Technology Guidance

Tenofovir alafenamide

for treating chronic hepatitis B infection

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended listing tenofovir alafenamide (TAF) on the Medication Assistance Fund (MAF) for treating chronic hepatitis B infection, due to unfavourable cost-effectiveness compared with tenofovir disoproxil fumarate (TDF) at the price proposed by the manufacturer.

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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 tenofovir alafenamide (TAF) for treating chronic hepatitis B infection. The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for TAF 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 subsidy considerations.

Clinical need

2.1. Chronic hepatitis B infection usually requires long-term drug treatment to prevent disease progression. In local clinical practice, either TAF, tenofovir disoproxil fumarate (TDF) or entecavir are used to manage chronic hepatitis B infection in line with international clinical practice guidelines. The Committee acknowledged that TDF and entecavir were already included in the MOH List of Subsidised Drugs and there was limited clinical need to subsidise an additional treatment option.

2.2. TAF and TDF are both prodrugs of tenofovir but have different pharmacokinetic profiles. Lower doses of TAF compared to TDF are required to achieve therapeutic levels of tenofovir. The Committee noted that some clinicians prefer to prescribe TAF in elderly patients or in patients who have, or are at risk of, developing renal dysfunction or bone disease because it is considered to have less bone and renal toxicity compared to TDF. However, unlike TDF, TAF is not recommended for use in adolescents, pregnant women or patients with decompensated cirrhosis due to a lack of study data in these patient groups.

Clinical effectiveness and safety

3.1. The Committee reviewed the available clinical evidence from two phase III randomised controlled trials (Study 108 and Study 110), which were conducted in treatment-naïve and treatment-experienced adults with chronic hepatitis B infection and compensated liver disease. Results for the primary efficacy endpoint in both trials showed that TAF was non-inferior to TDF in the proportions of patients who achieved viral suppression (hepatitis B virus DNA <29 IU/ml) at week 48.

3.2. The Committee noted that while patients who received TAF had smaller decreases in hip and spine bone mineral density and estimated glomerular filtration rate, as well as smaller increases in serum creatinine and proteinuria biomarkers at week 96 compared to patients who received TDF, no patients in either group developed treatment-related fractures, renal failure or other serious renal adverse events (AEs). In addition, the rates of AEs of any grade, serious AEs, and AEs leading to study drug discontinuation were all similar between groups. Consistent with other HTA agencies (e.g. CADTH, PBAC and PHARMAC), the Committee concluded that additional data from ongoing long-term follow-up studies would be required to determine whether the improvement in bone and renal surrogate outcomes seen with TAF in the trials were clinically relevant.

3.3. Based on the available clinical evidence, the Committee considered that TAF and TDF were comparable in clinical effectiveness and safety for treating chronic hepatitis B infection.

Cost effectiveness

4.1. No local published cost-effectiveness studies of TAF were identified. The Committee acknowledged that TAF and TDF were recommended for subsidy on a cost minimisation basis compared to entecavir by the PBAC (Australia). In view of comparable efficacy and safety with TDF, the Committee agreed that the cost-effectiveness of TAF would be acceptable if it was cost-minimised against TDF.

4.2. At the price offered by the manufacturer as part of their value-based pricing (VBP) proposal, the monthly cost of TAF was significantly higher compared to TDF generic formulation. Therefore, the Committee concluded that TAF was not cost-effective at the proposed price.

Estimated annual technology cost

5.1. The Committee noted that the annual cost impact was estimated to be less than SG$1 million in the first year of listing TAF on the Medication Assistance Fund (MAF).

Recommendations

6.1. Based on available evidence, the Committee recommended not listing TAF on the MAF in view of unfavourable cost-effectiveness compared with TDF at the price proposed by the manufacturer.

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 3 July 2020. 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.

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

Principal Head (HTA)
Agency for Care Effectiveness
Email: ACE_HTA@moh.gov.sg