Technology Guidance

Talquetamab

for relapsed or refractory multiple myeloma

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended talquetamab for inclusion on the MOH List of Subsidised Drugs for treating relapsed or refractory multiple myeloma in patients who have received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-cluster of differentiation 38 antibody, and have demonstrated disease progression on the last therapy. The decision was based on the uncertainty surrounding the extent of talquetamab's comparative effectiveness, unacceptable cost effectiveness compared with physician's choice of treatment, and the unacceptable price-volume agreement proposed by the company.

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

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Technology Evaluation

1.1. At the November 2025 meeting, the MOH Drug Advisory Committee ("the Committee") considered the technology evaluation of talquetamab for treating relapsed or refractory multiple myeloma (RRMM) in patients who have received at least three prior therapies, including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD), and an anti-cluster of differentiation 38 (CD38) antibody, and have demonstrated disease progression on the last therapy. The evaluation considered company's evidence submission by Johnson & Johnson for talquetamab (Talvey), and a review conducted by one of ACE's evidence review centres.

1.2. Expert opinion from clinicians at public healthcare institutions, the MOH Cancer Drug Subcommittee, and patient experts from local patient and voluntary organisations helped ACE ascertain the clinical value of talquetamab.

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. In Singapore, there are approximately 120 new patients diagnosed with multiple myeloma each year. It is estimated that 16 of these patients will require treatment at the fourth-line setting or beyond (4L+). In local practice, there is no standard treatment pathway for RRMM, and the choice of treatment is highly individualised, with patients typically cycling through various combination regimens across different treatment lines. Talquetamab monotherapy, a bispecific antibody, is expected to replace combination regimens including a PI, an IMiD, and/or an anti-CD38 antibody in 4L+ setting.

2.2. The submission appropriately nominated physician's choice of combination therapy as the comparator for the evaluation, which includes a basket of five regimens currently listed on the Cancer Drug List and are available for use in 4L+ RRMM: pomalidomide in combination with cyclophosphamide and dexamethasone (PCd); pomalidomide in combination with bortezomib and dexamethasone (PVd); isatuximab in combination with pomalidomide and dexamethasone (IsaPd); carfilzomib in combination with cyclophosphamide and dexamethasone (KCd); and carfilzomib in combination with dexamethasone (Kd).

2.3. The Committee considered 29 testimonials from local patients and carers about their lived experiences with multiple myeloma and the treatments they have received. The Committee acknowledged that multiple myeloma had a significant negative impact on patients' physical and mental well-being, with bone pain, muscle aches, fatigue, frequent infections, and fear of bone fractures and disease relapse, affecting their ability to work, socialise and maintain physical activities.

2.4. The Committee noted that patients were receiving different treatment regimens, and felt their treatments worked well with manageable side effects. Five patients had heard of talquetamab from their clinicians or other sources but had a limited understanding of its effectiveness or side effect profile. Most patients would be willing to accept the side effects of a new treatment if it can stop the cancer from worsening. However, they were unwilling to pay more for a new treatment without survival benefits. Overall, they considered that any new treatment for multiple myeloma should stop the cancer from worsening, be more affordable, improve quality of life, extend survival, and have manageable side effects.

Clinical effectiveness and safety

3.1. The Committee reviewed the clinical evidence for talquetamab from the ongoing Phase 1/2, open-label, single-arm trial (MonumenTAL-1). They noted that the company's requested listing for talquetamab was consistent with the approved HSA indication but broader than the evidence presented in the submission. Under the requested listing, treatment eligibility for talquetamab would be based on patients being triple-class exposed (TCE) to a PI, an IMiD and an anti-CD38 antibody. However, most participants in the MonumenTAL-1 trial received talquetamab after at least three prior lines of therapy, in addition to being TCE, and the comparative effectiveness of talquetamab's use in earlier lines was not evaluated in the submission.

3.2. The available evidence reported overall response rates (ORR) of 67% to 74% at a median follow-up exceeding 30 months, with median overall survival (OS) ranging from 28 to 34 months. However, as the evidence is derived from a single-arm trial, the interpretation of these endpoints remains limited.

3.3. In the absence of direct comparative evidence, the submission presented an unanchored indirect treatment comparison (ITC) between talquetamab (MonumenTAL-1) and real-world physician's treatment choice (RWPC) from two prospective observational studies (LocoMMotion and MoMMent), which served as a proxy for the nominated comparators. The comparative analysis only included participants who were TCE and had received at least three prior lines of therapy.

3.4. The results of the ITC favoured talquetamab for ORR, OS and progression-free survival (PFS) (Table 1). However, the Committee considered that there was substantial uncertainty associated with these findings. This was due to the inadequate adjustment for known prognostic variables and the inherent limitations of unanchored comparisons, which cannot control for unmeasured or unknown confounders. Furthermore, the generalisability of the RWPC arm to local clinical practice was limited, as IsaPd was underrepresented and some treatments included in the RWPC arm are not registered with HSA.

Table 11: Adjusted ITC results for talquetamab (MonumenTAL-1) and RWPC (LocoMMotion, MoMMent)

Outcomes	Talquetamab 0.4 mg/kg Q1W (n=143) versus RWPC arm (n=175)	Talquetamab 0.8 mg/kg Q2W (n=154) versus RWPC arm (n=175)
ORR		
RR (95% CI)	2.48 (1.78, 3.46), p<0.0001	2.38 (1.71, 3.33), p<0.0001
PFS		
HR (95% CI)	0.54 (0.41, 0.72), p<0.0001	0.48 (0.36, 0.64), p<0.0001
OS		
HR (95% CI)	0.38 (0.27, 0.53), p<0.0001	0.34 (0.23, 0.51), p<0.0001

Abbreviations: CI, confidence interval; HR, hazard ratio; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Q1W, once weekly; Q2W, once every two weeks; RR, rate ratio; RWPC, real-world physician's treatment choice.

3.5. In terms of safety, the Committee noted that the submission did not include a comparison of the safety outcomes between talquetamab and RWPC. Interpretation of safety outcomes was limited to the MonumenTAL-1 trial, in which the overall rates of cytokine-release syndrome and serious treatment-emergent adverse events were reported to be high.

3.6. The submission described talquetamab as superior in terms of effectiveness compared to RWPC in patients with TCE RRMM. The Committee considered the submission's claim was not adequately supported by the available evidence, as the extent of comparative effectiveness remains highly uncertain given the limitations of the unanchored ITC, including the high risk of bias and residual confounding. In terms of safety, the Committee considered that the high rates of serious treatment-emergent adverse events and cytokine-release syndrome observed in MonumenTAL-1 suggest that talquetamab may have an inferior safety profile compared to other treatments.

Cost effectiveness

4.1. The Committee considered the results of the submission's cost-utility analysis that compared talquetamab with RWPC in patients with TCE RRMM, based on the unanchored ITC. 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 relapsed or refractory multiple myeloma, who have received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy
Outcomes	Total and incremental direct medical costs; total and incremental LY gained; total and incremental QALYs; ICER
Perspective	Singapore healthcare system
Type of model	Partitioned survival model
Time horizon	5 years in the model base case, based on a median follow-up of 30.3 to 38.2 months in the MonumenTAL-1 trial
Health states	Pre-progression; post-progression; death
Cycle length	1 week
Extrapolation methods used to generate results	Talquetamab OS and PFS were based on the weighted KM data from the 0.4 mg/kg Q1W cohort and the 0.8 mg/kg Q2W cohort in MonumenTAL-1. RWPC OS and PFS were based on ATT-adjusted KM data from LocoMMotion/MoMMent. The parametric models used in the model base case were as follows: • Talquetamab ○ OS: lognormal ○ PFS: lognormal • RWPC ○ OS: loglogistic ○ PFS: loglogistic
Health-related quality of life	• Health state utilities were derived from the EQ-5D-5L data reported in the MonumenTAL-1 trial, using UK-specific weights, and mapped to EQ-5D-3L (pre-progression = 0.705; post-progression = 0.631).
Types of healthcare resources included	• Drug and drug administration • Disease management cost • Healthcare resource use • Subsequent treatment costs • AE management costs

Abbreviations: ATT, average treatment effect on the treated; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; KM, Kaplan-Meier; LYs, life years; OS, overall survival; PFS, progression-free survival; Q1W, once weekly; Q2W, once every two weeks; QALYs, quality-adjusted life years; RWPC, real-world physician's treatment choice.

4.2. The base-case incremental cost-effectiveness ratio (ICER) in the submission was between SG$325,000 and SG$365,000 per quality-adjusted life year (QALY) gained. However, the Committee considered the ICER to be highly uncertain and likely underestimated, in view of the following:

- The submitted model was largely limited by the uncertainty in the comparative effectiveness between talquetamab and RWPC, which was informed by the unanchored ITC.

- The parametric functions selected to model OS for the talquetamab (lognormal) and RWPC (loglogistic) arms did not fit the trial data well and resulted in overly optimistic long-term OS for the talquetamab arm.

- The patient-reported health state utilities used in the model were subject to high risk of bias due to the open-label, non-comparative design of the trial, and lacked face validity across cohorts.

- The submission applied treatment costs based on the two-weekly dosing of talquetamab, which was inconsistent with the clinical data used in the model that incorporated both the two-weekly and the once-weekly dosing regimens. The submission also applied inaccurate drug costs and administration charges for talquetamab and the comparators.

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 choice of extrapolations for OS and PFS, applying alternative health state utilities and updating cost inputs. These changes substantially increased the ICER to more than SG$365,000 per QALY gained. However, the uncertainty in the cost-effectiveness results cannot be fully addressed in view of the limitations with the clinical evidence.

4.4. The Committee noted that based on one-way sensitivity analysis of the revised economic evaluation, the key model drivers were body weight, time horizon, and utility values for the progression-free and progressed disease health states. When the model parameters were varied within their uncertainty ranges, the ICERs remained unfavourably high.

4.5. Overall, the Committee considered that talquetamab did not represent a cost-effective use of healthcare resources for treating patients with TCE RRMM 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 increase from between SG$5 million and SG$10 million in the first year, to more than SG$10 million in the fifth year of listing talquetamab on the MOH List of Subsidised Drugs for treating TCE RRMM.

5.2. The Committee considered that the submission's financial estimates were high due to the inclusion of a broader patient population (TCE RRMM) as compared to the submitted evidence (TCE RRMM at 4L+ setting), double counting of patients in the calculation, and overestimation of the treatment duration. 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 from the first year to the fifth year of listing. The Committee also considered that the submission's price-volume agreement caps were unacceptably high and inadequate to provide budget certainty.

Recommendations

6.1. Based on available evidence, the Committee recommended not listing talquetamab on the MOH List of Subsidised Drugs for treating RRMM in patients who have received at least three prior therapies, including a PI, an IMiD, and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy. The decision was based on the uncertainty surrounding the extent of talquetamab's comparative effectiveness, unacceptable cost effectiveness compared with physician's choice of treatment, and the unacceptable price-volume agreement proposed by the company.

ANNEX

Recommendations by the MOH Drug Advisory Committee

Drug preparation	Company-proposed clinical indication	Subsidy class	MediShield Life claim limit per month
Talquetamab 3 mg/1.5 mL and 40 mg/1.0 mL solution for injection	Talquetamab as monotherapy for patients with relapsed or refractory multiple myeloma who have received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy.	Not recommended for subsidy	Not recommended for MediShield Life claims