Technology Guidance

Atogepant and rimegepant

for prophylaxis of migraine

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended the following medications for inclusion on the MOH List of Subsidised Drugs, due to their uncertain comparative clinical effectiveness and substantially higher prices versus subsidised alternatives:

- Atogepant for prophylaxis of chronic migraine; and
- Atogepant or rimegepant for prophylaxis of episodic migraine.

Published: 4 June 2025

Factors considered to inform the recommendations for funding

Technology evaluation

1.1. At the March 2025 meeting, the MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of atogepant and rimegepant for prophylaxis of migraine. The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from public healthcare institutions and patient experts from local patient and voluntary organisations. Published clinical and economic evidence for atogepant and rimegepant was considered in line with their respective registered indications.

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 funding considerations.

Clinical need

2.1. Migraine is characterised by recurrent attacks of headache that are typically moderate to severe in intensity and may be accompanied by other symptoms. It can be broadly classified as chronic or episodic. A chronic migraine (CM) is defined as 15 or more headache days per month, of which at least eight days are with migraine. An episodic migraine (EM) is defined as fewer than 15 headache days per month.

2.2. Several subsidised drugs are available for the prophylaxis of CM and EM. They include oral drugs such as beta-blockers, antidepressants and antiepileptics that are available on the MOH Standard Drug List (SDL). In addition, botulinum toxin A (Botox) intramuscular injection and galcanezumab subcutaneous injection are listed on the Medication Assistance Fund (MAF) for prophylaxis of migraine in adults with inadequate response, intolerance or contraindication to at least three migraine prophylactic medications. Botulinum toxin A (Botox) is indicated for CM prophylaxis, while galcanezumab is indicated for CM and EM prophylaxis.

2.3. The Committee recognised that gepants are a new class of oral medicines that counteract the pathophysiology of migraine. In Singapore, atogepant is approved for prophylaxis of CM and EM, while rimegepant is approved for prophylaxis of EM.

2.4. The Committee agreed that atogepant or rimegepant could benefit patients who cannot receive or are averse to injectable treatments. Nonetheless, they considered the overall local clinical need for the gepants to be low, given that botulinum toxin A (Botox) and galcanezumab are already subsidised as later-line therapies for migraine prophylaxis.

2.5. The Committee considered three testimonials from local patient experts about living with migraine and their experience with different treatments. They heard that migraine and its associated symptoms such as giddiness and vomiting significantly impacted their ability to work and carry out daily activities. The Committee noted that the patients welcomed new treatment options for migraine that could reduce symptoms, have fewer side effects, are more affordable and most importantly, reduce the frequency of migraine attacks.

Clinical effectiveness and safety

3.1. The Committee agreed that botulinum toxin A (Botox) and galcanezumab were the appropriate comparators for atogepant for CM prophylaxis. For EM prophylaxis, atogepant and rimegepant were compared with galcanezumab and each other. The Committee reviewed the clinical evidence from randomised controlled trials of atogepant, rimegepant, botulinum toxin A (Botox) and galcanezumab for prophylaxis of CM and/or EM.

3.2. It was noted that most of the trials were placebo-controlled, and only CHALLENGE-MIG included active treatment arms (rimegepant versus galcanezumab). In the absence of head-to-head trials comparing all the relevant interventions and comparators, network meta-analyses (NMAs) were conducted to assess the comparative clinical effectiveness between the treatments.

3.3. The Committee noted several limitations with the NMAs, including the assumption that the placebo oral tablets used in the atogepant and rimegepant trials were equivalent to placebo injections used in the botulinum toxin A (Botox) and galcanezumab trials. In addition, transitivity was limited due to significant heterogeneity across the trials in terms of endpoint assessments, permitted concomitant migraine prophylactic treatments, and participants' prior exposure to prophylactic treatments. The Committee also noted the limited data in the NMAs specific to the proposed positioning of atogepant or rimegepant in the local setting, which is after at least three migraine prophylactic medications.

3.4. Atogepant or rimegepant versus placebo
The Committee noted that direct and indirect evidence showed that both atogepant (for CM and EM) and rimegepant (for EM only) were superior to placebo in reducing monthly migraine days (MMDs) following 3 months of treatment. However, they did not consider the reductions to be clinically meaningful, because the treatment differences did not meet the previously accepted minimal clinically important difference of two days.

3.5. Direct and indirect evidence also showed that atogepant and rimegepant were superior to placebo in increasing the proportion of patients who achieved at least a 50% reduction in MMDs (≥50% responder rate) at 3 months of treatment.

3.6. Atogepant versus botulinum toxin A (Botox) and galcanezumab for CM prophylaxis
The Committee reviewed indirect evidence comparing atogepant with botulinum toxin A (Botox) and with galcanezumab. While the evidence showed no statistically significant differences in terms of MMD reduction and ≥50% responder rate between these treatments, the Committee noted that a non-inferiority claim could not be supported. They heard that the point estimates consistently favoured both botulinum toxin A (Botox) and galcanezumab over atogepant. Furthermore, the upper bound of the 95% confidence interval (CI) for the change in MMDs exceeded the non-inferiority margin of two days.

3.7. The Committee heard that the treatment comparison network was sparsely populated and that the evidence for atogepant relied on a single trial (PROGRESS) with limited applicability to the local setting. They also noted the NMA results had wide confidence intervals that could not exclude clinically important differences between treatments.

3.8. Overall, the Committee considered that, for CM prophylaxis, the comparative effectiveness of atogepant versus botulinum toxin A (Botox) and galcanezumab remained uncertain.

3.9. Atogepant or rimegepant versus galcanezumab and each other for EM prophylaxis
The Committee noted that indirect evidence between atogepant and galcanezumab, and between atogepant and rimegepant showed no significant difference in terms of MMD reduction and ≥50% responder rate While the results suggested non-inferiority between these treatments, the Committee acknowledged that there was significant inconsistency across the network with substantial differences between direct and indirect evidence for the rimegepant comparisons.

3.10. Between rimegepant and galcanezumab, the Committee noted that both direct and indirect evidence showed no significant difference in terms of MMD reduction and ≥50% responder rate. However, they heard that results from CHALLENGE-MIG appeared inconsistent with other data. Specifically, CHALLENGE-MIG showed similar MMD reductions for both rimegepant and galcanezumab (-4.4 and -4.8 days, mean difference 0.4 days, 95% CI -0.1 to 0.8), despite rimegepant's modest effect versus placebo (mean difference -0.8 days) and galcanezumab's larger effect versus placebo (mean difference -2.2 days) in their respective placebo-controlled trials. The Committee also noted that sensitivity analyses excluding CHALLENGE-MIG in the NMA was conducted to explore the impact of inconsistency, which resulted in a statistically significant difference that favoured galcanezumab over rimegepant in terms of MMD reduction.

3.11. Overall, the Committee considered that, for EM prophylaxis, the comparative effectiveness of atogepant or rimegepant versus galcanezumab and each other remained uncertain.

3.12. Safety

The Committee noted that atogepant and rimegepant were well-tolerated compared with placebo. The most frequently reported adverse events (AEs) for both drugs were nausea, constipation and fatigue.

3.13. The Committee also noted that indirect evidence showed no significant difference among atogepant, rimegepant, botulinum toxin A (Botox) and galcanezumab in terms of treatment-related AEs, serious AEs and AEs leading to treatment discontinuation. However, atogepant and rimegepant were associated with more gastrointestinal events, whereas botulinum toxin A (Botox) and galcanezumab were associated with more injection site reactions. Hence, the Committee considered that atogepant and rimegepant had a different safety profile than botulinum toxin A (Botox) and galcanezumab.

Cost effectiveness

4.1. Given the uncertain comparative clinical effectiveness of the gepants versus botulinum toxin A (Botox) or galcanezumab, the Committee considered that the treatment costs of atogepant or rimegepant should be lower than the treatment costs of already subsidised alternatives. This approach aligns with reference HTA agencies that have recommended atogepant and/or rimegepant based on their lower comparative costs versus other migraine prophylactic treatments.

4.2. The companies of atogepant and rimegepant were invited to submit pricing proposals for their products for funding consideration. At the proposed prices, the 2-year treatment costs with atogepant or rimegepant were substantially higher than subsidised alternatives (botulinum toxin A (Botox) and galcanezumab). Hence, the Committee considered that both atogepant and rimegepant were unlikely to represent an acceptable use of healthcare resources.

Estimated annual technology cost

5.1. The Committee noted that the cost impact to the public healthcare system was estimated to be less than SG$1 million per year in the first five years of listing atogepant on the MOH List of Subsidised Drugs for prophylaxis of CM and EM.

5.2. The cost impact to the public healthcare system was estimated to be less than SG$1 million per year in the first five years of listing rimegepant on the MOH List of Subsidised Drugs for prophylaxis of EM.

Recommendations

6.1. Based on available evidence, the Committee recommended not listing atogepant or rimegepant on the MOH List of Subsidised Drugs for prophylaxis of migraine. This decision was based on the uncertain comparative clinical effectiveness and substantially higher prices of atogepant or rimegepant versus subsidised alternatives.