

Technology Guidance

Brexucabtagene autoleucel

for relapsed or refractory B-cell precursor acute lymphoblastic leukaemia

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended brexucabtagene autoleucel for inclusion on the MOH Cell, Tissue and Gene Therapy Product (CTGTP) List for treating adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia. The decision was based on the unfavourable cost effectiveness compared with blinatumomab, and the unacceptable price-volume agreement proposed by the company.

Technology Evaluation

- 1.1. At the July 2026 meeting, the MOH Drug Advisory Committee (“the Committee”) considered the technology evaluation of brexucabtagene autoleucel (“brexucabtagene”) for relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (r/r B-ALL). The evaluation considered the company’s evidence submission by Gilead Sciences Singapore for brexucabtagene (Tecartus), and a review conducted by one of ACE’s evidence review centres.
- 1.2. Expert opinion from clinicians at public healthcare institutions and the MOH Cancer Drug Subcommittee helped ACE ascertain the clinical value of brexucabtagene. Local patient and voluntary organisations were also invited to provide their lived experiences to inform the evaluation, however, no submissions were received.
- 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. B-ALL is characterised by the abnormal proliferation of immature B-cell lymphoblasts in the bone marrow and blood. Brexucabtagene is a chimeric antigen receptor T-cell (CAR-T) therapy that targets CD19-expressing tumour cells and is approved for adult patients aged 18 years and above with r/r B-ALL. It may be used with curative intent or as a bridge to allogeneic stem cell transplantation. Approximately 17 adult patients would be eligible for treatment with brexucabtagene each year in Singapore.
- 2.2. In local practice, adult patients with r/r B-ALL typically receive blinatumomab, inotuzumab ozogamicin (InO), or salvage chemotherapy. Outcomes with current treatments remain variable, with some patients experiencing disease progression or further relapse. The Committee agreed that blinatumomab, the most commonly used treatment, was the main comparator.

- 2.3. The Committee noted that tisagenlecleucel, another CAR-T therapy, is currently included on the MOH Cell, Tissue and Gene Therapy Product (CTGTP) List for younger patients aged 2 to 25 years with r/r B-ALL. The Committee therefore acknowledged the potential value of an additional treatment option for adult patients with r/r B-ALL and considered that funding of brexucabtagene may improve access to care.

Clinical effectiveness and safety

- 3.1. The Committee reviewed the clinical evidence for brexucabtagene from a Phase I/II, open-label, single-arm trial (ZUMA-3) in adult patients with r/r B-ALL. At a median follow-up of 3.5 years, the primary endpoint of overall complete remission (OCR) by central assessment was achieved in 73% of patients (95% confidence interval [CI] 62% to 82%) in the modified intention-to-treat (mITT) population. At follow-up of 5 years, the median overall survival (OS) was 25.6 months (95% CI 16.2 to 60.4 months).
- 3.2. In the absence of direct comparative evidence, the submission presented a matching-adjusted indirect comparison (MAIC) of brexucabtagene (ZUMA-3) versus blinatumomab (TOWER), InO and salvage chemotherapy (both from INO-VATE), and an indirect treatment comparison (ITC) of brexucabtagene versus standard of care from a retrospective cohort study (SCHOLAR-3). The Committee considered that both analyses were associated with significant methodological limitations, including substantial reductions in effective sample size due to limited population overlap across studies, potential risks of bias and transitivity concerns.
- 3.3. The Committee noted that, across all MAIC comparisons, brexucabtagene demonstrated numerically longer median OS and event-free survival (EFS) than comparator treatments. However, the differences were not consistently statistically significant. For the ITC, brexucabtagene was associated with a higher likelihood of achieving OCR compared with standard of care (odds ratio 10.5, 95% CI 2.3 to 48.7), but these findings were limited by the small sample size and the inclusion of only a limited proportion of patients from ZUMA-3.
- 3.4. In terms of safety, the submission did not present a comparative analysis of safety outcomes between brexucabtagene and comparator treatments. The Committee noted that adverse events of special interest, including cytokine release syndrome, neurologic events, and cytopenias, were consistent with the known safety profile of other CAR-T therapies.

- 3.5. The submission described brexucabtagene as superior in effectiveness to comparator treatments for adult patients with r/r B-ALL. Based on the available evidence, the Committee considered the submission's claim reasonable, but the magnitude of clinical benefit remained uncertain. The Committee considered the relative safety of brexucabtagene versus comparator treatments was uncertain, although a different safety profile is reasonable given the distinct treatment modalities.

Cost effectiveness

- 4.1. The Committee noted that the submission included cost-utility analyses (CUAs) comparing brexucabtagene with (1) blinatumomab; (2) InO; and (3) salvage chemotherapy.
- 4.2. As blinatumomab was the main comparator for the evaluation, the Committee considered the results of the submission's CUA that compared brexucabtagene with blinatumomab for adult patients with r/r B-ALL, based on the ZUMA-3 study. 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	Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia
Outcomes	Total and incremental direct medical costs; total and incremental LY gained; total and incremental QALYs; ICER
Perspective	Singapore healthcare system
Type of model	Decision tree followed by partitioned survival model
Time horizon	Lifetime (37 years) in the base case
Health states	EFS; PD; death
Cycle length	1 week
Extrapolation methods used to generate results	EFS and OS curves were informed by a MAIC using the ZUMA-3 trial for the brexucabtagene arm and the TOWER trial for the blinatumomab arm. The MAIC-adjusted KM curves were used for the brexucabtagene arm. The curves were fitted using standard parametric distributions and flexible spline models in the base case before the application of a cure point at 5 years. For brexucabtagene OS, as the KM curve was available till year 5, no modelled curve was fitted and the KM curve was used until the cure point. • EFS for brexucabtagene = gamma distribution • EFS for blinatumomab = 1-knot normal • OS for brexucabtagene = KM curve • OS for blinatumomab = 1-knot normal A cure point was assumed at year 5, after which, a SMR of 1.09 derived from a study of newly diagnosed large B-cell lymphoma was applied on top of general population mortality rate.

Component	Description
Health-related quality of life	Utilities for the EFS and PD health state were based on EQ-5D-5L data from ZUMA-3 mITT population and mapped to EQ-5D-3L using UK weights (van Hout et al., 2012). • Pre-infusion: 0.78 • EFS: 0.82 • PD: 0.75 Utilities for the cured health state were assumed to follow general population utilities
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; EFS, event-free survival; ICER, incremental cost-effectiveness ratio; KM, Kaplan-Meier; LY, life year; mITT, modified intention-to-treat; OS, overall survival; PD, progressed disease; QALY, quality-adjusted life year; SMR, standardised mortality ratio.

4.3. The base-case incremental cost-effectiveness ratio (ICER) in the submission was between SG\$15,000 and SG\$45,000 per quality-adjusted life year (QALY) gained for brexucabtagene compared with blinatumomab. However, the Committee considered the ICER to be highly uncertain and likely underestimated, in view of the following:

- The modelled comparative treatment effectiveness was based on the unanchored MAIC in para 3.2, which introduces substantial uncertainty into the model.
- The cure assumptions applied at the five-year mark were overly optimistic.
 - Patients who experienced disease progression could still transition to the cured health state and accrue a lifetime of benefits.
 - The standardised mortality ratio applied, based on a study of patients with newly diagnosed large B-cell lymphoma, likely underestimated mortality for the relapsed or refractory disease population.
 - The submission assumed the QALYs of cured patients would match the general population despite the cumulative toxicity of prior therapies and disease burden.
- The lifetime horizon compounded the uncertainties within the model, including those related to the unanchored MAIC and cure assumptions.
- The submission applied different drug costs and healthcare resource utilisation inputs arising from alternative data sources and assumptions, which favoured brexucabtagene.

- The results lacked face validity. Incremental QALYs for brexucabtagene were primarily accrued in the progressed disease health state, despite the poor prognosis of this population and limited evidence that benefits would be maintained following disease relapse relative to comparator treatments.
- 4.4. The Committee considered the respecified base case, which addressed the uncertainties in the company's model. Key changes included revisions to cure assumptions, time horizon, and drug and administration costs. These changes increased the ICER to between SG\$165,000 and SG\$205,000 per QALY gained compared with blinatumomab. The Committee noted that the respecified base case could not address the uncertainty arising from the use of an unanchored MAIC.
 - 4.5. The Committee noted that based on one-way sensitivity analysis of the respecified base case, the key model drivers were time horizon and the cost of brexucabtagene. When these parameters were varied within their uncertainty ranges, the ICERs remained high and unfavourable.
 - 4.6. The Committee also noted that the Australian Medical Services Advisory Committee has recommended funding of brexucabtagene for r/r B-ALL, with pricing consistent with other publicly funded CAR-T therapies.
 - 4.7. Overall, the Committee considered that brexucabtagene did not represent a cost-effective use of healthcare resources for adult patients with r/r B-ALL 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\$1 million and SG\$3 million over the first five years of listing brexucabtagene on the MOH CTGTP List for treating adult patients with r/r B-ALL.
- 5.2. The Committee considered that the submission's financial estimates were high and uncertain as the submission did not account for patients who undergo leukapheresis but do not ultimately receive brexucabtagene infusion. Based on the respecified budget impact model, the annual cost to the public healthcare system was estimated to be between SG\$1 million and SG\$3 million over the first five years of listing. The Committee also considered that the submission's price-volume agreement (PVA) caps were unacceptably high and inadequate to provide budget certainty.

Recommendations

- 6.1. Based on available evidence, the Committee recommended not listing brexucabtagene on the MOH CTGTP List for treating adult patients with r/r B-ALL. The decision was based on the unfavourable cost effectiveness compared with blinatumomab, and the unacceptable PVA proposed by the company.

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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 guidelines 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.

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