Technology Guidance

Lenvatinib and sorafenib

for treating advanced hepatocellular carcinoma

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 advanced unresectable hepatocellular carcinoma in patients with adequate liver function as assessed by the Child-Pugh scoring system.

Funding status

Sorafenib 200 mg tablet is recommended for inclusion on the MOH Standard Drug List (SDL) and lenvatinib 4 mg and 10 mg capsules are recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication when used according to HSA-recommended dosing regimens.

SDL subsidy for sorafenib will be implemented from 4 January 2022, while MAF assistance for lenvatinib will be implemented from 1 September 2022.

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

Updated: 1 June 2026

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 patients with advanced unresectable hepatocellular carcinoma. 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. Approximately 740 patients are diagnosed with liver cancer each year in Singapore, and hepatocellular carcinoma (HCC) accounts for about 90% of all cases. In local clinical practice, lenvatinib and sorafenib may be used as initial systemic therapy in patients with advanced unresectable HCC. Clinicians may also consider these drugs as a subsequent-line treatment option if they have not been used in an earlier setting.

2.2. The Committee noted that HCC typically occurs in patients with cirrhosis and hepatic impairment. Therefore, the treatment approach and prognosis of patients will depend not only on the tumour stage but also on the underlying liver function. In local practice, the use of lenvatinib and sorafenib is limited to patients who have adequate liver function as assessed by the Child-Pugh scoring system.

2.3. In view of the therapeutic gap in the MOH List of Subsidised Drugs, the Committee acknowledged the clinical need to consider lenvatinib and sorafenib 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 three phase III randomised controlled trials (RCTs) that were conducted in patients with advanced unresectable HCC who had not received previous systemic therapy and had Child-Pugh liver function class A.

3.2. Two of the RCTs showed that sorafenib was superior to placebo in terms of overall survival (OS). The third RCT was a head-to-head study which showed that lenvatinib was non-inferior in OS to sorafenib, but not superior over sorafenib. The median OS was 13.6 and 12.3 months in the lenvatinib and sorafenib groups, respectively (hazard ratio 0.92, 95% CI 0.79 - 1.06). For the secondary endpoints, a longer median progression-free survival and higher objective response rate were observed in the lenvatinib group compared to the sorafenib group.

3.3. In the head-to-head study, the overall rates of treatment-emergent adverse events were similar between lenvatinib and sorafenib, although they had different safety profiles. Lenvatinib was associated with more events of hypertension, proteinuria and dysphonia, while sorafenib was associated with more events of palmar-plantar erythrodysaesthesia, diarrhoea and alopecia.

3.4. Given that lenvatinib and sorafenib were non-inferior in OS, the Committee considered that both drugs were clinically comparable for treating HCC but acknowledged their different safety profiles. They also heard that CADTH (Canada) concluded both drugs were likely to be similar in efficacy with different toxicity profiles, and PBAC (Australia) considered that lenvatinib was non-inferior in effectiveness and safety to sorafenib while noting the differences in their safety profiles.

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 the evaluations of overseas HTA agencies for lenvatinib and sorafenib in patients with HCC. However, given that the drug prices used in the evaluations were not published or had included confidential discounts from the manufacturers, it was unknown whether the prices were comparable to those in Singapore and if the results were generalisable.

4.2. The Committee noted that, at the local proposed prices, the average monthly treatment cost of lenvatinib was higher than that of sorafenib. Nonetheless, the prices of both drugs were comparable to prices in overseas reference jurisdictions. Hence, both drugs were likely to represent cost-effective treatments for HCC.

4.3. In view of acceptable cost-effectiveness at the proposed prices, the Committee agreed that an SDL listing for sorafenib and a broad MAF listing for lenvatinib (not restricted to patients with untreated advanced HCC) were acceptable to allow flexibility in treatment protocols.

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 advanced unresectable HCC was estimated to be:

- Sorafenib (SDL): less than SG$1 million; and
- Lenvatinib (MAF): between SG$1 million to less than SG$3 million.

Recommendations

6.1. On the basis of the 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 advanced unresectable HCC in view of clinical need and favourable clinical and cost effectiveness.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Approved clinical indications	Subsidy class (implementation date)	Eligible for MediShield Life claims (implementation date)
Sorafenib 200 mg tablet	Treatment of advanced unresectable hepatocellular carcinoma in patients with adequate liver function as assessed by the Child-Pugh scoring system.	SDL (4 Jan 2022)	Yes[1] (1 Sep 2022)
Lenvatinib 4 mg and 10 mg capsules	Treatment of advanced unresectable hepatocellular carcinoma in patients with adequate liver function as assessed by the Child-Pugh scoring system, when used according to HSA-recommended dosing regimens.	MAF (1 Sep 2022)	Yes[1] (1 Sep 2022)

Abbreviations: SDL, Standard Drug List; MAF, Medication Assistance Fund.
[1]Please refer to MOH's website for the MediShield Life claim limit starting from the implementation date.

VERSION HISTORY

Guidance on lenvatinib and sorafenib for treating advanced hepatocellular carcinoma

This Version History is provided to track any updates or changes to the guidance following the first publication date. It is not part of the guidance.

1. **Publication of guidance**

   Date of Publication 4 Jan 2022

2. **Guidance updated to reflect MediShield Life claims eligibility**

   Date of Publication 1 Jun 2026

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.

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