Botulinum toxin A

for treating focal spasticity of the upper or lower limbs in children with cerebral palsy

Technology Guidance from the MOH Drug Advisory Committee

Guidance recommendations

The Ministry of Health's Drug Advisory Committee has recommended:

- ✓ *Clostridium botulinum toxin* type A neurotoxin complex (Botox) 50 U and 100 U injection vials for treating children, aged 2 years or older, with focal spasticity of the upper or lower limbs (including dynamic equinus foot deformity) due to cerebral palsy, and who:
  - do not have significant joint contractures, i.e. the affected joint is not permanently fixed in position due to shortening of the target muscle; and
  - are concurrently receiving ongoing supportive therapy, e.g. physiotherapy or occupational therapy.

Botulinum toxin type A must be administered by a physician specialising in paediatric neurological disorders or paediatric rehabilitation with experience in administering botulinum toxin type A.

Subsidy status

Clostridium botulinum toxin type A neurotoxin complex (Botox) 50 U and 100 U injection vials are recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication.

MAF **does not** apply to Botox 200 U injection vial, Dysport 300 U and 500 U injection vials, and Xeomin 50 U and 100 U injection vials.

Published on 2 September 2019

Factors considered to inform the recommendations for subsidy

Technology evaluation

1.1 The MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of botulinum toxin type A for treating focal spasticity of the upper or lower limbs in children with cerebral palsy. The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from public healthcare institutions. Published clinical and economic evidence for two brands of botulinum toxin type A (Botox and Dysport) was considered. As the use of Xeomin in children has not been approved by the Health Sciences Authority (HSA), this brand of botulinum toxin type A was not considered in the evaluation.

1.2 The evidence was used to inform the Committee's deliberations around four core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Clinical effectiveness and safety of the technology;
- Cost-effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives; and
- Estimated annual technology cost and the number of patients likely to benefit from the technology.

1.3 Additional factors, including social and value judgments, may also inform the Committee's subsidy considerations.

Clinical need

2.1 In children with cerebral palsy, there is high clinical need for effective treatments for focal spasticity of the upper and lower limbs (including dynamic equinus foot deformity). The Committee acknowledged that use of botulinum toxin type A for these conditions currently constitutes standard of care in local practice, in line with international clinical guidelines.

2.2 Local clinical experts considered Botox and Dysport to be clinically comparable for treating focal spasticity in children with cerebral palsy.

Clinical effectiveness and safety

3.1 The Committee acknowledged that the dosing of botulinum toxin type A is individualised based on patient need, and unit doses are not equivalent among brands. Given the uncertainty surrounding the dose relativity between Botox and Dysport, the Committee accepted a dose relativity of around 1:3 between Botox and Dysport in line with ratios used by local clinicians, results from dose conversion studies and the therapeutic relativity accepted in Australia (PBAC) for focal spasticity in children.

3.2 The Committee considered published clinical studies which showed that the concurrent use of botulinum toxin type A with supportive therapy (e.g. physiotherapy or occupational therapy) was clinically effective in reducing muscle spasticity and allowing achievement of functional goals in children with upper limb focal spasticity and dynamic equinus foot deformity. Although clinical data were limited for lower limb focal spasticity, there was some evidence showing benefit of botulinum toxin type A in reducing spasticity in calf muscles and hip adductors in children with cerebral palsy. The Committee acknowledged that there was a high clinical need for effective treatment for patients with lower limb spasticity and considered that the benefit of botulinum toxin type A in these patients outweighed the risks.

3.3 The Committee noted that botulinum toxin type A was generally well-tolerated in all studies.

3.4 The Committee considered that the clinical outcomes for each brand of botulinum toxin type A (Botox or Dysport) were consistent across the studies, and concluded that they were clinically comparable in terms of their efficacy and safety profiles for treating focal spasticity in children with cerebral palsy.

Cost-effectiveness

4.1 The Committee noted that there were no local cost-effectiveness studies of botulinum toxin type A in children with focal spasticity due to cerebral palsy. However, the Committee concluded that it was likely to be cost-effective for this population, given they had previously determined that it was cost-effective for a related indication (focal spasticity of the upper limbs due to stroke) in adults.

4.2 The manufacturers of both brands of botulinum toxin A offered price discounts as part of value-based pricing (VBP) discussions. The Committee agreed that Botox was the most cost-effective treatment option based on appropriate dose conversion ratios.

Estimated annual technology cost

5.1 The Committee estimated the annual cost impact to be less than SG$500,000 in the first year of listing Botox 50U and 100U injection vials on the MAF for children with focal spasticity.

Recommendation

6.1 Based on available evidence, the Committee recommended botulinum toxin type A (Botox) 50 U and 100 U injection vials be listed on the MAF for treating focal spasticity of the upper or lower limbs (including dynamic equinus foot deformity) in children with cerebral palsy, in view of favourable clinical and cost-effectiveness, and the high clinical need to subsidise this treatment to ensure appropriate patient care.

6.2 Botox 200 U injection vial and Dysport 300 U and 500 U injection vials were not recommended due to their higher costs compared with Botox 50 U and 100 U injection vials that were not justified by the clinical outcomes they provide over Botox 50 U and 100 U injection vials.

6.3 Xeomin 50 U and 100 U injection vials are not approved for use in children with focal spasticity and are not recommended for subsidy.