Technology Guidance

[GUIDANCE IS OUTDATED AND HAS BEEN WITHDRAWN ON 2 JANUARY 2024.]

# Regorafenib and sunitinib

## for treating advanced gastrointestinal stromal tumours

**Technology Guidance from the MOH Drug Advisory Committee**



## Guidance Recommendations

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

- ✓ Regorafenib 40 mg tablet for treating patients with locally advanced, unresectable or metastatic gastrointestinal stromal tumours (GISTs) who have been previously treated with imatinib mesylate.

### Subsidy status

Regorafenib 40 mg tablet is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication with effect from 4 January 2022.

MAF assistance **does not** apply to sunitinib 12.5 mg, 25 mg, 37.5 mg and 50 mg capsules when used for treating GISTs.

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

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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 sunitinib and regorafenib for treating gastrointestinal stromal tumours (GISTs). 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 and/or specific clinical criteria defined by local experts to reflect local clinical practice. Additional expert opinion was obtained from the MOH Oncology Drug Subcommittee (ODS) who assisted ACE ascertain the clinical value of sunitinib and regorafenib 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 37 patients are diagnosed with GIST each year in Singapore and 30% to 60% are diagnosed with metastatic or recurrent disease. Imatinib is the standard of care and first-line treatment for metastatic GISTs. In local clinical practice, sunitinib and regorafenib are used for patients whose disease progresses on imatinib. The Committee agreed that there was a clinical need to improve affordability of treatments used after imatinib to ensure appropriate patient care.

## Clinical effectiveness and safety

3.1. Sunitinib

The Committee reviewed the available clinical evidence (A618-1004) and considered that sunitinib was superior to placebo based on a statistically significant longer time to tumour progression in patients who had been previously treated with imatinib. While there was no statistically significant difference in overall survival (OS) at the final analysis, the Committee noted that the trial was unblinded early at the interim analysis and participants could switch from placebo to sunitinib, potentially confounding the OS results.

3.2. The Committee noted that the most common adverse events with sunitinib were fatigue, diarrhoea, skin discolouration, nausea, anorexia, dysgeusia and hand-foot skin reaction.

3.3. Regorafenib

The Committee reviewed the available clinical evidence (GRID) and considered that regorafenib was superior to placebo based on a statistically significant improvement in progression free survival (PFS) in patients who had been previously treated with imatinib and sunitinib. Similar to sunitinib, while there was no statistically significant difference in OS, the Committee noted that significant crossover of patients from placebo to regorafenib could have confounded the results.

3.4. The Committee noted that the most common adverse events for regorafenib were hand-foot skin reaction, hypertension and diarrhoea.

## Cost effectiveness

4.1. Sunitinib

In the absence of a local cost-effectiveness evaluation, the Committee reviewed results from evaluations conducted by overseas HTA agencies. The incremental cost effectiveness ratios (ICERs) for sunitinib were high in Australia (PBAC: AU$45,000 to AU$75,000 per QALY) and the UK (NICE: £31,800 per QALY) compared to placebo. The Committee noted that the price proposed by the manufacturer for sunitinib was higher than in overseas reference jurisdictions and compared to regorafenib; therefore it was unlikely that sunitinib would be cost effective in the local context for treating GIST.

4.2. Regorafenib

The Committee noted that the PBAC (Australia) did not recommend regorafenib for patients who have previously been treated with imatinib and sunitinib as the ICER was uncertain and likely to be underestimated (AU$15,000 to AU$45,000 per QALY gained). NICE (UK) considered that the most plausible ICER was between £40,000 to £48,000 per QALY gained. Despite the ICERs reported overseas, the Committee acknowledged that at the local prices proposed by the manufacturers, the treatment cost of regorafenib was comparable with overseas reference jurisdictions and lower

than that of sunitinib, and it was likely to represent a cost-effective option for subsequent-line treatment for GIST following disease progression in the local context.

## Estimated annual technology cost

5.1. The Committee noted that the annual cost impact for regorafenib was estimated to be less than SG$1 million in the first year of listing on the MAF based on local epidemiological rates.

## Recommendations

6.1. Based on available evidence, the Committee recommended regorafenib 40 mg tablet be listed on the MAF for treating patients with locally advanced, unresectable or metastatic GISTs who have been previously treated with imatinib mesylate, in view of the clinical need, favourable clinical effectiveness and lower cost of treatment compared with sunitinib.

6.2. The Committee did not recommend sunitinib for listing on the MAF in view of unfavourable cost-effectiveness at the proposed price.



## ANNEX

**Recommendations by the MOH Drug Advisory Committee**

| Drug preparation | Clinical indications | Subsidy class (implementation date) | MediShield Life claim limit per month (implementation date) |
|---|---|---|---|
| Regorafenib 40 mg tablet | Treatment of patients with locally advanced, unresectable or metastatic gastrointestinal stromal tumours (GISTs) who have been previously treated with imatinib mesylate. | MAF (4 Jan 2022) | $1800 (1 Sep 2022) |
| Sunitinib 12.5 mg, 25 mg, 37.5 mg and 50 mg capsules | Treatment of patients with unresectable and/or metastatic malignant gastrointestinal stromal tumours (GISTs) who have had an inadequate response to imatinib mesylate treatment due to resistance or intolerance. | Not recommended for subsidy | $1600 (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 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*



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