

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Proposed Health Technology Appraisal

### Botulinum toxin type A for treating upper and lower limb spasticity associated with stroke

#### Draft scope (pre-referral)

#### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of botulinum toxin type A preparations (Botox, Dysport and Xeomin) within their licensed indication for treating upper and lower limb spasticity associated with stroke.

#### Background

Spasticity is a state of increased muscle tone that causes resistance to movement and impaired reflex function. It leads to stiffness, fibrosis and atrophy in muscles. Spasticity has a disabling effect through pain and reduced movement and mobility, which can result in difficulties with walking, sitting, standing, and other everyday activities. The effects of spasticity can also increase the risk of falls and consequent fractures. Up to 89% of people with spasticity associated with stroke report total or partial inability to work.

In England, approximately 110,000 people have a stroke each year and between 19 and 38% of them (up to 41,800 people) are affected by spasticity. Of the people who have spasticity associated with stroke, 79% report spasticity in the elbow, 66% report spasticity in the wrist, 50% report spasticity in the hip, 54% report spasticity in the knee, and 66% report spasticity in the ankle. These figures suggest that around 33,000 people in England each year have a stroke that results in upper limb spasticity and around 27,600 people in England each year have a stroke that results in lower limb spasticity.

Treatment for spasticity associated with stroke includes oral medications such as muscle relaxants (baclofen, tizanidine, and dantrolene) and anxiolytics (benzodiazepines), and physiotherapy (as recommended in NICE clinical guideline 162, 'Stroke rehabilitation'). There are 3 botulinum toxin type A preparations that have a marketing authorisation for treating upper limb spasticity (Botox, Dysport and Xeomin). Only Botox has a marketing authorisation for treating lower limb spasticity.

#### The technology

Botulinum toxin type A is a purified neurotoxin complex derived from the bacterium *Clostridium botulinum*. It stops muscle overactivity by inhibiting the release of acetylcholine. It is given as an injection.

Botox (Allergan) has a marketing authorisation in the UK for the treatment of wrist and hand disability due to upper limb spasticity associated with stroke in

adults and ankle disability due to lower limb spasticity associated with stroke in adults.

Dysport (Ipsen) has a marketing authorisation in the UK for the treatment of arm symptoms associated with focal spasticity in conjunction with physiotherapy.

Xeomin (Merz Pharma UK) has a marketing authorisation in the UK for the treatment of post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults.

<p><b>Interventions</b></p>	<p>Upper limb spasticity</p> <ul style="list-style-type: none"> <li>• Botox</li> <li>• Dysport</li> <li>• Xeomin</li> </ul> <p>Lower limb spasticity</p> <ul style="list-style-type: none"> <li>• Botox</li> </ul>
<p><b>Populations</b></p>	<ul style="list-style-type: none"> <li>• Adults with upper limb spasticity associated with stroke.</li> <li>• Adults with lower limb spasticity associated with stroke.</li> </ul>
<p><b>Comparators</b></p>	<p><b>Upper limb spasticity</b></p> <ul style="list-style-type: none"> <li>• The technologies will be compared with each other.</li> <li>• Established clinical management without botulinum type A preparations (Botox, Dysport and Xeomin) including oral medications such as muscle relaxants and anxiolytics and physiotherapy.</li> </ul> <p><b>Lower limb spasticity</b></p> <p>Established clinical management without Botox including oral medications such as muscle relaxants and anxiolytics and physiotherapy.</p>
<p><b>Outcomes</b></p>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• movement and/or mobility</li> <li>• pain</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>

<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<b>Other considerations</b>	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p>Related Guidelines:</p> <p>Clinical Guideline No. 162, Jun 2013, 'Stroke rehabilitation: long-term rehabilitation after stroke.' Review Proposal Date TBC.</p> <p>Related Quality Standards:</p> <p>Quality Standard No. 2, Jun 2010, 'Stroke'. Review date TBC.</p> <p>Related NICE Pathways:</p> <p>NICE Pathway: Stroke, Pathway created: May 2011. <a href="http://pathways.nice.org.uk/pathways/stroke">http://pathways.nice.org.uk/pathways/stroke</a></p>
<b>Related National Policy</b>	<p>NHS England. 2013/14 NHS Standard Contract for Specialised Vascular Services (Adults). A04/S/a.</p>

### Questions for consultation

Is Dysport used for treating upper limb spasticity associated with stroke in clinical practice?

Have all relevant comparators for botulinum toxin type A (Botox, Dysport and Xeomin) been included in the scope?

- Which treatments are considered to be established clinical practice in England for upper limb spasticity associated with stroke?
- Which treatments are considered to be established clinical practice in England for lower limb spasticity associated with stroke?

Have all relevant outcomes for botulinum toxin type A (Botox, Dysport and Xeomin) for treating upper limb spasticity associated with stroke been included in the scope?

Have all relevant outcomes for Botox for treating lower limb spasticity associated with stroke been included in the scope?

Are there any subgroups of people in whom botulinum toxin type A (Botox, Dysport and Xeomin) is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider botulinum toxin type A (Botox, Dysport and Xeomin) will fit into the existing NICE pathway, [Stroke](#)?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which botulinum toxin type A (Botox, Dysport and Xeomin) is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider botulinum toxin type A (Botox, Dysport and Xeomin) to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of botulinum toxin type A (Botox, Dysport and Xeomin) can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Multiple Technology Appraisal (MTA) Process. We welcome comments on the appropriateness of

appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at [http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology\\_appraisal\\_process\\_guides.jsp](http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp))