiazepines
- Systemic therapies are mainly used in treatment of generalised hyperhidrosis
Background continued:

Botulinum toxin A (BTX-A) (Botox®)

- BTX-A blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. When injected intradermally, BTX-A produces temporary chemical denervation of the sweat gland resulting in local reduction in sweating.

- BTX-A is the best-studied treatment to date for focal hyperhidrosis, and local intradermal injections of BTX-A have been used since 1996 as a minimally invasive treatment for focal hyperhidrosis, with numerous studies documenting safety, efficacy, effectiveness, and extremely high levels of patient satisfaction, especially when other treatment options have proven ineffective.

- It is only licensed for the treatment of severe axillary hyperhidrosis that is inadequately managed by /unresponsive to topical agents.

- Effectiveness: In 2018, a Health Technology assessment was published for the treatment of hyperhidrosis in secondary care. A systematic review and economic model, including a value-of-information (VOI) analysis was carried out.

- ‘Fifty studies were included in the effectiveness review: 32 randomised controlled trials (RCTs), 17 non-RCTs and one large prospective case series. Most studies were small, rated as having a high risk of bias and poorly reported. The interventions assessed in the review were iontophoresis, BTX, anticholinergic medications, curettage and newer energy-based technologies that damage the sweat gland (e.g. laser, microwave). There is moderate-quality evidence of a large statistically significant effect of BTX on axillary hyperhidrosis symptoms, compared with placebo. There was weak but consistent evidence for iontophoresis for palmar hyperhidrosis. Evidence for other interventions was of low or very low quality. For axillary hyperhidrosis cost-effectiveness results indicated that iontophoresis, BTX, medication, curettage and ETS was the most cost-effective sequence (probability 0.8), with an incremental cost-effectiveness ratio of £9304 per quality-adjusted life-year.’
References:


5. Stolman LP. Hyperhidrosis: medical and surgical treatment. Eplasty. 2008:8 e22


18. DTB. Treatments for excessive armpit sweating. Drug & Therapeutics Bulletin


20. NICE Clinical Knowledge Summaries. https://cks.nice.org.uk/hyperhidrosis