

Technology Guidance

Bevacizumab biosimilar for treating different types of cancer

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Bevacizumab biosimilar (Mvasi) 100 mg/4 mL and 400 mg/16 mL concentrate for solution for infusion in line with its registered indications or local clinical protocols for treating:
 - Persistent, recurrent or metastatic cervical cancer when used with platinum-based chemotherapy plus paclitaxel;
 - Metastatic colorectal cancer when used with fluoropyrimidine-based chemotherapy;
 - Malignant glioma (WHO Grade III and IV) after relapse or disease progression following prior therapy;
 - Previously untreated, unresectable, locally advanced, recurrent or metastatic non-squamous non-small-cell lung cancer when used with carboplatin and paclitaxel;
 - Previously untreated, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer in patients who have suboptimally debulked Stage III disease with more than 1 cm of residual disease or Stage III unresectable or Stage IV disease;
 - Recurrent, platinum-sensitive, epithelial ovarian, fallopian tube, or primary peritoneal cancer when used with carboplatin and gemcitabine or paclitaxel;
 - Recurrent, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer when used with paclitaxel, topotecan or pegylated liposomal doxorubicin; and
 - Advanced homologous recombination deficiency (HRD) positive high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer as maintenance treatment in combination with olaparib in patients who are in complete or partial response to first-line platinum-based chemotherapy in combination with bevacizumab biosimilar.

Subsidy status

Bevacizumab biosimilar (Mvasi) 100 mg/4 mL and 400 mg/16 mL concentrate for solution for infusion are recommended for inclusion on the MOH Standard Drug List (SDL) for the abovementioned indications with effect from 1 April 2022.

SDL subsidy **does not** apply to any formulations or strengths of bevacizumab reference biologic (Avastin) or other brands of bevacizumab biosimilars.

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

Updated: 12 July 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 bevacizumab biosimilar (Mvasi) for treating different types of cancer. 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 Mvasi was considered in line with its registered indications or specific clinical criteria defined by clinical experts to reflect its use in local practice.
- 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. A biosimilar is a biological therapeutic product with proven similar physicochemical characteristics, biological activity, safety and efficacy to the reference biological product. Mvasi is a biosimilar of bevacizumab and its reference biologic is Avastin.
- 2.2. The Committee noted that bevacizumab-containing regimens represented the standard of care for many cancer indications in local practice, and available clinical evidence for Avastin had already been reviewed in separate technology evaluations. The Committee agreed that the availability of cheaper biosimilar products could improve treatment affordability for patients and would lead to cost savings to the healthcare system.
- 2.3. The Committee noted that position statements from international professional bodies and overseas HTA agencies support the use of bevacizumab biosimilars if they have regulatory approval, the prescribing decision is shared between the patient and the clinician, and patients are closely monitored for efficacy and safety outcomes.

- 2.4. Local clinical experts confirmed that they would prescribe a bevacizumab biosimilar if the clinical evidence showed that it was non-inferior to the reference biologic and it was more affordable for their patients.

Clinical effectiveness and safety

- 3.1. The Committee heard that the clinical development programme for Mvasi to show therapeutic equivalence to Avastin was based on a pivotal phase III randomised controlled trial (MAPLE) in adults with non-small-cell lung cancer (NSCLC), and two phase I pharmacokinetic (PK) studies in healthy adults.
- 3.2. The Committee heard that a real-world observational cohort study was ongoing in the United States, to assess the clinical effectiveness and safety of Mvasi compared to Avastin in patients with metastatic colorectal cancer. In addition, two retrospective studies have reviewed patients with different types of cancer who switched from Avastin to Mvasi, however, clinical outcomes have not been published yet.
- 3.3. In the MAPLE trial, Mvasi was shown to be equivalent in efficacy to Avastin for the primary endpoint of objective response rate (ORR), which fell within the predefined equivalence margin. Progression-free survival and overall survival rates were also comparable between treatment groups. The Committee considered that ORR was an appropriate primary endpoint as it is an objective measure of anti-tumour activity and less likely to be affected by confounding factors.
- 3.4. The Committee noted that the safety profile, immunogenicity and PK properties of Mvasi were comparable to those of Avastin in the MAPLE trial and PK studies. They also acknowledged that patients in the MAPLE trial had stage IV or recurrent metastatic non-squamous NSCLC and represented a sensitive population for detecting clinically meaningful differences between Mvasi and Avastin. Overall, based on the available evidence, the Committee agreed that Mvasi was therapeutically equivalent to Avastin for treating NSCLC.
- 3.5. The Committee noted that no randomised controlled trials had been conducted for Mvasi in other cancer types. Nonetheless, they considered that an extrapolation of therapeutic equivalence to all other HSA-approved cancer indications of Avastin was acceptable given the mechanism of action, PK, route of administration, immunogenicity and toxicity of bevacizumab were expected to be similar across clinical indications.
- 3.6. The Committee acknowledged that local and international regulatory agencies had concluded that there were sufficient justifications to support therapeutic equivalence between Mvasi and Avastin, and to also approve Mvasi for the same indications as Avastin, despite a lack of clinical evidence.

Cost-effectiveness

- 4.1. Based on the value-based pricing proposals submitted for subsidy consideration, the Committee noted that Mvasi was more cost-effective than Avastin on a cost-minimisation basis and was likely to represent an acceptable use of healthcare resources.
- 4.2. No local economic analyses of bevacizumab biosimilar were identified. The Committee reviewed a budget impact analysis from Europe, which estimated substantial cost savings from the introduction of bevacizumab biosimilar when a conservative 20% price reduction from the reference biologic was assumed. The Committee agreed that cost savings were also likely in the Singapore context, based on the local prices of both products.

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 Mvasi on the SDL for treating different types of cancer in line with clinical practice was estimated to be between SG\$1 million to less than SG\$3 million.
- 5.2. Depending on the rate of uptake of the biosimilar in the public healthcare institutions, the Committee noted that estimated cost savings from patients switching from Avastin to Mvasi were likely to be at least SG\$30 million over five years.

Additional considerations

- 6.1. In view of the potential cost savings to patients who use Mvasi instead of Avastin, and the low risk of inappropriate use given the well-established role of bevacizumab in different local cancer treatment protocols, the Committee considered that an SDL listing for Mvasi was appropriate to encourage uptake.

Recommendations

- 7.1. Based on available evidence, the Committee recommended bevacizumab biosimilar (Mvasi) 100 mg/4 mL and 400 mg/16 mL concentrate for solution for infusion be listed on the SDL for treating different cancer indications in line with clinical practice, in view of the clinical need, and favourable clinical and cost-effectiveness.
- 7.2. The Committee did not recommend bevacizumab reference biologic (Avastin) for subsidy due to unfavourable cost-effectiveness compared to Mvasi.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation (Brand)	Clinical indications	Subsidy class (implementation date)	MediShield Life claim limit per month (implementation date)
Bevacizumab biosimilar (Mvasi) 100 mg/4 mL and 400 mg/16 mL concentrate for solution for infusion	For cancer treatment	SDL (1 Apr 2022)	\$600 (1 Sep 2022)
Bevacizumab reference biologic (Avastin) 100 mg/4 mL and 400 mg/16 mL concentrate for solution for infusion	For cancer treatment	Not recommended for subsidy	\$600 (1 Sep 2022)

Abbreviation: SDL, Standard Drug List.

VERSION HISTORY

Guidance on bevacizumab biosimilar for treating different types of cancer

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 1 Apr 2022
- 2. Guidance updated with the MediShield Life claim limit for bevacizumab**
Date of Publication 12 Jul 2022

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 13 December 2021 and 16 June 2022. 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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