Technology Guidance

Sacituzumab govitecan

for unresectable locally advanced or metastatic HR-positive, HER2-negative breast cancer

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended sacituzumab govitecan for inclusion on the MOH List of Subsidised Drugs for treating patients with unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting. The decision was based on the unfavourable cost effectiveness of sacituzumab govitecan compared with chemotherapy, and the unacceptable price-volume agreement proposed by the company.

Clinical indication, subsidy class and MediShield Life claim limit for sacituzumab govitecan are provided in the Annex.

Updated: 16 September 2025

Company-led submission

1.1. At the November 2024 meeting, the MOH Drug Advisory Committee ("the Committee") considered the technology evaluation of sacituzumab govitecan for treating unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer in patients who have received endocrine-based therapy (ET) and at least two additional systemic therapies in the metastatic setting. The evaluation included the company's evidence submission and a review by one of ACE's evidence review centres.

1.2. Expert opinion obtained from the MOH Cancer Drug Subcommittee and patient experts from local patient and voluntary organisations assisted ACE in ascertaining the clinical value of sacituzumab govitecan.

1.3. 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.

1.4. Additional factors, including social and value judgments, may also inform the Committee's funding considerations.

Clinical need

2.1. The Committee heard that each year in Singapore, approximately 544 patients are diagnosed with HR-positive, HER2-negative unresectable locally advanced or metastatic breast cancer (uBC or mBC). Most patients with disease progression on ET and/or targeted therapies will receive a taxane followed by single-agent chemotherapy (e.g. capecitabine, eribulin, gemcitabine or vinorelbine). Sacituzumab govitecan is most likely to replace single-agent chemotherapy in clinical practice.

2.2. The Committee considered testimonials from 14 local patient experts about living with advanced or metastatic breast cancer and their experience with different treatments. They heard that breast cancer had negatively impacted their emotional and mental health, and their ability to work and take care of loved ones, affecting family relationships for some. The side effects of treatments also affected their lives and daily activities, and the financial burden of treatments caused them to feel worried and stressed. None of the patients had experience with sacituzumab govitecan, but they considered that any new treatments for breast cancer should be more affordable, able to stop cancer from worsening, prolong their time living with cancer, improve quality of life and have manageable side effects.

Clinical effectiveness and safety

3.1. The company requested a listing based on the HSA-approved indication. The Committee heard local clinicians' inputs that the use of sacituzumab govitecan in local practice was aligned with the HSA-approved indication (i.e. for patients who have received ET and at least two additional systemic therapies which could include targeted therapy). The Committee considered it was reasonable to consider listing of sacituzumab govitecan in line with the approved HSA indication, which did not restrict its use to after at least two additional lines of chemotherapy following ET (i.e. eligibility criteria of the pivotal TROPiCS-02 trial).

3.2. The Committee reviewed the clinical evidence, presented in the company's submission, from two phase III, randomised, open-label trials (TROPiCS-02 and EVER-132-002). Both trials compared sacituzumab govitecan with treatment of physician's choice (TPC), which comprised single-agent chemotherapy including capecitabine, eribulin, gemcitabine or vinorelbine, in patients with HR-positive, HER2-negative uBC or mBC whose disease had progressed after ET and two to four prior chemotherapy regimens for metastatic disease.

3.3. At median follow-up of 12.5 months for TROPiCS-02 and 13.4 months for EVER-132-002, sacituzumab govitecan led to statistically significant improvements in median progression-free survival (PFS) and overall survival (OS) compared with TPC (Table 1). However, the Committee considered the magnitude of benefit to be modest (Table 1).

Table 1: Results of PFS and OS in TROPiCS-02 and EVER-132-002

	TROPiCS-02 (median follow-up: 10.22 months; data cut-off: 3 January 2022)		EVER-132-002 (median follow-up: 13.4 months; data cut-off: 30 April 2023)	
	SG (N=272)	**TPC (N=271)**	**SG (N=166)**	**TPC (N=165)**
PFS by BICR				
Events, n/N (%)	170/272 (62.5%)	159/271 (58.7%)	122/166 (73.5%)	122/165 (73.9%)
Median PFS, months (95% CI)	5.5 (4.2 to 7.0)	4.0 (3.1 to 4.4)	4.3 (4.1 to 5.7)	4.2 (2.8 to 4.2)
Hazard ratio (95% CI), p-value[a]	**0.66 (0.53, 0.83), p=0.0003**		**0.671 (0.517, 0.870), p=0.003**	
	TROPiCS-02 (median follow-up: 12.48 months; data cut-off: 1 July 2022)		**EVER-132-002 (median follow-up: 13.4 months; data cut-off: 30 April 2023)**	
	SG (N=272)	**TPC (N=271)**	**SG (N=166)**	**TPC (N=165)**
OS				
Events, n/N (%)	191/272 (70.2%)	199/271 (73.4%)	67/166 (40.4%)	89/165 (53.9%)
Median OS, months (95% CI)	14.4 (13.0 to 15.7)	11.2 (10.1 to 12.7)	21.0 (16.5 to NE)	15.3 (13.2 to 18.1)
Hazard ratio (95% CI), p-value[a,b]	**0.79 (0.65, 0.96), p=0.02**		**0.64 (0.47, 0.88), p=0.0061**	

Abbreviations: BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Bold indicates statistically significant result.
[a] Derived using log rank test.
[b] Nominal p-value reported.

3.4. The Committee noted that the open-label design of both trials could have introduced bias and may have influenced patients' responses to quality-of-life questionnaires to favour sacituzumab govitecan. In addition, in TROPiCS-02, the number of non-evaluable patients for health-related quality of life (HRQoL) assessment was higher in the TPC arm (n=61) compared to the sacituzumab govitecan arm (n=36). It was uncertain how the missing data influenced the results.

3.5. In terms of safety, the Committee heard that sacituzumab govitecan was associated with a statistically significant, higher incidence of grade ≥3 treatment-emergent adverse events (TEAEs) compared with TPC (TROPiCS-02: 73.9% vs 60.2%; EVER-132-002: 81.8% vs 69.5%). More patients in the sacituzumab govitecan arm of both trials also experienced study drug interruption from TEAEs compared with TPC (TROPiCS-02: 66.4% vs 43.8%; EVER-132-002: 67.9% vs 40.2%). The most common TEAEs of any grade reported with sacituzumab govitecan were neutropenia, diarrhoea, nausea and fatigue.

3.6. The submission described sacituzumab govitecan as superior to TPC in terms of effectiveness, and tolerable in terms of safety for patients with previously treated, endocrine-resistant HR-positive, HER2-negative uBC or mBC. Based on the evidence submitted, the Committee concluded that the magnitude of clinical benefit provided by sacituzumab govitecan compared with TPC was considered modest. In terms of safety, the Committee considered the safety of sacituzumab govitecan to be inferior to TPC.

Cost effectiveness

4.1. The Committee considered the submission's cost-utility analysis that compared sacituzumab govitecan with TPC for HR-positive, HER2-negative uBC or mBC in patients who have received ET and at least two additional systemic therapies in the metastatic setting, based on the TROPiCS-02 trial. Key components of the base-case economic evaluation provided in the submission are summarised in Table 2.

Table 2: Key components of the company-submitted base-case economic evaluation

Component	Description
Type of analysis	Cost-utility analysis
Population	Patients with HR-positive, HER2-negative uBC or mBC who have received ET and at least two additional systemic therapies in the metastatic setting
Outcomes	Total and incremental LYs gained; total and incremental QALYs gained; total and incremental direct medical costs; ICER
Perspective	Singapore healthcare system
Type of model	Partitioned survival model
Time horizon	7 years in the model base case, based on a median follow up of 10.2 months for PFS and 12.48 months for OS in the TROPiCS-02 trial (mean follow up was 14.4 months)
Health states	PF, PD, death
Cycle length	Weekly
Extrapolation methods used to generate results	KM data for PFS, OS and ToT were extrapolated using jointly fitted standard parametric survival functions. The base case used the following distributions: • PFS = Log-normal (with direct use of KM until 14.4 months) • OS = Log-logistic (with direct use of KM until 14.4 months) • ToT = Exponential (with direct use of KM until 14.4 months)
Health-related quality of life	EQ-5D-5L based utilities from TROPiCS-02 cross-walked to EQ-5D-3L were used, with treatment-specific utilities in the PF health state. • PF health state: SG = 0.761, TPC = 0.738 • PD: SG/TPC = 0.711
Types of healthcare resources included	• Drug and drug administration • Disease management cost • Healthcare resource use • Subsequent treatment costs • AE management costs

Abbreviations: AE, adverse event; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; ICER, incremental cost-effectiveness ratio; KM, Kaplan-Meier, LY, life year; OS, overall survival; PD, progressed disease; PF, progression-free; PFS, progression-free survival; QALY, quality-adjusted life year; SG, sacituzumab govitecan; TPC, treatment of physician's choice; ToT, time on treatment; uBC or mBC: unresectable locally advanced or metastatic breast cancer

4.2. The base-case incremental cost-effectiveness ratio (ICER) in the submission was between SG$205,000 and SG$245,000 per quality-adjusted life year (QALY) gained. However, the Committee considered the ICER to be highly uncertain and likely underestimated, given the following:

- The submission used a vial size of 200 mg although the HSA product insert stated a vial size of 180 mg.

- The submission applied treatment-specific utility values to the progression-free (PF) health state by reasoning that a statistically significantly longer median time-to-deterioration in EORTC QLQ-C30 global health status and fatigue domain scores with sacituzumab govitecan vs TPC was observed. Given the issues with the HRQoL data (see para 3.4), the Committee considered it was more appropriate to apply treatment-independent utility values for the PF health state.

- The submission applied a 14.4-month cut-off time point at which the OS curves for both arms switched from the observed Kaplan-Meier (KM) curve to the extrapolated curve. The Committee noted that the KM estimates beyond 14.4 months still contained enough at-risk patients for a meaningful interpretation of the KM plot, and it was more appropriate to consider a later cut-off time point for OS before switching to the extrapolated curve.

4.3. The Committee considered the revised base case, which accounted for several uncertainties in the company's model. Key changes to the economic model included reducing the vial size for sacituzumab govitecan to 180 mg, applying treatment-independent utility values, and changing the cut-off time point at which the extrapolated curve was used for OS. These changes substantially increased the ICER to more than SG$365,000 per QALY gained.

4.4. The Committee noted that based on a one-way sensitivity analysis of the revised base case, the key model drivers were factors relating to the treatment cost of sacituzumab govitecan and utility values in the PF health state. When the model parameters were varied within their uncertainty ranges, the ICERs remained unfavourably high.

4.5. Overall, the Committee considered that sacituzumab govitecan did not represent a cost-effective use of healthcare resources for previously treated patients with HR-positive, HER2-negative uBC or mBC, at the price proposed by the company.

Estimated annual technology cost

5.1. Using an epidemiological approach, the submission estimated that the annual cost impact to the public healthcare system would be between SG$5 million and SG$10 million over the first five years of listing sacituzumab govitecan on the MOH List of Subsidised Drugs for patients with previously treated HR-positive, HER2-negative uBC or mBC.

5.2. The Committee considered that the submission estimates and price-volume agreement (PVA) caps were high, due to an overestimation of eligible patients, omission of relative dose intensity and dose delays. Based on the revised budget impact model, the annual cost impact to the public healthcare system was estimated to be between SG$1 million and SG$3 million in the first year of listing.

Recommendations

6.1. Based on the evidence submitted, the Committee recommended not listing sacituzumab govitecan on the MOH List of Subsidised Drugs for treating patients with HR-positive, HER2-negative uBC or mBC who have received ET and at least two additional systemic therapies in the metastatic setting. The decision was based on the unfavourable cost effectiveness of sacituzumab govitecan compared with TPC, and the unacceptable PVA proposed by the company.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Approved clinical indication	Subsidy class	MediShield Life claim limit per month (implementation date)
Sacituzumab govitecan 180 mg powder for solution for infusion	Treatment of patients with unresectable locally advanced or metastatic HR-positive, HER2-negative breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.	Not recommended for subsidy	$1,800 (1 Nov 2025)

VERSION HISTORY

Guidance on sacituzumab govitecan for unresectable locally advanced or metastatic HR-positive, HER2-negative breast 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 17 Feb 2025

2. **Guidance updated to include sacituzumab govitecan on the Cancer Drug List**

   Date of Publication 16 Sep 2025

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 www.ace-hta.gov.sg/about

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