Technology Guidance

Calcitonin gene-related peptide (CGRP) monoclonal antibodies

for prophylaxis of migraine

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Galcanezumab 120 mg/mL solution for injection in pre-filled pen for prophylaxis of migraine in adults who have at least four migraine days a month prior to commencement of treatment with galcanezumab. Patients must have experienced an inadequate response, intolerance, or a contraindication to at least three migraine prophylactic medications. Treatment with galcanezumab should be stopped after 12 weeks if:
  a) in episodic migraine, the number of migraine days per month does not reduce by at least 50% compared with baseline;
  b) in chronic migraine, the number of migraine days per month does not reduce by at least 30% compared with baseline.

Funding status

Galcanezumab 120 mg/mL solution for injection in pre-filled pen is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication from 1 August 2024.

MAF assistance **does not** apply to galcanezumab 100 mg/mL solution for injection in pre-filled syringe, or any formulations or strengths of eptinezumab, erenumab or fremanezumab.

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Factors considered to inform the recommendations for funding

Technology evaluation

1.1. At the March 2024 meeting, the MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of four calcitonin gene-related peptide monoclonal antibodies (CGRP mAbs; eptinezumab, erenumab, fremanezumab and galcanezumab) for prophylaxis of migraine in adults. 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 the CGRP mAbs was considered in line with their registered indications.

1.2. For galcanezumab, only the 120 mg/mL pre-filled pen was included in the current evaluation. The 100 mg/mL pre-filled syringe is not indicated for migraine prophylaxis.

1.3. 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.

1.4. 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 episodic or chronic. An episodic migraine (EM) is defined as fewer than 15 headache days per month. A chronic migraine (CM) is defined as 15 or more headache days per month, of which at least eight days are with migraine.

2.2. In local clinical practice, prophylaxis of migraine is considered for adults who have CM, or EM with at least four migraine days per month. Several subsidised drugs are available for the prophylaxis of EM and CM, including 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 is listed on the Medication Assistance Fund (MAF) for prophylaxis of CM in adults with

inadequate response, intolerance or contraindication to at least three migraine prophylactic medications.

2.3. The Committee recognised that CGRP mAbs have a different mechanism of action from currently available migraine prophylactic medications as they target the CGRP pathway to prevent migraine. Three of the CGRP mAbs are subcutaneous injections that can be self-administered at home. The fourth, eptinezumab, is administered by intravenous infusion.

2.4. The Committee agreed it was appropriate to consider CGRP mAbs for funding as a later-line therapy alongside Botox, for patients who have inadequate response to at least three migraine prophylactic medications. The Committee heard that in overseas jurisdictions, CGRP mAbs are reimbursed for prophylaxis of EM and CM in this subgroup of patients.

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 associated symptoms such as giddiness and vomiting significantly impacted patients' ability to work and carry out daily activities. The Committee noted that none of the patients had experience with a CGRP mAb, but they 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 reviewed the clinical evidence from randomised controlled trials of eptinezumab, erenumab, fremanezumab and galcanezumab for prophylaxis of EM and CM in patients with and without previous drug failure. The evidence from the overall populations showed that CGRP mAbs were superior to placebo in reducing monthly migraine days (MMDs) or monthly migraine headache days (MMHDs) at 3 to 6 months of treatment.

3.2. Post hoc subgroup analyses reviewed by reference HTA agencies also suggested that, in patients who previously received at least three migraine prophylactic medications, CGRP mAbs provided clinically meaningful reductions in MMDs or MMHDs compared with placebo.

3.3. The Committee noted that, in the absence of head-to-head trials, reference HTA agencies reviewed indirect treatment comparisons among the four CGRP mAbs (for prophylaxis of EM and CM), and against Botox (for prophylaxis of CM), in patients who had received at least three prophylactic medications. While the analyses were associated with uncertainty, the results suggested that CGRP mAbs were likely to be comparable to one another and Botox, in efficacy and safety. The Committee also heard that these findings were consistent with local clinical expert opinion.

Cost effectiveness

4.1. The Committee agreed that a cost-minimisation approach was appropriate to assess the cost effectiveness of CGRP mAbs versus one another and Botox for migraine prophylaxis. The Committee noted that galcanezumab had the lowest 2-year treatment cost among the CGRP mAbs. At the proposed price, its cost effectiveness was also acceptable versus Botox.

4.2. When compared with prices in overseas reference jurisdictions, the Committee considered galcanezumab likely to represent an acceptable use of healthcare resources for prophylaxis of EM and CM in patients who had received at least three migraine prophylactic medications.

Estimated annual technology cost

5.1. The Committee noted that the annual cost impact to the public healthcare system was estimated to be less than SG$1 million in the first five years of listing galcanezumab on the MOH List of Subsidised Drugs.

Recommendations

6.1. Based on available evidence, the Committee recommended galcanezumab 120 mg/mL solution for injection in pre-filled pen be listed on the MAF for prophylaxis of migraine in adults who have at least four migraine days a month and have experienced an inadequate response, intolerance, or a contraindication to at least three migraine prophylactic medications, given its clinical need and acceptable clinical and cost effectiveness.

6.2. The Committee recommended not listing eptinezumab, erenumab and fremanezumab on the MOH List of Subsidised Drugs due to unacceptable cost effectiveness compared with galcanezumab.

Agency for Care Effectiveness - ACE Agency for Care Effectiveness (ACE)

About the Agency

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

This guidance 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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