

Technology Guidance

Icatibant and sebetralstat for treating hereditary angioedema attacks

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Icatibant 30 mg/3 mL solution for injection in pre-filled syringe for treating acute attacks of hereditary angioedema (HAE) in patients aged 2 years and older with confirmed diagnosis of C1-esterase inhibitor deficiency. Patient must be treated by, or in consultation with, a specialist physician experienced in the diagnosis and management of HAE.

Funding status

Icatibant 30 mg/3 mL solution for injection in pre-filled syringe is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication from 1 December 2026.

MAF assistance **does not** apply to sebetralstat for treating HAE attacks.

Technology evaluation

- 1.1. At the July 2026 meeting, the MOH Drug Advisory Committee (“the Committee”) considered the evidence presented for the technology evaluation of icatibant and sebetrastat for treating hereditary angioedema (HAE) attacks. 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 icatibant and sebetrastat was considered in line with their 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. Approximately 40 patients in Singapore have been diagnosed with hereditary angioedema (HAE), a genetic disorder primarily caused by *SERPINE1* mutations resulting in C1-esterase inhibitor (C1-INH) deficiency and excess bradykinin, leading to recurrent, unpredictable episodes of tissue swelling. Attacks may affect the face, extremities, genitals, gastrointestinal tract or upper airway, causing severe pain and functional impairment. Upper-airway swelling can be life-threatening, and untreated attacks typically last two to five days.
- 2.2. International clinical practice guidelines recommend early on-demand treatment of HAE attacks, as prompt treatment can shorten symptom duration, prevent attack progression, and reduce morbidity and mortality. In Singapore, plasma-derived C1-INH is currently the only subsidised on-demand therapy under the Medication Assistance Fund (MAF). As it requires intravenous (IV) infusion, patients must attend a hospital emergency department for treatment during an attack.

- 2.3. The Committee acknowledged the clinical need for alternative on-demand therapies such as icatibant (subcutaneous injection) and sebetralstat (oral tablet), which patients can carry and self-administer for timelier treatment. The availability of these treatment options was expected to reduce the need for hospital visits, although some patients might still present to the hospital for severe attacks or if rescue treatment with plasma-derived C1-INH was required following use of icatibant or sebetralstat.
- 2.4. The Committee considered five testimonials from local patients and carers describing the substantial physical and emotional burden of HAE and their treatment experiences. Respondents highlighted limitations of plasma-derived C1-INH, particularly around portability and ease of access. One patient had received icatibant and found it effective with minimal side effects, while none of the patients had experience with sebetralstat. Overall, respondents preferred self-administered treatments over hospital-based IV infusions, citing greater convenience and faster access during acute attacks. They valued treatments that could provide rapid symptom relief, reduce hospital visits, support daily activities, and were easy to administer and affordable.

Clinical effectiveness and safety

- 3.1. Icatibant and sebetralstat versus placebo
The Committee reviewed the clinical evidence for icatibant and sebetralstat for treating HAE attacks in patients with a confirmed diagnosis of C1-INH deficiency. The Committee noted that the clinical trials of icatibant and sebetralstat differed in their efficacy endpoints and administration settings: icatibant was administered by a healthcare professional at the study site or hospital, whereas sebetralstat was self-administered by patients in the community setting.
- 3.2. For icatibant, two randomised controlled trials (FAST-1 and FAST-3) compared icatibant 30 mg against placebo in adults. In FAST-1, icatibant did not show a statistically significant improvement over placebo for the primary endpoint, median time to onset of symptom relief (2.5 versus 4.6 hours; $p=0.14$), although the Committee noted that early use of rescue medication may have confounded the results. In FAST-3, icatibant demonstrated significant improvements over placebo for median time to onset of symptom relief (2.0 versus 19.8 hours; $p<0.001$) and almost complete symptom relief (8.0 versus 36.0 hours; $p=0.012$). The Committee also considered the single-arm study (HGT-FIR-086) in children and adolescents, which reported rapid symptom relief consistent with the response observed in adults.

- 3.3. For sebetralstat, the Committee reviewed the placebo-controlled trial (KONFIDENT) in adolescents and adults. Sebetralstat 300 mg significantly reduced the median time to beginning of symptom relief compared with placebo (1.61 versus 6.72 hours; $p < 0.001$) and shortened the time to complete symptom resolution ($p = 0.002$). The proportion of attacks with complete resolution within 24 hours was also higher with sebetralstat than placebo (42.5% versus 27.4%).
- 3.4. In terms of safety, icatibant and sebetralstat were generally well-tolerated in the trials. The most common adverse event reported with icatibant was injection-site reactions such as skin irritation, swelling, and pain, which were generally mild to moderate in severity and resolved without further intervention. For sebetralstat, the most common adverse event was headache, which was non-serious and self-limiting.
- 3.5. On-demand therapies versus one another
The Committee acknowledged that no head-to-head trials have compared the three on-demand therapies: icatibant, sebetralstat, and plasma-derived C1-INH.
- 3.6. For icatibant, the Committee noted that CDA (Canada) and MSAC (Australia) had considered indirect treatment comparisons (ITCs) versus plasma-derived C1-INH, but both HTA agencies considered the analyses limited by substantial heterogeneity across the included clinical trials. Despite uncertainty in the comparative clinical effectiveness of icatibant versus plasma-derived C1-INH, both agencies considered cost-minimisation analyses reasonable in their funding deliberations.
- 3.7. For sebetralstat, the Committee noted that, at the time of the evaluation, no reference HTA agency had reviewed ITCs versus plasma-derived C1-INH or icatibant.
- 3.8. Overall, based on available evidence, the Committee considered that the comparative clinical effectiveness of icatibant, sebetralstat, and plasma-derived C1-INH remained uncertain.

Cost effectiveness

- 4.1. Based on the pricing proposal submitted for icatibant, the Committee noted that the average costs of treating an HAE attack with icatibant, with or without additional rescue treatment with plasma-derived C1-INH, were lower than the costs of using plasma-derived C1-INH alone. The analysis accounted for drug and administration costs, as well as the estimated need for rescue treatment and hospitalisation. The Committee therefore considered icatibant likely to represent an acceptable use of healthcare resources in Singapore for treating HAE attacks.

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 in the first year of listing icatibant on the MOH List of Subsidised Drugs for treating HAE attacks.

Recommendations

- 6.1. In view of the clinical need, acceptable clinical effectiveness and acceptable use of healthcare resources, the Committee recommended listing icatibant 30 mg/3 mL solution for injection in pre-filled syringe on the MAF for treating acute attacks of HAE in patients aged 2 years and older with confirmed diagnosis of C1-INH deficiency.
- 6.2. To govern appropriate use of icatibant, the Committee also recommended that patients must be treated by, or in consultation with, a specialist physician experienced in the diagnosis and management of HAE.
- 6.3. The Committee recommended not listing sebetralstat on the MOH List of Subsidised Drugs for treating HAE attacks, due to uncertainty in its comparative clinical and cost effectiveness relative to alternative treatments.

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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 guidelines, and education.

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.

The 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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