Technology Guidance

Tislelizumab

for treating locally advanced or metastatic non-squamous non-small-cell lung cancer without EGFR or ALK genomic tumour aberrations

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

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

- ✓ Tislelizumab 100 mg/10 mL concentrate for solution for infusion, in combination with platinum-doublet chemotherapy, for untreated locally advanced or metastatic non-squamous non-small-cell lung cancer (NSCLC), in patients whose tumours have programmed death-ligand 1 (PD-L1) expression on ≥50% of tumour cells, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase genomic tumour aberrations. Patients with locally advanced non-squamous NSCLC must not be candidates for surgical resection or platinum-based chemoradiation.

Funding status

Tislelizumab 100 mg/10 mL concentrate for solution for infusion is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication from 1 September 2025.

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

Published: 1 August 2025

Company-led submission

1.1. At the June 2025 meeting, the MOH Drug Advisory Committee ("the Committee") considered the technology evaluation of tislelizumab, in combination with platinum-doublet chemotherapy (TIS+CHEMO), for untreated locally advanced or metastatic non-squamous non-small-cell lung cancer (NSCLC), in patients whose tumours have programmed death-ligand 1 (PD-L1) expression on ≥50% of tumour cells, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumour aberrations. 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 tislelizumab.

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. Each year, approximately 300 patients in Singapore are diagnosed with locally advanced or metastatic non-squamous NSCLC, with no EGFR- or ALK-positive mutations. Around one-third of them have PD-L1 expression on 50% of their tumour cells.

2.2. The Committee noted that several programmed death-1 (PD-1) or PD-L1 [PD-(L)1] checkpoint inhibitors, in combination with chemotherapy, are already subsidised for first-line treatment of advanced non-squamous NSCLC, including atezolizumab in combination with bevacizumab and chemotherapy (ATEZO+BEV+CHEMO), and atezolizumab or pembrolizumab in combination with chemotherapy (ATEZO+CHEMO or PEM+CHEMO). Nivolumab in combination with ipilimumab and chemotherapy is listed on the Cancer Drug List without subsidy and is not routinely used due to higher costs and associated toxicities.

2.3. The Committee considered that funding TIS+CHEMO, another PD-(L)1 checkpoint inhibitor combination therapy, would be reasonable if it provides a more affordable treatment option with comparable health benefits.

2.4. The Committee considered 13 testimonials from local patients and carers about their lived experiences with NSCLC and the different treatments. The Committee acknowledged that NSCLC had a significant negative impact on patients' emotional health from the uncertainty regarding their prognosis and the symptoms they experienced impacting their ability to work, socialise, and carry out many daily activities. The Committee heard that none of the respondents were familiar with tislelizumab, but most would be willing to accept the side effects of a new treatment if it effectively reduced disease progression, was affordable, prolonged their lifespan, stopped the cancer from worsening, and had manageable side effects.

Clinical effectiveness and safety

3.1. The company requested a listing for patients with PD-L1 expression on ≥50% tumour cells, which aligned with the approved HSA indication. The Committee noted that there was no direct clinical trial evidence comparing TIS+CHEMO with the comparator PD-(L)1 checkpoint inhibitor combination therapies. The submission was based on a phase III, open-label randomised controlled trial comparing TIS+CHEMO with chemotherapy (RATIONALE-304), and indirect treatment comparisons (ITCs) of TIS+CHEMO versus ATEZO+BEV+CHEMO (IMpower150), ATEZO+CHEMO (IMpower130, IMpower150) and PEM+CHEMO (KEYNOTE-189, KEYNOTE-021) in patients with PD-L1 expression ≥50%.

3.2. The Committee heard that in the RATIONALE-304 trial, TIS+CHEMO demonstrated clinically meaningful improvements in progression-free survival (PFS) and overall survival (OS) compared to chemotherapy in the PD-L1 expression ≥50% population, at the median follow-up of 45.0 months (April 2023 data cut-off).

3.3. The Committee noted that results from the ITCs showed favourable hazard ratios (HRs) for TIS+CHEMO over ATEZO+BEV+CHEMO, ATEZO+CHEMO and PEM+CHEMO. However, TIS+CHEMO's treatment effect may have been overestimated due to poor performance of the chemotherapy arm in RATIONALE-304, underpowered PD-L1 ≥50% subgroups and transitivity issues across trials. Overall, based on the network meta-analysis fixed-effects model and Bucher ITCs, OS HRs met the non-inferiority margin, supporting non-inferiority of TIS+CHEMO versus each comparator PD-(L)1 checkpoint inhibitor combination therapy.

3.4. In terms of safety, the Committee heard the ITCs were limited by differences across trials in treatment duration. The Committee noted that the adverse event profile of TIS+CHEMO was generally consistent with the known safety profile of PD-(L)1 checkpoint inhibitor combination therapies.

3.5. Based on the available evidence, the Committee considered that the submission's claim of non-inferior effectiveness and safety for TIS+CHEMO versus comparator PD-(L)1 checkpoint inhibitor combination therapies was reasonable. This was in line with the New Zealand Pharmacology and Therapeutics Advisory Committee's conclusion that there was a class effect across PD-(L)1 checkpoint inhibitor combination therapies for the first-line treatment of advanced NSCLC.

Cost effectiveness

4.1. The submission presented a cost-minimisation analysis that compared TIS+CHEMO with ATEZO+BEV+CHEMO, ATEZO+CHEMO and PEM+CHEMO. The base-case results indicated that over a two-year time horizon, TIS+CHEMO was cost-saving compared to each PD-(L)1 checkpoint inhibitor combination therapy.

4.2. The Committee agreed that the cost savings were likely overestimated, due to overestimation of comparator drug costs, inappropriate assumptions of treatment durations and relative dose intensities, and inclusion of adverse event management costs. The Committee noted that TIS+CHEMO remained cost-saving in the revised base case and across scenario analyses, but with reduced estimates.

4.3. Overall, the Committee considered tislelizumab to be acceptable use of healthcare resources in local setting.

Estimated annual technology cost

5.1. Using an epidemiological approach, the submission estimated that the annual cost impact to the public healthcare system would increase from less than SG$1 million in the first year, to between SG$1 million and SG$3 million in the fifth year following listing of TIS+CHEMO on the MOH List of Subsidised Drugs for untreated locally advanced or metastatic non-squamous NSCLC, in patients whose tumours have PD-L1 expression on ≥50% tumour cells with no EGFR or ALK genomic tumour aberrations.

5.2. The Committee considered that the submission's estimates were overestimated, due to the inclusion of patients who switched to TIS+CHEMO after starting a comparator PD-(L)1 checkpoint inhibitor combination therapy, optimistic uptake rates and a substantially longer treatment duration for TIS+CHEMO compared to RATIONALE-304. Based on the revised budget impact model, the annual cost impact to the public healthcare system was estimated to be less than SG$1 million in each of the first five years of listing TIS+CHEMO. The company agreed with the revised estimates.

5.3. Overall, the Committee acknowledged that the company's proposal was adequate to manage the uncertainty of the overall budget impact.

Recommendations

6.1. The Committee recommended tislelizumab 100 mg/10 mL concentrate for solution for infusion be listed on the Medication Assistance Fund, for use in combination with platinum-doublet chemotherapy for untreated non-squamous locally advanced or metastatic NSCLC, in patients whose tumours have PD-L1 expression on ≥50% of tumour cells, with no EGFR or ALK genomic tumour aberrations. The decision was based on acceptable clinical effectiveness and safety versus comparator PD-(L)1 checkpoint inhibitor combination therapies, an acceptable pricing proposal by the company, and potential cost savings to the healthcare system.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Approved clinical indication	Subsidy class (implementation date)	MediShield Life claim limit per month (implementation date)
Tislelizumab 100 mg/10 mL concentrate for solution for infusion	Tislelizumab in combination with platinum-doublet chemotherapy, for untreated locally advanced or metastatic non-squamous non-small-cell lung cancer (NSCLC), in patients whose tumours have PD-L1 expression on ≥50% of tumour cells, with no EGFR or ALK genomic tumour aberrations. Patients with locally advanced non-squamous NSCLC must not be candidates for surgical resection or platinum-based chemoradiation.	MAF (1 Sep 2025)	$1,800 (1 Sep 2025)

Abbreviation: MAF, Medication Assistance Fund.

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

© Agency for Care Effectiveness, Ministry of Health, Republic of Singapore
All rights reserved. Reproduction of this publication in whole or in part in any material form is prohibited without the prior written permission of the copyright holder. Requests to reproduce any part of this publication should be addressed to:

Agency for Care Effectiveness, Ministry of Health, Singapore
Email: ACE_HTA@moh.gov.sg

In citation, please credit "Agency for Care Effectiveness, Ministry of Health, Singapore" when you extract and use the information or data from the publication.