Botulinum toxin A (Dysport) for hyperhidrosis of the axillae

LAY SUMMARY

Hyperhidrosis is the medical term for excessive sweating, most commonly affecting the palms of the hands, soles of the feet and the axillae (armpits). Although hyperhidrosis is not life-threatening, it increases the risk of skin infections and has a significant impact on the quality of life of those affected.

Botulinum toxin A is a treatment which can reduce sweating in people with hyperhidrosis. It is injected directly into the skin of the armpit, blocking the nerves in the skin that trigger sweating.

Botulinum toxin A has been studied and has been found to be safe and effective in treating people with hyperhidrosis. If this formulation of botulinum toxin A (Dysport) is licensed for axillary hyperhidrosis, it will provide an additional treatment option for people with this distressing condition.

NIHR HSRIC ID: 12081
TARGET GROUP

- Hyperhidrosis of the axillae – following failure of topical therapy.

TECHNOLOGY

DESCRIPTION

Botulinum toxin A (Dysport; Azzalure; AbobotulinumtoxinA; BoNT-A; BTX-A-HAC NG; Reloxin) is a purified neurotoxin formulation that when injected locally, blocks cutaneous nerve conduction by inhibiting the release of acetylcholine at the sweat glands. Botulinum toxin A is administered via intradermal injection at an initial dose of 100 units (U) per axilla. If the desired effect is not attained, up to 200 U may be administered for subsequent injections. The maximum dose administered must not exceed 200 U per axilla.

Botulinum toxin A (as Dysport) is licensed in the EU for:

- spastic equinus foot deformity due to spasticity in adults following a stroke,
- focal spasticity affecting the upper limbs in adults,
- local symptomatic treatment of spasticity affecting upper and/or lower limbs in adults,
- dynamic equinus foot deformity due to spasticity in paediatric cerebral palsy,
- local symptomatic treatment of spasticity affecting the lower limbs in children,
- spasmodic torticollis,
- blepharospasm,
- hemifacial spasm,
- moderate to severe glabellar lines.

Other preparations of botulinum toxin A are licensed in the EU for:

- axillary hyperhidrosis,
- prophylaxis of headaches in adults with chronic migraine,
- temporary improvement of moderate to severe wrinkles between the eyebrows in adults under 65 years,
- temporary improvement of moderate to severe crow’s feet,
- bladder dysfunction.

Botulinium toxin A (as Dysport) is also in phase II clinical trials for Gilles de la Tourette’s syndrome.

INNOVATION and/or ADVANTAGES

If licensed, botulinum toxin A (as Dysport) will be the second preparation of botulinum toxin A that is specifically licensed for axillary hyperhidrosis.

DEVELOPER

Ipsen Limited.

AVAILABILITY, LAUNCH OR MARKETING

In phase III clinical trials.
PATIENT GROUP

BACKGROUND

Hyperhidrosis is characterised by sweating in excess of that needed for normal thermoregulation\(^1\). It is classified as primary (idiopathic) or secondary hyperhidrosis, with the primary form having no association with any underlying condition, whilst secondary hyperhidrosis may be attributed to a number of other conditions, including endocrine disturbances, drugs, certain malignancies and central nervous system abnormalities\(^2\). Hyperhidrosis is further classified anatomically as focal or generalised.

Primary hyperhidrosis tends to be focal and usually affects the palms, soles, axilla or face\(^3\). Whilst not life-threatening, hyperhidrosis can increase the risk of cutaneous infection and have a significant social and psychological impact on the person affected\(^4\). Anxiety about social situations and relationships, and problems with daily living, such as an inability to hold a pen at work, can affect quality of life\(^1\). The exact mechanism underlying hyperhidrosis is poorly understood but it is thought to be caused by sympathetic overstimulation of the eccrine sweat glands\(^4\).

NHS or GOVERNMENT PRIORITY AREA

This topic is relevant to the following Department of Health policy area:

- Long term health conditions.

CLINICAL NEED and BURDEN OF DISEASE

The prevalence of hyperhidrosis is estimated at 1%, although the actual figure is likely to be much higher, due to low levels of reporting to primary care\(^1\). It can present at any age, with an estimated prevalence of 1.6% in teenagers\(^1\). The palms, soles and axillae are the most commonly affected sites\(^4\). In upper limb hyperhidrosis, the axillae alone are affected in 37%, the hands and axillae in 43%, and the hands alone in 20%\(^4\). Onset of axillary hyperhidrosis is more common after the onset of puberty, and is almost certainly linked to the development of sweat glands\(^1\). In 2014-15, there were 3,036 hospital admissions in England due to hyperhidrosis (ICD10 R61), accounting for 3,130 finished consultant episodes and 904 bed days\(^5\).

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE Guidance


Other Guidance

- Clinical Knowledge Summary. Hyperhidrosis. 2013\(^6\).
CURRENT TREATMENT OPTIONS

Initial treatment for hyperhidrosis should include lifestyle and behavioural advice, as well as topical agents, with a referral to a dermatologist if this approach fails\(^1\). Treatments in secondary care include modified topical therapies (including emollients, corticosteroids, aluminium salts and glutaraldehyde or formaldehyde), iontophoresis or surgery\(^6\). Botulinum toxin A (as Botox) is licensed for axillary hyperhidrosis but is frequently not funded by Clinical Commissioning Groups for NHS use\(^a\), and is mostly given in private clinics\(^6\).

EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>095/DYS7MH50; botulinum toxin A; phase II.</th>
<th>Botulinum toxin A vs placebo; phase II.</th>
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<tbody>
<tr>
<td>Sponsor</td>
<td>Ipsen Limited.</td>
<td>Ipsen Limited.</td>
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<tr>
<td>Status</td>
<td>Published.</td>
<td>Published.</td>
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<tr>
<td>Source of information</td>
<td>Publication(^7).</td>
<td>Publication(^8).</td>
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<tr>
<td>Location</td>
<td>Germany.</td>
<td>Germany.</td>
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<tr>
<td>Design</td>
<td>Randomised.</td>
<td>Randomised, placebo-controlled.</td>
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<tr>
<td>Participants</td>
<td>n=43; aged 19-64 yrs; hyperhidrosis; sweat production &gt;50mg/min on ≥2 occasions; failure of 4 weeks daily topical therapy with aluminium chloride solution.</td>
<td>n=145; hyperhidrosis; sweat production &gt;50mg/min on ≥2 occasions; failure of 4 wks daily topical therapy with aluminium chloride solution.</td>
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<tr>
<td>Schedule</td>
<td>Randomised to botulinum toxin A at 100 U or 200 U via 10 intradermal injections to the axilla at wks 0 and 48.</td>
<td>All participants received botulinum toxin A at 200 U or placebo via intradermal injection, allocated randomly to left or right axilla on day 1, followed by botulinum toxin A at 100 U injected into the axilla that had previously been treated with placebo on day 14.</td>
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<td>Follow-up</td>
<td>96 wks follow-up.</td>
<td>14 wks follow-up.</td>
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<td>Primary outcome/s</td>
<td>Sweat production.</td>
<td>Sweat production.</td>
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<tr>
<td>Key results</td>
<td>Both doses significantly reduced sweat production at wk 2, and by wk 48 sweat production returned to baseline levels. Following second treatment, both doses were equally effective at any follow-up point, with sweat production at wk 96 being significantly lower than wk 48.</td>
<td>For botulinum toxin A and placebo, respectively: at day 14, sweat production mean rates (±SE), 24±27 mg/min vs 144±113 mg/min (mean difference, 111mg/min, 95% CI 91-132, p&lt;0.001); at day 28, following injection into the axillae previously treated with placebo, sweat production mean rate fell to 32±39 mg/min (p&lt;0.001). For botulinum toxin A at 200 U and 100 U doses respectively, mean reduction in sweating at 14 days after treatment, 76.5% vs 81.4% (p=0.04); when two doses compared, 2.1% had equal reductions in sweating with both doses, 44.1% had a greater reduction with 100 U, and 53.8% had a greater reduction with 200 U.</td>
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\(^a\) Expert personal communication.
Horizon Scanning Research & Intelligence Centre

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<th>Adverse effects (AEs)</th>
<th>Minor AEs included stinging during injection, skin irritation and mild fatigue following injection.</th>
<th>Temporary AEs included headache, muscle soreness of the shoulder girdle, increased facial sweating, and axillary itching.</th>
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<td>Expected reporting date</td>
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**ESTIMATED COST and IMPACT**

**COST**

The cost of botulinum toxin A for hyperhidrosis is not yet known. The cost of botulinum toxin A (Dysport) for the treatment of chronic migraine is £92.40 for a 300 U vial.

**IMPACT - SPECULATIVE**

**Impact on Patients and Carers**

☐ Reduced mortality/increased length of survival  ☑ Reduced symptoms or disability  ☐ No impact identified

☐ Other:

**Impact on Health and Social Care Services**

☑ Increased use of existing services: requires access to, and availability of specialised services for this condition.  ☐ Decreased use of existing services

☐ Re-organisation of existing services  ☐ Need for new services

☐ Other:  ☑ None identified

**Impact on Costs and Other Resource Use**

☐ Increased drug treatment costs  ☐ Reduced drug treatment costs

☐ Other increase in costs:  ☐ Other reduction in costs:

☐ Other:  ☑ None identified

**Other Issues**

☑ Clinical uncertainty or other research question identified: an expert notes there is a significant and largely hidden clinical need for patients with hyperhidrosis because many CCGs do not fund this service. Patients often struggle to be referred and often have psychological issues as a result of this ongoing condition. A psychological study in this patient group would be informative.

☐ None identified

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b Expert personal opinion.
REFERENCES