HAUTE AUTORITÉ DE SANTÉ

NEUROLOGY
New indication
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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

BOTOX (botulinum toxin type A), muscle relaxant

Minor clinical added value in the treatment of idiopathic overactive bladder in adults

Main points

- BOTOX has Marketing Authorisation in adults in the treatment of idiopathic overactive bladder associated with symptoms including three episodes of urinary incontinence with urinary urgency in 3 days, number of urinations ≥ 8 in adults not adequately managed with anticholinergics (after 3 months of treatment) or intolerant to anticholinergic treatment and properly conducted physiotherapy.
- After 12 weeks of treatment, its efficacy was demonstrated by comparison with placebo. Clinical data in men are very limited (12% of men in the phase III studies).
- It has not been assessed by comparison with mirabegron (BETMIGA). Its role in relation to functional neuromodulation has still to be determined.
- In the absence of long-term clinical data, the duration of the therapeutic effect seems unpredictable and the number of reinjections needed to obtain an optimal therapeutic response has still to be established. The long-term safety profile (including the risk of urinary retention and/or urinary infections) is not known.

Pre-existing indications

BOTOX also has Marketing Authorisation:

- In adults, in the treatment of neurogenic detrusor overactivity leading to urinary incontinence which is not adequately managed by anticholinergic treatment in patients with spinal-cord injuries and patients with multiple sclerosis who are self-catheterising to empty their bladder.
- In adults and children over 12 years of age, in oculomotor dysfunction: strabismus, recent oculomotor paralysis, recent thyrotoxic myopathy, blepharospasm, hemifacial spasm, spasmodic torticollis, severe axillary hyperhidrosis that is resistant to local treatments and has a substantial psychological and social impact.
- In adults and children aged 2 years and above, in the local symptomatic treatment of spasticity of the upper and/or lower limbs.

This summary does not cover these indications.

Therapeutic use

- In the treatment of refractory idiopathic overactive bladder, with urinary incontinence and in cases where at least three months' treatment with an anticholinergic has failed, BETMIGA (mirabegron) is an alternative. Functional electrostimulation, surgery (including neuromodulation of the sacral roots in the event of resistance to drug treatments), palliative treatments (protectors, urine collection devices, urinary catheter, penile sheaths, etc.) can also be considered as alternatives to drug treatments for urinary incontinence in the event of inefficacy, contraindications or adverse effects, and in severe cases. Enterocystoplasty for enlargement of the bladder is a third-line treatment.
- **Role of the medicinal product in the therapeutic strategy**

BOTOX is a 2nd-line treatment in case drug treatment with an anticholinergic and/or with mirabegron fails, and is an alternative to minimally invasive surgical techniques.

Clinical data

- Two randomised, double-blind, multicentre, placebo-controlled studies were carried out in patients with overactive bladder, with symptoms including urinary incontinence, urinary urge incontinence and pollakiuria. They included

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patients who had had at least 3 episodes of urinary incontinence caused by urinary urge on 3 consecutive days (a mean of between 5 and 5.7 episodes on inclusion) and urination at least 8 times a day (mean between 11 and 12 times on inclusion).

- In the 12th week, the number of episodes of urinary incontinence per 24 h was reduced by 1.65 or by 1.91 by comparison with placebo in each of these studies.
- At the end of the 12 weeks' follow-up and by comparison with placebo, an improvement in favour of BOTOX was also observed in the following secondary endpoints: daily frequency of urination, number of episodes of urinary urge incontinence, nocturia and quality of life. The volume voided was also significantly larger.
- The main adverse effects are urinary tract infections and urinary retention necessitating self-catheterisation.

Benefit of the medicinal product

- The actual benefit* of BOTOX is substantial.
- BOTOX provides a minor clinical added value** (CAV IV) in the treatment of overactive bladder in patients in whom drug and non-drug treatments have failed (behavioural treatments and rehabilitation of the perineum and the sphincter).
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 23 July 2014 (CT-13729) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means "no clinical added value".

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