Technology Guidance

Review of cancer drugs

for treating advanced urothelial carcinoma

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Avelumab 200 mg/10 mL concentrate for solution for infusion; and
- ✓ Pembrolizumab 100 mg/4 mL solution for infusion

for treating advanced urothelial carcinoma (UC) in line with specific clinical criteria.

Funding status

Avelumab 200 mg/10 mL concentrate for solution for infusion is recommended for inclusion on the Medication Assistance Fund (MAF) for maintenance treatment of locally advanced or metastatic UC that has not progressed with first-line platinum-based chemotherapy when used in line with the treatment regimen outlined in the Annex.

Pembrolizumab 100 mg/4 mL solution for infusion is recommended for inclusion on the MAF for treating patients with locally advanced or metastatic UC after receiving platinum-based chemotherapy. Patients must not have received prior treatment with a PD-1/PD-L1 inhibitor for locally advanced or metastatic UC.

MAF assistance for the abovementioned treatments will be implemented from 1 September 2022.

MAF assistance **does not** apply to pembrolizumab when used for patients with untreated PD-L1-positive UC who are unable to receive cisplatin-based chemotherapy, or erdafitinib when used for treating UC with FGFR3 genetic alterations.

Clinical indications, subsidy class and MediShield Life claims eligibility for all drugs included in the evaluation 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 avelumab, erdafitinib and pembrolizumab for treating locally advanced or metastatic urothelial carcinoma (UC). 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 all 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. Urothelial carcinomas occur in urothelial cells that line the urinary bladder, renal pelvis, ureter and urethra. Approximately 190 patients are diagnosed with UC each year in Singapore.

2.2. Patients with locally advanced or metastatic UC have poor prognosis, with median survival of approximately 14 months. In local practice, these patients commonly receive cisplatin- or carboplatin-based chemotherapy as initial treatment. Carboplatin-based chemotherapy is used mainly in patients who are unable to receive cisplatin due to renal impairment, poor performance status, or other comorbidities. For certain patients who are cisplatin-ineligible and have PD-L1-positive tumours, treatment with pembrolizumab may be considered.

2.3. For patients who have not experienced disease progression with first-line platinum-based chemotherapy, maintenance treatment with avelumab may be considered as an alternative to watchful waiting. However, if there is disease progression during or after platinum-based chemotherapy, subsequent-line treatment options include chemotherapy (e.g., gemcitabine, paclitaxel) and pembrolizumab.

2.4. For certain patients whose tumours have susceptible fibroblast growth factor receptor 3 (FGFR3) genetic alterations, and who have disease progression during or following at least one line of prior chemotherapy, treatment with erdafitinib may be considered.

2.5. While gemcitabine, paclitaxel, cisplatin- and carboplatin-based chemotherapy are currently subsidised, the Committee acknowledged the clinical need to consider avelumab, erdafitinib and pembrolizumab for subsidy to allow flexibility in treatment protocols and improve affordability for patients.

Clinical effectiveness and safety

3.1. Patients who are cisplatin-ineligible with untreated PD-L1-positive UC
The Committee reviewed the available clinical evidence for pembrolizumab from a phase II single-arm trial (KEYNOTE-052) in cisplatin-ineligible patients with untreated, locally advanced or metastatic UC. Results from a subgroup analysis in patients whose tumours expressed PD-L1 with a combined positive score (CPS) ≥10 showed an ORR of 47% and median OS of 18.5 months. The most common grade 3 or 4 treatment-related adverse events reported in the overall population were fatigue, increased alkaline phosphatase (ALP), colitis, and muscle weakness.

3.2. Overall, the Committee considered that the clinical benefit of pembrolizumab for this indication was uncertain due to limitations of the data from a non-comparative trial and subgroup analysis.

3.3. Maintenance treatment of UC that has not progressed with first-line platinum-based chemotherapy
The Committee reviewed the clinical evidence for avelumab maintenance therapy from a phase III randomised controlled trial (JAVELIN Bladder 100) in patients with locally advanced or metastatic UC that had not progressed with first-line platinum-based chemotherapy.

3.4. Results showed that the addition of avelumab to best supportive care (BSC) improved median OS by 7.1 months compared with BSC alone in the overall population. The OS benefit was also observed in all prespecified subgroups, including patients with PD-L1-positive tumours. The most common grade ≥3 adverse events reported in the avelumab group were urinary tract infection, anaemia, fatigue, and haematuria. Overall, the Committee agreed that avelumab was a clinically effective maintenance treatment for patients with UC.

3.5. Patients with UC who have received platinum-based chemotherapy
The Committee reviewed the clinical evidence for pembrolizumab from a phase III randomised controlled trial (KEYNOTE-045) in patients with locally advanced or metastatic UC that had progressed after platinum-based chemotherapy.

3.6. Results showed that pembrolizumab improved median OS by 2.8 months compared with chemotherapy (docetaxel, paclitaxel or vinflunine) in the ITT population. The OS benefit was also shown in all subgroups examined, including patients with different PD-L1 expression levels. The safety profile of pembrolizumab was favourable compared to chemotherapy, with a lower incidence of grade ≥3 treatment-related adverse events reported in the pembrolizumab group. Overall, the Committee agreed that pembrolizumab was clinically effective for treating UC that has progressed after platinum-based chemotherapy.

3.7. Previously treated patients who have UC with FGFR3 genetic alterations
The Committee reviewed the available evidence for erdafitinib from a phase II single-arm trial (BLC2001) in patients who had locally advanced or metastatic UC with a prespecified FGFR genetic alteration, and who had disease progression during or following at least one line of prior chemotherapy.

3.8. In the overall population, erdafitinib was associated with an ORR of 40% and median OS of 11.3 months. Based on the type of genetic alteration, the ORR was 41% among 64 patients with FGFR3 mutations, and 11% among 18 patients with FGFR3 fusions. In terms of safety, the most common grade ≥3 adverse events of any cause were hyponatremia, stomatitis and asthenia.

3.9. Given the limitations of the study design and small sample size, the Committee considered that the results could not be interpreted in a clinically meaningful manner. However, they heard that there was an ongoing, randomised phase III trial (THOR, expected completion April 2024) comparing the use of erdafitinib versus chemotherapy or pembrolizumab, which is expected to provide more robust evidence to determine the clinical benefit of erdafitinib for treating UC with FGFR genetic alterations.

Cost effectiveness

4.1. The manufacturers of avelumab, erdafitinib and pembrolizumab were invited to submit value-based pricing (VBP) proposals for their products for subsidy consideration.

4.2. Patients who are cisplatin-ineligible with untreated PD-L1-positive UC
In the absence of local economic studies, the Committee reviewed evaluations from overseas HTA agencies for pembrolizumab. NICE (UK) and CADTH (Canada) considered that the cost-effectiveness estimates were uncertain when pembrolizumab was compared with carboplatin plus gemcitabine because the treatments were not directly compared in a clinical trial, making it difficult to establish the true magnitude of clinical benefit.

4.3. In view of the uncertainties raised by NICE and CADTH, the Committee considered that pembrolizumab was unlikely to represent a cost-effective treatment option locally for this indication.

4.4. Maintenance treatment of UC that has not progressed with first-line platinum-based chemotherapy

The Committee reviewed a local cost-effectiveness analysis (CEA) conducted by ACE that compared maintenance avelumab plus BSC versus BSC alone in patients with UC that had not progressed with first-line platinum-based chemotherapy. Results showed that avelumab plus BSC was associated with a base-case incremental cost-effectiveness ratio (ICER) of more than SG$105,000 per quality-adjusted life year (QALY) gained. However, following VBP discussions, the Committee concluded that an MAF listing for avelumab was appropriate in view of acceptable cost-effectiveness across all subsidised indications[1-2] at the proposed price that was also comparable to prices in overseas reference jurisdictions.

4.5. Patients with UC who have received platinum-based chemotherapy

In the absence of local economic studies, the Committee reviewed evaluations from overseas HTA agencies for pembrolizumab for treating patients with UC who have received platinum-based chemotherapy. Based on the evaluation from CADTH, pembrolizumab was not cost-effective versus docetaxel or paclitaxel. However, the results were not considered to be generalisable to the Singapore context as the drug price used in the analysis was higher than the local proposed price.

4.6. In the evaluations from NICE and PBAC (Australia), the drug prices used in the analyses were not published or included confidential discounts, thus it was unknown whether the results were generalisable to the Singapore context.

4.7. The Committee recalled that pembrolizumab provided an OS benefit compared with chemotherapy in the pivotal trial, and they considered that the treatment cost of pembrolizumab when capped at a maximum duration of 2 years at the proposed price was likely to be an acceptable use of healthcare resources in the local setting for treating UC that has progressed after platinum-based chemotherapy.

4.8. Previously treated patients who have UC with FGFR3 genetic alterations

No published local or overseas economic studies of erdafitinib for treating UC with FGFR genetic alterations were identified. However, given the uncertain clinical benefit, the Committee considered that erdafitinib was unlikely to represent a cost-effective treatment option at the price proposed by the manufacturer.

[1] ACE technology guidance for Review of cancer drugs for treating advanced renal cell cancer
[2] Update of MOH List of Subsidised Drugs to include treatments for various cancer conditions

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 avelumab and pembrolizumab on the MAF was estimated to be less than SG$1 million each when used for the following indications:

- Avelumab for maintenance treatment of UC that has not progressed with first-line platinum-based chemotherapy; and
- Pembrolizumab for treating patients with UC after receiving platinum-based chemotherapy.

Recommendations

6.1. Patients who are cisplatin-ineligible with untreated PD-L1-positive UC

Based on available evidence, the Committee did not recommend pembrolizumab for listing on MAF due to uncertain clinical benefit and cost effectiveness for treating patients who are cisplatin-ineligible with untreated PD-L1-positive UC.

6.2. Maintenance treatment of UC that has not progressed with first-line platinum-based chemotherapy

In view of clinical need, and acceptable clinical and cost effectiveness, the Committee recommended avelumab 200 mg/10 mL concentrate for solution for infusion be listed on MAF for maintenance treatment of UC that has not progressed with first-line platinum-based chemotherapy.

6.3. Patients with UC who have received platinum-based chemotherapy

In view of clinical need, and acceptable clinical and cost effectiveness, the Committee recommended pembrolizumab 100 mg/4 mL solution for infusion be listed on MAF for treating patients with locally advanced or metastatic UC after receiving platinum-based chemotherapy.

6.4. Previously treated patients who have UC with FGFR3 genetic alterations

The Committee did not recommend erdafitinib for listing on MAF due to uncertain clinical benefit and cost effectiveness in previously treated patients who have UC with FGFR3 genetic alterations.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Clinical indications	Subsidy class (implementation date)	Eligible for MediShield Life claims (implementation date)
Patients who are cisplatin-ineligible with untreated PD-L1-positive UC			
Pembrolizumab 100 mg/4 mL solution for infusion	Treatment of patients with locally advanced or metastatic urothelial carcinoma whose tumours express PD-L1 with a combined positive score (CPS) ≥10, and who are not eligible for cisplatin-containing chemotherapy.‡	Not recommended for subsidy	Yes[1] (1 Sep 2022)
Maintenance treatment of UC that has not progressed with first-line platinum-based chemotherapy			
Avelumab 200 mg/10 mL concentrate for solution for infusion	Maintenance treatment of locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-based chemotherapy. Avelumab may be given at a dose of 10 mg/kg up to a maximum of 800 mg, every 2 weeks.	MAF (1 Sep 2022)	Yes[1] (1 Sep 2022)
Patients with UC who have received platinum-based chemotherapy			
Pembrolizumab 100 mg/4 mL solution for infusion	Treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) after receiving platinum-containing chemotherapy. Patients must not have received prior treatment with a PD-1/PD-L1 inhibitor for locally advanced or metastatic UC.‡	MAF (1 Sep 2022)	Yes[1] (1 Sep 2022)
Previously treated patients who have UC with FGFR3 genetic alterations			
Erdafitinib 3 mg, 4 mg and 5 mg tablets	Treatment of patients with locally advanced or metastatic urothelial carcinoma, whose tumours have susceptible FGFR3 genetic alterations, and who have disease progression during or following at least one line of prior systemic therapy. Erdafitinib is not recommended for the treatment of patients who are eligible for and have not received PD-1 or PD-L1 inhibitor therapy.^	Not recommended for subsidy	Yes[1] (1 Sep 2022)

Abbreviations: MAF, Medication Assistance Fund; PD-1/PD-L1, Programmed Cell Death 1/ Programmed Cell Death Ligand 1; FGFR3, fibroblast growth factor receptor 3
‡revised clinical indication with effect from 1 Aug 2025.
^revised clinical indication with effect from 1 April 2026.
[1] Please refer to MOH's website for the MediShield Life claim limit starting from the implementation date.

VERSION HISTORY

Guidance on review of cancer drugs for treating advanced urothelial 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	12 Jul 2022
2.	**Guidance updated to revise the clinical indication for pembrolizumab** Date of Publication	2 Jan 2024
3.	**Guidance updated to revise the clinical indication for pembrolizumab** Date of Publication	1 Aug 2025
4.	**Guidance updated to revise the clinical indication for erdafitinib** Date of Publication	1 Apr 2026
5.	**Guidance updated to reflect MediShield Life claims eligibility for all drugs** 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.

Find out more about ACE at https://www.ace-hta.gov.sg/about-us/

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