

Lenvatinib and sorafenib for treating differentiated thyroid cancer

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Sorafenib 200 mg tablet; and
- ✓ Lenvatinib 4 mg and 10 mg capsules

for treating locally advanced or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer.

Subsidy status

Sorafenib 200 mg tablet is recommended for inclusion on the MOH Standard Drug List (SDL) for the abovementioned indication with effect from 4 January 2022.

Lenvatinib 4 mg and 10 mg capsules are recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication with effect from 1 September 2022.

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

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 lenvatinib and sorafenib for treating locally advanced or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC). 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. The Committee noted that approximately 360 patients are diagnosed with DTC each year in Singapore. Most patients can be cured with surgery, followed by radioactive iodine (RAI) or thyroxine therapy. However, some patients have locally advanced or metastatic disease that is refractory to RAI therapy and is clinically progressive or symptomatic. These patients are treated with lenvatinib or sorafenib in local clinical practice, in line with international clinical practice guidelines. The Committee acknowledged the clinical need to consider these drugs for subsidy to improve treatment affordability and ensure appropriate patient care.

Clinical effectiveness and safety

- 3.1. The Committee reviewed the available clinical evidence from randomised placebo-controlled trials for lenvatinib (SELECT) and sorafenib (DECISION). In both trials,

lenvatinib and sorafenib were superior to placebo in terms of progression-free survival (a surrogate endpoint), but not in overall survival. The Committee noted that the overall survival analyses in both trials could have been confounded, given that the majority of patients who were randomised to receive placebo had crossed over to receive the active drug after disease progression.

- 3.2. The Committee agreed that in the absence of a head-to-head study, the superiority of one drug over the other could not be concluded. Moreover, an indirect treatment comparison between lenvatinib and sorafenib was not considered appropriate in view of heterogeneity between the SELECT and DECISION trial populations.
- 3.3. In terms of safety, the Committee noted that lenvatinib and sorafenib had different adverse event profiles in the trials. Lenvatinib was associated with more events of hypertension, diarrhoea, fatigue and decreased appetite compared to placebo. Sorafenib was associated with more events of hand-foot skin reaction, diarrhoea, alopecia and rash compared to placebo. The Committee heard that local experts considered lenvatinib and sorafenib to be suitable for different patients depending on their comorbidities.

Cost effectiveness

- 4.1. The manufacturers of lenvatinib and sorafenib were invited to submit value-based pricing (VBP) proposals for their products for subsidy consideration. In the absence of local cost-effectiveness studies, the Committee reviewed evaluations from overseas HTA agencies. Although lenvatinib and sorafenib were not found to be cost-effective by NICE (UK) and CADTH (Canada), the Committee considered that the results were unlikely to be generalisable to the Singapore context as the drug costs used in the overseas evaluations were higher compared to local drug acquisition costs.
- 4.2. The Committee noted that, at the local proposed prices, the monthly treatment cost of sorafenib was lower than that of lenvatinib. They also acknowledged that the proposed prices of both drugs were comparable to prices in overseas reference jurisdictions. Therefore, they agreed that both drugs were likely to represent cost-effective treatments for DTC.

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 sorafenib on SDL and lenvatinib on MAF for treating locally advanced or metastatic, progressive, RAI-refractory DTC was estimated to be less than SG\$1 million each.

Recommendations

- 6.1. Based on available evidence, the Committee recommended sorafenib 200 mg tablet be listed on SDL, and lenvatinib 4 mg and 10 mg capsules be listed on MAF for treating locally advanced or metastatic, progressive, RAI-refractory DTC, in view of the therapeutic gap in the MOH List of Subsidised Drugs, and favourable clinical and cost effectiveness.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Clinical indications	Subsidy class (implementation date)	MediShield Life claim limit per month (implementation date)
Sorafenib 200 mg tablet	Treatment of locally advanced or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer	SDL (4 Jan 2022)	\$1200 (1 Sep 2022)
Lenvatinib 4 mg and 10 mg capsules	Treatment of locally advanced or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer	MAF (1 Sep 2022)	\$1200 (1 Sep 2022)

Abbreviations: SDL, Standard Drug List; 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 and 2 July 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

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