Technology Guidance

Trastuzumab deruxtecan

for treating HER2-positive advanced gastric cancer after two or more therapies

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended trastuzumab deruxtecan (T-DXd) for inclusion on the MOH List of Subsidised Drugs for treating human epidermal growth factor receptor 2 (HER2)-positive locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma in patients who have received two or more prior therapies. The decision was based on the unfavourable cost-effectiveness of T-DXd at the price proposed by the company compared with chemotherapy.

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

Updated: 1 September 2023

Factors considered to inform the recommendations for funding

Technology evaluation

1.1. The MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of trastuzumab deruxtecan (T-DXd) for treating human epidermal growth factor receptor 2 (HER2)-positive locally advanced or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma in patients who have received two or more prior therapies. The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from public healthcare institutions. Clinical and economic evidence for T-DXd was considered in line with its registered indication. Additional expert opinion was obtained from the MOH Cancer Drug Subcommittee (CDS) who assisted ACE to ascertain the clinical value of T-DXd 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 funding considerations.

Clinical need

2.1. The Committee noted that approximately 540 patients are diagnosed with gastric or GEJ cancer each year in Singapore, and adenocarcinomas represent over 80% of these cancers. About 10 to 20% of advanced gastric or GEJ cancers have overexpression of HER2.

2.2. The Committee acknowledged that at the time of evaluation, T-DXd was the only HER2-targeted drug approved by the Health Sciences Authority (HSA) for third- or subsequent-line treatment of patients with HER2-positive advanced gastric or GEJ adenocarcinoma. Local clinicians confirmed that prior to T-DXd being approved, patients usually received chemotherapy (irinotecan or a taxane), nivolumab or trifluridine/tipiracil as a third- or subsequent-line treatment for advanced gastric or GEJ adenocarcinoma, irrespective of HER2 status. In view of the limited targeted treatment options available, the Committee agreed that there was a clinical need to consider T-DXd for funding to improve treatment affordability and ensure appropriate patient care.

2.3. The Committee heard that T-DXd had also been investigated as a second-line treatment for HER2-positive advanced gastric cancer (DESTINY-Gastric04), hence, there may be changes to its place in therapy overtime. However, given that this indication has not been approved by HSA yet, the Committee acknowledged that it was outside the scope of the current evaluation.

Clinical effectiveness and safety

3.1. The Committee reviewed the available clinical evidence from a phase II randomised controlled trial (DESTINY-Gastric01) that compared T-DXd with physician's choice of chemotherapy (irinotecan or paclitaxel) in 187 patients with HER2-positive locally advanced or metastatic gastric or GEJ adenocarcinoma who had received two or more prior therapies.

3.2. At a median follow-up of 18.5 months, T-DXd improved overall survival (OS) by 3.6 months (hazard ratio [HR] 0.60, 95% CI 0.42 to 0.86) and progression free survival (PFS) by 2.1 months (HR 0.47, 95% CI 0.31 to 0.71) compared with chemotherapy.

3.3. In terms of safety, T-DXd was associated with more grade ≥3 treatment-emergent adverse events (TEAEs) compared with chemotherapy (85.6% vs 56.5%), The most commonly reported TEAEs were decreased neutrophil count, anaemia, and decreased white blood cell count. Drug-related interstitial lung disease occurred in 16 patients (12.8%) in the T-DXd group compared with no cases in the chemotherapy group.

3.4. Overall, the Committee considered that, as a third- or subsequent-line treatment for HER2-positive advanced gastric or GEJ adenocarcinoma, T-DXd provided superior efficacy but had an inferior safety profile compared with chemotherapy.

Cost effectiveness

4.1. The Committee reviewed a cost-effectiveness analysis conducted by ACE that compared T-DXd with chemotherapy, as a third- or subsequent-line treatment in patients with HER2-positive advanced gastric cancer. At the price proposed by the company, T-DXd had a high base-case incremental cost-effectiveness ratio (ICER) of more than SG$365,000 per quality-adjusted life year (QALY) gained. Results from sensitivity and scenario analyses showed that the ICERs remained above SG$325,000 per QALY gained when model parameters were varied across the range of possible values.

4.2. Therefore, at the price proposed by the company, the Committee agreed that T-DXd did not represent a cost-effective treatment compared with chemotherapy, for HER2-positive advanced gastric cancer after two or more therapies.

Estimated annual technology cost

5.1. The Committee noted that the annual cost impact to the public healthcare system was estimated to be less than SG$1 million in the first year of including T-DXd on the MOH List of Subsidised Drugs as a third- or subsequent-line treatment for HER2-positive advanced gastric or GEJ adenocarcinoma.

Recommendations

6.1. Based on available evidence, the Committee recommended not listing T-DXd on the MOH List of Subsidised Drugs for treating HER2-positive locally advanced or metastatic gastric or GEJ adenocarcinoma in patients who have received two or more prior therapies. The decision was based on the unfavourable cost-effectiveness of T-DXd at the price proposed by the company compared with chemotherapy.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Clinical indication	Subsidy class	MediShield Life claim limit per month (implementation date)
Trastuzumab deruxtecan 100 mg powder for concentrate for solution for infusion	Treatment of HER2-positive locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma in patients who have received two or more prior regimens, including a trastuzumab-based regimen.	Not recommended for subsidy	$2400 (1 Nov 2023)

VERSION HISTORY

Guidance on trastuzumab deruxtecan for treating HER2-positive advanced gastric cancer after two or more therapies

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 Jul 2023

2. **Guidance updated to include trastuzumab deruxtecan on the Cancer Drug List**

Date of Publication	1 Sep 2023

Agency for Care Effectiveness - ACE Agency for Care Effectiveness (ACE)