Technology Guidance

Bevacizumab

for treating persistent, recurrent or metastatic cervical cancer

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended bevacizumab reference biologic (Avastin) for subsidy for treating persistent, recurrent or metastatic cervical cancer in view of unfavourable cost effectiveness compared with bevacizumab biosimilar (Mvasi) at the price proposed by the manufacturer.

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 reference biologic (Avastin) for treating persistent, recurrent or metastatic cervical 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 bevacizumab 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 bevacizumab 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 subsidy considerations.

1.4. The technology evaluation of bevacizumab biosimilar (Mvasi) for treating different types of cancer in line with its registered indications is discussed in a separate guidance.

Clinical need

2.1. Approximately 215 patients are diagnosed with cervical cancer each year in Singapore. In local practice, patients who have persistent, recurrent or metastatic cervical cancer are treated with chemotherapy (cisplatin or carboplatin plus paclitaxel), with or without bevacizumab.

2.2. The Committee noted that cisplatin-based regimens are more commonly used than carboplatin-based regimens in local practice. The latter are used as an alternative for patients who are unable to have cisplatin treatment (e.g., elderly patients or those with impaired renal function).

2.3. The Committee heard that the HSA-approved indication for bevacizumab allows its use in combination with either cisplatin plus paclitaxel or topotecan plus paclitaxel for treating cervical cancer, however, local clinicians confirmed that topotecan is no longer used due to the risk of myelosuppression.

2.4. While cisplatin, carboplatin and paclitaxel are already subsidised, the Committee acknowledged the clinical need to consider bevacizumab for subsidy to allow flexibility in treatment protocols and improve affordability for patients.

Clinical effectiveness and safety

3.1. The Committee reviewed the available clinical evidence for bevacizumab from three clinical trials conducted in patients with persistent, recurrent or metastatic cervical cancer.

3.2. In a phase III randomised controlled trial (GOG 240), bevacizumab in combination with chemotherapy (cisplatin-paclitaxel or topotecan-paclitaxel) led to an improvement in median overall survival (OS) of 3.5 months compared to chemotherapy alone. Subgroup analyses also showed an OS benefit when bevacizumab-cisplatin-paclitaxel was compared to cisplatin-paclitaxel.

3.3. In terms of safety, the addition of bevacizumab to chemotherapy increased the incidence of hypertension, thromboembolic events and gastrointestinal fistulas compared to chemotherapy alone, but there was no significant reduction in health-related quality of life.

3.4. In a phase II single-arm trial (CECILIA), bevacizumab in combination with carboplatin-paclitaxel showed similar efficacy and safety results as those observed with bevacizumab-cisplatin-paclitaxel in the GOG 240 trial.

3.5. In a phase III randomised controlled trial (JCOG0505), carboplatin-paclitaxel was non-inferior in terms of overall survival compared to cisplatin-paclitaxel for treating cervical cancer.

3.6. Overall, the Committee agreed that the use of bevacizumab in combination with chemotherapy (cisplatin or carboplatin plus paclitaxel) for treating persistent, recurrent or metastatic cervical cancer was adequately supported.

Cost effectiveness

4.1. The Committee acknowledged that they had established therapeutic equivalence between bevacizumab reference biologic (Avastin) and bevacizumab biosimilar (Mvasi) in a separate technology evaluation, and that a cost-minimisation approach was appropriate to assess the cost effectiveness of Avastin. At the price proposed by the manufacturer, Avastin did not represent a cost-effective treatment option compared to Mvasi.

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 Avastin on the MOH Standard Drug List (SDL) or Medication Assistance Fund (MAF) for treating cervical cancer was estimated to be less than SG$1 million.

Recommendations

6.1. Based on available evidence, the Committee did not recommend bevacizumab reference biologic (Avastin) for subsidy for treating persistent, recurrent or metastatic cervical cancer due to unfavourable cost effectiveness compared with bevacizumab biosimilar (Mvasi) at the price proposed by the manufacturer.

6.2. The Committee noted that Mvasi had been recommended for listing on the SDL for treating different types of cancer, including cervical cancer, as part of a separate review, with subsidy implementation effective from 1 April 2022.

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	Bevacizumab biosimilar in combination with platinum-based chemotherapy plus paclitaxel for treating persistent, recurrent or metastatic cervical cancer.	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	Bevacizumab in combination with platinum-based chemotherapy plus paclitaxel for treating persistent, recurrent or metastatic cervical cancer.	Not recommended for subsidy	$600 (1 Sep 2022)

Abbreviation: SDL, Standard Drug List.

VERSION HISTORY

Guidance on bevacizumab for treating persistent, recurrent or metastatic cervical 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 16 March 2021, 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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