Technology Guidance

Vutrisiran

for transthyretin amyloid cardiomyopathy

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Vutrisiran 25 mg/0.5 mL injection for transthyretin amyloid cardiomyopathy.

Funding status

Vutrisiran 25 mg/0.5 mL injection is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication from 1 September 2026.

Patient must be undergoing treatment with vutrisiran as a monotherapy (i.e. not in combination with any other disease modifying medicines for amyloidosis disorders), and treatment should be used in line with the additional clinical criteria listed in the Annex.

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Technology evaluation

1.1. At the April 2026 meeting, the MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of vutrisiran for treating transthyretin amyloid cardiomyopathy (ATTR-CM). 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. Clinical and economic evidence for vutrisiran was considered in line with its registered 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 funding considerations.

Clinical need

2.1. ATTR-CM is an underdiagnosed, progressive disease caused by the deposition of misfolded transthyretin (TTR) amyloid fibrils in the myocardium, which results in heart failure. ATTR-CM may be hereditary or wild-type, and untreated disease is associated with a poor prognosis. The Committee heard that approximately 150 patients diagnosed with ATTR-CM are currently receiving active follow-up care in public healthcare institutions. However, the actual number of patients is likely higher due to underdiagnosis of the condition.

2.2. The Committee acknowledged that while tafamidis, an oral TTR stabiliser indicated only for ATTR-CM, is the current first-line treatment in local practice, there remains a need for alternative treatments, particularly for patients with mixed cardiomyopathy/polyneuropathy (CM/PN) phenotypes. Vutrisiran is a gene-silencing therapy that reduces TTR protein production by degrading TTR mRNA in hepatocytes. It is administered via subcutaneous injection once every three months and is HSA-approved for ATTR-CM and for stage 1 or 2 hereditary transthyretin amyloidosis with polyneuropathy (hATTR-PN).

2.3. The Committee considered eleven testimonials from local patients and carers and acknowledged that ATTR-CM had a significant negative impact on patients' lives. Symptoms such as fatigue, breathlessness, and mobility issues impact their ability to work, socialise and carry out many daily activities.

2.4. The Committee heard that most respondents were receiving tafamidis and felt that it helped to slow disease progression, and improve appetite and energy. One respondent reported no perceived benefit. Some patients with mixed CM/PN phenotypes also received patisiran (an exemption drug indicated for hATTR-PN only), but highlighted the burden of frequent hospital visits for infusions. Most respondents were aware of vutrisiran through their clinicians or patient support groups, and hoped that it could provide a more convenient treatment option. Overall, respondents considered that any new treatment for ATTR-CM should be more affordable, improve daily functioning and energy levels, and enable greater independence and quality of life.

Clinical effectiveness and safety

3.1. The Committee reviewed published clinical evidence from one phase III randomised controlled trial (HELIOS-B) comparing vutrisiran with placebo in patients with ATTR-CM. The trial recruited adults with wild-type or hereditary ATTR-CM, including both tafamidis-naïve patients and those receiving background tafamidis therapy at baseline.

3.2. The Committee heard that at 36-month follow-up, vutrisiran demonstrated statistically significant reductions versus placebo in the primary composite endpoint of all-cause mortality and recurrent cardiovascular events. These reductions occurred in both the overall population (including 40% receiving background tafamidis) and among patients not receiving background tafamidis. Secondary outcomes including 6-minute walk test distance, health-related quality of life scores, and all-cause mortality also showed statistically significant improvements in both populations. Furthermore, the Committee noted that vutrisiran was well-tolerated and showed an acceptable safety profile compared with placebo, with the most frequently reported adverse events being cardiovascular-related and likely reflecting the underlying disease rather than treatment-related effects.

3.3. However, in the subgroup of patients receiving tafamidis at baseline, vutrisiran did not demonstrate statistically significant benefit on the primary end point compared with placebo, and the trial was not powered for this analysis. Hence, the Committee considered that there was inadequate evidence to support any additive benefit of vutrisiran when added on to tafamidis.

3.4. In the absence of direct evidence comparing vutrisiran and tafamidis, the Committee considered indirect treatment comparisons reviewed by NICE (UK) and CDA (Canada). These showed no statistically significant differences in clinical effectiveness between the two treatments.

3.5. Overall, the Committee considered that vutrisiran demonstrated superior efficacy versus placebo with a tolerable safety profile, and is likely to have similar efficacy and comparable safety to tafamidis in patients with ATTR-CM.

Cost effectiveness

4.1. Given the comparable efficacy and safety of vutrisiran and tafamidis, the Committee agreed that a cost-minimisation analysis was appropriate for evaluating the cost effectiveness of vutrisiran. The Committee noted that vutrisiran was the more cost-effective option and the proposal was adequate to manage the uncertainty of the overall budget impact. The Committee also heard that the proposed price was comparable to those in overseas reference jurisdictions and considered vutrisiran to be 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 between SG$1 million and SG$3 million in the first year and between SG$3 million and SG$5 million in the fifth year of listing vutrisiran on the MOH List of Subsidised Drugs for treating ATTR-CM.

Recommendations

6.1. Based on available evidence, the Committee recommended vutrisiran 25 mg/0.5 mL injection be listed on the MAF for ATTR-CM, in view of the high clinical need, favourable clinical effectiveness and acceptable cost effectiveness at the price proposed.

ANNEX

MAF clinical criteria for vutrisiran for treating transthyretin amyloid cardiomyopathy (ATTR-CM)

Treatment of transthyretin amyloid cardiomyopathy (ATTR-CM):

Additional clinical criteria (initial):
The patient on initial application for transthyretin amyloid cardiomyopathy (ATTR-CM):

- has history of hospitalisation due to heart failure, or clinical evidence of heart failure that requires treatment with a diuretic for improvement; and
- a New York Heart Association (NYHA) Class I to III heart failure; and
- has end-diastolic interventricular septal wall thickness of at least 12 mm; and
- an estimated glomerular filtration rate (eGFR) of at least 30 mL/min/1.73 m2.

Diagnosis of ATTR-CM must be confirmed by documented evidence of transthyretin precursor protein through:

- histological confirmation with either immunohistochemistry or mass spectrometry; or
- grade 2 or 3 bone scintigraphy in addition to negative results for monoclonal protein on all of the following tests: serum and urine immunofixation and serum free light chains.

Patient must be undergoing treatment with this drug as a monotherapy (i.e. not in combination with any other disease modifying medicines for amyloidosis disorders).

The above criteria are valid for 6 months. To continue treatment, please reapply under 'Renewal'.

Additional clinical criteria (renewal):

The patient on subsequent reapplication for ATTR-CM:

- does not have persistent NYHA Class IV heart failure.

Reassessment should be conducted every 6 months and treatment continued only if there is clear evidence of ongoing clinical benefit.

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

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 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.

Find out more about ACE at https://www.ace-hta.gov.sg/about-us/

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