Technology Guidance

Cabozantinib in combination with nivolumab

for previously untreated advanced renal cell cancer

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended cabozantinib in combination with nivolumab for inclusion on the MOH List of Subsidised Drugs for previously untreated advanced renal cell cancer in view of unfavourable cost-effectiveness compared with alternative treatments.

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

Published: 1 August 2023

Factors considered to inform the recommendations for funding

Technology evaluation

1.1. The MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of cabozantinib in combination with nivolumab for previously untreated advanced renal cell cancer (RCC). 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 the combination regimen was considered in line with its registered indication. Additional expert opinion was obtained from the MOH Oncology Drug Subcommittee (ODS) who assisted ACE ascertain the clinical value of the treatment regimen and provided clinical advice on its 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 funding considerations.

Clinical need

2.1. The Committee acknowledged that RCC is the most common type of kidney cancer among adults in Singapore with approximately 160 patients diagnosed with advanced and/or metastatic RCC each year. The Committee noted that only 20% of patients with stage IV disease live for up to 5 years and acknowledged that there was a high clinical need to consider treatments for subsidy to improve affordability and ensure appropriate patient care.

2.2. In local clinical practice, the Committee noted that tyrosine kinase inhibitors (TKIs) and immune checkpoint inhibitors are standard of care for previously untreated advanced and/or metastatic RCC, in line with international clinical practice guidelines. The Committee acknowledged that these treatments, including immune-oncology (IO)/TKI combinations, are included in the MOH List of Subsidised Drugs for previously untreated advanced renal cell cancer (RCC).[1]

[1] Update of MOH List of Subsidised Drugs to include treatments for various cancer conditions

Clinical effectiveness and safety

3.1. The Committee reviewed the available clinical evidence for cabozantinib plus nivolumab from a phase III randomised controlled trial (CHECKMATE 9ER) in patients with previously untreated advanced RCC.

3.2. At a median follow up of 18.1 months, results showed that cabozantinib plus nivolumab led to superior progression-free survival compared to sunitinib. Median overall survival was not reached in either arm at the time of data analysis.

3.3. The Committee noted that cabozantinib plus nivolumab was associated with more grade ≥3 adverse events (AEs) and immune-related AEs compared to sunitinib.

3.4. The Committee noted that there was no head-to-head randomised controlled trial comparing cabozantinib plus nivolumab with other IO/TKI combinations (avelumab plus axitinib or pembrolizumab plus axitinib). The Committee acknowledged that indirect comparisons were limited due to differences in study follow-up, and agreed that there was insufficient evidence to support a claim of superiority of one combination over another. Conservatively, the Committee considered all three IO/TKI combinations were likely to be clinically comparable.

Cost effectiveness

4.1. The Committee agreed that a cost minimisation approach (CMA) was appropriate to assess the cost-effectiveness of cabozantinib plus nivolumab compared with other IO/TKI combinations in view of their comparable efficacy.

4.2. Based on the prices proposed by the companies, the Committee noted that the cost of cabozantinib plus nivolumab was considerably higher than other IO/TKI combinations, driven by the higher cost of cabozantinib versus other TKIs. The cost of other TKIs was also expected to lower further over time with the availability of generic alternatives. Therefore, the Committee agreed that cabozantinib plus nivolumab was unlikely to represent a cost-effective treatment option for previously untreated advanced RCC compared to alternative treatments.

Estimated annual technology cost

5.1. The Committee noted that the annual cost impact to the public healthcare system was estimated to be between SG$5 million to less than SG$10 million in the first year of listing cabozantinib plus nivolumab on the MAF for previously untreated advanced RCC.

Recommendations

6.1. Based on available evidence, the Committee recommended not including cabozantinib plus nivolumab on the MOH List of Subsidised Drugs for untreated advanced RCC due to unfavourable cost-effectiveness compared with alternative treatments.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Clinical indications	Subsidy Class (implementation date)	MediShield Life claim limit per month (implementation date)
Cabozantinib 20 mg, 40 mg and 60 mg tablets plus nivolumab concentrate for solution for infusion (40 mg/4mL, 100 mg/10mL)	Cabozantinib in combination with nivolumab for untreated advanced renal cell carcinoma. Treatment with nivolumab should be stopped at 2 years, or earlier if disease progresses.	Not recommended for subsidy	$3000* (1 Sep 2022)

* change in MSHL claim limit with effect from 1 Aug 2023

VERSION HISTORY

Guidance on cabozantinib in combination with nivolumab for previously untreated advanced renal cell 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 31 Aug 2022

2. **Guidance updated with the increased MSHL claim limit for the combination**

   Date of Publication 1 Aug 2023

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.

This guidance is based on the evidence available to the MOH Drug Advisory Committee as at 20 May 2022 and 14 April 2023. 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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