Technology Guidance

Dabrafenib in combination with trametinib

for treating BRAF V600 mutation-positive anaplastic thyroid cancer

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Dabrafenib 50 mg and 75 mg capsules in combination with trametinib 0.5 mg and 2 mg tablets for treating locally advanced or metastatic anaplastic thyroid cancer in patients with a BRAF V600 mutation and with no satisfactory locoregional treatment options.

Subsidy status

Dabrafenib 50 mg and 75 mg capsules and trametinib 0.5 mg and 2 mg tablets are recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication with effect from 4 January 2022.

Clinical indications, subsidy class and MediShield Life claim limits for both drugs are provided in the Annex.

Published: 4 January 2022

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 dabrafenib in combination with trametinib for treating patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with a BRAF V600 mutation and with no satisfactory locoregional treatment options. The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for both drugs was considered in line with their registered indications. Additional expert opinion was obtained from the MOH Oncology Drug Subcommittee (ODS) who assisted ACE ascertain the clinical value of the drugs under evaluation and provided clinical advice on their appropriate and effective use based on the available clinical evidence.

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. Anaplastic thyroid cancer (ATC) is a rare and aggressive cancer, accounting for only 1-2% of all thyroid cancer diagnoses. The median survival from diagnosis is about 5 months, and the 12-month survival rate is about 20%. In Singapore, approximately 7 patients are diagnosed with ATC each year, and between 20-50% of ATCs harbour BRAF V600 mutations.

2.2. The Committee noted that dabrafenib in combination with trametinib is currently the only HSA-approved treatment for locally advanced or metastatic ATC with a BRAF V600 mutation. In local practice, this combination therapy is used in patients who have no satisfactory locoregional treatment options, in line with international clinical practice guidelines. The Committee acknowledged the high clinical need to consider this treatment for subsidy to improve affordability and ensure appropriate patient care.

Clinical effectiveness and safety

3.1. The Committee reviewed the clinical evidence from a phase II, non-randomised trial that included 16 patients who were treated with dabrafenib and trametinib for ATC with BRAF V600 mutations. The confirmed overall response rate was 69% (11 of 16 patients; 95% CI 41% - 89%), and 7 patients had durable responses that were ongoing at the time of data cut-off. The median duration of response, progression-free survival, and overall survival endpoints were not reached as a result of ongoing responses, but the 12-month Kaplan-Meier estimates were 90%, 79%, and 80%, respectively.

3.2. In terms of safety, the combination treatment was generally well-tolerated as evaluated in 100 patients across seven rare tumour types. The common adverse events reported were fatigue, pyrexia and nausea.

3.3. Based on available evidence, the Committee considered that the combination treatment had shown acceptable clinical effectiveness and safety in patients with ATC, although there were uncertainties in the results given the limitations of the study design, small sample size, and lack of long-term overall survival data.

Cost effectiveness

4.1. The manufacturer of dabrafenib and trametinib was invited to submit value-based pricing (VBP) proposals for subsidy consideration. No published local or overseas cost-effectiveness studies of dabrafenib and trametinib for treating ATC were identified. However, the Committee acknowledged that the local proposed prices of these drugs were comparable to prices in overseas reference jurisdictions. Hence, they considered that dabrafenib in combination with trametinib was likely to represent a cost-effective treatment for ATC in the local context.

Estimated annual technology cost

5.1. Based on local epidemiological rates and estimated drug utilisation in the public healthcare institutions, the annual cost impact in the first year of listing dabrafenib and trametinib on MAF for treating ATC was estimated to be less than SG$1 million.

Recommendations

6.1. Based on available evidence, the Committee recommended dabrafenib 50 mg and 75 mg capsules and trametinib 0.5 mg and 2 mg tablets be listed on MAF for treating locally advanced or metastatic ATC in patients with a BRAF V600 mutation and with no satisfactory locoregional treatment options, in view of the unmet clinical need, absence of treatment alternatives, acceptable clinical and cost effectiveness, and reasonable budget impact at the proposed prices.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Clinical indication	Subsidy class (implementation date)	MediShield Life claim limit per month (implementation date)
Dabrafenib 50 mg and 75 mg capsules, and trametinib 0.5 mg and 2 mg tablets	Dabrafenib in combination with trametinib for treating locally advanced or metastatic anaplastic thyroid cancer in patients with a BRAF V600 mutation and with no satisfactory locoregional treatment options.	MAF (4 Jan 2022)	$3800 (1 Sep 2022)

Abbreviation: MAF, Medication Assistance Fund.

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 16 March 2021. 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

Chief HTA Officer
Agency for Care Effectiveness
Email: ACE_HTA@moh.gov.sg