Technology Guidance

# Botulinum toxin A

## for the prophylaxis of headaches in adults with chronic migraine

**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 the prophylaxis of headaches in adults with chronic migraine who have had an inadequate response, intolerance, or contraindication to at least three migraine prophylactic medications.

Botulinum toxin type A must be administered by a neurologist.

### 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 assistance **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.

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# 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 A (Botox) for the prophylaxis of headaches in adults with chronic migraine. The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for botulinum toxin A was considered in line with its registered indication, and in adults who have had an inadequate response, intolerance, or contraindication to at least three migraine prophylactic medications. Other brands of botulinum toxin A (Dysport and Xeomin) were not considered for subsidy as they have not been approved by HSA for this indication.

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. Chronic migraine is defined as headaches occurring on at least 15 days per month (of which at least eight days are with migraine), for more than three months. It is a debilitating condition which significantly affects health-related quality of life. In local clinical practice, botulinum toxin A is routinely used as an option for the prophylaxis of headaches in adults with chronic migraine after one or more oral medications have failed to provide relief. The Committee acknowledged that there are currently no subsidised treatments for chronic migraine after failure of oral prophylactic medications. Therefore, they agreed that there was a clinical need to consider botulinum toxin A for subsidy for these patients to improve treatment affordability, and ensure appropriate patient care.

## Clinical effectiveness and safety

3.1. The Committee reviewed published clinical evidence from two pivotal trials (PREEMPT 1 and 2), and noted that botulinum toxin A reduced the number of headache and migraine days per month (~2 days) compared with placebo.

3.2. The Committee also noted that compared to placebo, botulinum toxin A demonstrated a significant decrease in disability and improved functioning as measured by a change in total Headache Impact Test-6 (HIT-6) scores, and statistically significantly improved health-related quality of life as measured by changes in three Migraine-Specific Quality of Life questionnaire (MSQ) role function domains (restrictive, preventive, and emotional).

3.3. While the magnitude of treatment effects was small, the Committee acknowledged that any improvement was likely to be clinically meaningful for patients, and could help reduce headache-related disability.

3.4. The Committee noted that the occurrence of adverse events in the clinical trials was higher in patients receiving botulinum toxin A compared to placebo, of which the most common adverse events were neck pain and muscular weakness. However, these adverse events were typically mild to moderate in severity, and resolved without sequelae.

## Cost effectiveness

4.1. In the absence of local cost-effectiveness studies, the Committee reviewed published economic analyses by overseas reference HTA agencies (NICE (UK), PBAC (Australia), and CADTH (Canada)) which compared botulinum toxin A to best supportive care at different lines of treatment for chronic migraine. Despite uncertainties in the cost-effectiveness estimates, all three HTA agencies considered botulinum toxin A to be cost-effective in patients who had failed three or more prior prophylactic medications, and all agencies recommended botulinum toxin A for subsidy for these patients. The Committee also noted that NHI (Taiwan) had reimbursed botulinum toxin A for chronic migraine in this patient subgroup.

4.2. The Committee noted that the manufacturer had previously reduced the price of Botox to achieve subsidy listings for other indications which were comparable to overseas prices, and were likely cost-effective in the local context including for the chronic migraine indication.

## Estimated annual technology cost

5.1. The Committee estimated the annual cost impact was less than SG$1 million in the first year of listing Botox 50 U and 100 U injection vials on the MAF for adults with chronic migraine.

## Recommendations

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 the prophylaxis of headaches in adults with chronic migraine, given its acceptable clinical and cost-effectiveness, and clinical need for this treatment to ensure appropriate patient care.

**About the Agency**

The Agency for Care Effectiveness (ACE) was established by the Ministry of Health (Singapore) to drive better decision-making in healthcare through health technology assessment (HTA), clinical guidance, and education.

As the national HTA agency, ACE conducts evaluations to inform government subsidy decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

This guidance is based on the evidence available to the MOH Drug Advisory Committee as at 18 August 2021. It is not, and should not be regarded as, a substitute for professional or medical advice. Please seek the advice of a qualified healthcare professional about any medical condition. The responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

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