

Technology Guidance

Clesrovimab

for prevention of respiratory syncytial virus-associated lower respiratory tract disease in infants during their first RSV season

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended clesrovimab for inclusion on the MOH Subsidised Vaccine List (SVL) for prevention of respiratory syncytial virus (RSV)-associated lower respiratory tract disease in infants during their first RSV season. The decision was based on the unfavourable cost effectiveness of clesrovimab compared with no immunisation.

Technology Evaluation

- 1.1. At the July 2026 meeting, the MOH Drug Advisory Committee (“the Committee”) considered the technology evaluation of clesrovimab for the prevention of respiratory syncytial virus (RSV)-associated lower respiratory tract disease (LRTD) in infants during their first RSV season. The evaluation considered the evidence submission by MSD for clesrovimab (Enflonsia), and a review conducted by one of ACE’s evidence review centres. The use of clesrovimab for the prevention of RSV-associated LRTD in children during their second RSV season was not HSA-registered at the time of evaluation and hence outside the scope of this evaluation.
- 1.2. Expert opinion from clinicians at public healthcare institutions (PHIs), and the Expert Committee on Immunisation (ECI) helped ACE ascertain the clinical value of clesrovimab.
- 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 RSV is a common cause of respiratory illness in infants and young children in Singapore, with infants at high risk of severe disease particularly susceptible to poor outcomes such as hospitalisation and death. They include those born preterm or with chronic lung disease, congenital heart disease, neuromuscular disorders or who are immunocompromised.
- 2.2 The Committee had previously considered the clinical need for RSV immunisation at its April 2026 meeting during its review of nirsevimab, a long-acting monoclonal antibody (mAb) administered directly to infants to provide passive immunisation against RSV. The Committee also noted that an infant’s first RSV season refers to the first year of life, given the absence of a clearly defined RSV season in Singapore.

- 2.3 The Committee recalled the previously considered treatment context, including that RSV immunisation is not routine practice for the general infant population and no RSV immunisation products are included on the MOH Subsidised Vaccine List (SVL). The Committee noted that nirsevimab was not recommended for subsidy at the April 2026 meeting, while RSVpreF, a maternal vaccine administered to pregnant individuals to stimulate maternal production of antibodies that provides passive immunisation to infants via transplacental transfer, was being considered concurrently at the July 2026 meeting. For high-risk subgroups, palivizumab remains a short-acting mAb option for RSV prevention. These considerations were taken into account in the Committee's July 2026 review of clesrovimab, another long-acting mAb for RSV prevention.

Clinical effectiveness and safety

Clesrovimab versus no immunisation

- 3.1. The Committee reviewed the clinical evidence in the company submission from a randomised controlled trial (RCT; CLEVER), which compared clesrovimab to no immunisation in healthy infants born at ≥ 29 weeks' gestational age.
- 3.2. The RCT showed that clesrovimab led to statistically significant relative risk reductions (RRRs) of 60.4% (95% confidence interval [CI] 44.1 to 71.9) for medically attended RSV lower respiratory tract infection (MA RSV-LRTI), and 84.2% (95% CI 66.6 to 92.6) for RSV hospitalisation, both at 150 days, compared with no immunisation. The absolute risk reductions corresponded with a number needed to immunise of 26 for MA RSV-LRTI and 50 for RSV hospitalisation at 150 days.
- 3.3. The Committee noted there was a lack of comparative RCT evidence between clesrovimab and no immunisation in high-risk infants. The submission claimed that clesrovimab's efficacy versus no immunisation in high-risk infants was comparable to that in healthy infants, based on similar pharmacokinetic exposure in the CLEVER and SMART (clesrovimab versus palivizumab in high-risk infants) RCTs. However, this was considered speculative. The Committee further noted the lack of comparative RCT evidence for the sequential use of clesrovimab following maternal vaccination.
- 3.4. Based on the available evidence, the Committee concluded that while the submission's claim of superior efficacy of clesrovimab compared to no immunisation in all infants was considered reasonable, the magnitude of efficacy in high-risk infants remained uncertain.
- 3.5. In terms of safety, the adverse event (AE) rates were largely similar across treatment arms. The Committee noted that injection-site AEs were the main difference between placebo in the CLEVER trial and no immunisation in clinical practice. The most frequently reported AEs with clesrovimab included irritability, upper respiratory tract infection and drowsiness.

Clesrovimab versus nirsevimab

- 3.6 In the absence of head-to-head trials, the Committee reviewed a matching adjusted indirect comparison (MAIC) presented in the submission, based on RCTs for nirsevimab (MELODY, nirsevimab Phase 2b) that compared nirsevimab with no immunisation in healthy infants born at ≥ 29 weeks' gestational age.
- 3.7 While the MAIC results for MA RSV-LRTI and RSV hospitalisation at 150 days were not statistically significantly different, with 95% CIs crossing the null, the Committee considered that the submission's claim of non-inferior efficacy for clesrovimab versus nirsevimab was not adequately supported. This was because the MAIC was derived from trials that were neither designed nor powered to demonstrate non-inferiority.
- 3.8 Furthermore, the MAIC drew on results from the more favourable post-hoc analyses from the CLEVER trial rather than the pre-specified analyses. While outcome definitions for the post-hoc analyses aligned more closely with the nirsevimab trials, the post-hoc selection of events may have introduced bias, alongside incomplete reporting of the MAIC methodology. The Committee also noted the absence of evidence for clesrovimab versus nirsevimab in high-risk infants.
- 3.9 The comparative safety of clesrovimab versus nirsevimab remained uncertain, as safety outcomes were not included in the submission's MAIC. Nevertheless, rates of treatment-related AEs in the CLEVER and nirsevimab trials were low in healthy infants.

Clesrovimab versus RSVpreF

- 3.10 In the absence of head-to-head trials, the Committee heard that the submission did not present any indirect comparisons for clesrovimab versus RSVpreF, citing poor exchangeability of the trials. Hence, the comparative efficacy and safety of clesrovimab versus RSVpreF remained uncertain.

Clesrovimab versus palivizumab

- 3.11 The Committee considered direct evidence from the SMART RCT that studied clesrovimab versus palivizumab in high-risk infants. While SMART showed numerically comparable event rates across efficacy outcomes for both treatment arms, the trial was not powered to demonstrate non-inferiority, and event rates were low.
- 3.12 Overall, the Committee concluded that the submission's claim of comparable efficacy and safety of clesrovimab versus palivizumab in high-risk infants was not adequately supported due to limitations with the SMART trial.

Cost effectiveness

- 4.1 The Committee considered the results of the submission's cost-utility analysis (CUA) that compared clesrovimab with no immunisation for the prevention of RSV in infants during their first season. Key components of the base-case economic evaluation provided in the submission are summarised in Table 1.

Table 1: Key components of the company-submitted base-case economic evaluation

Component	Description
Type of analysis	Cost-utility analysis
Population	Resident infant population in Singapore during their first RSV season (age 0-12 months) stratified into six mutually exclusive subgroups by gestational age at birth and high-risk conditions: • full-term (≥ 37 wGA, 91.01%), • late preterm (35-36 wGA, 4.08%), • moderately preterm (32-34 wGA, 3.36%), • very preterm (29-31 wGA, 0.65%), • extremely preterm (< 29 wGA, 0.39%), and • infants of any gestational age with CHD or CLD (with CHD 0.25% and CLD 0.26% of births reported).
Intervention	Clesrovimab administered at discharge
Outcomes	Total and incremental direct medical costs; total and incremental QALYs; ICER
Perspective	Singapore healthcare system
Type of model	Static decision tree model
Time horizon	1 year, based on outcomes reported at 6 months in the trials. Lifetime QALYs loss due to RSV-associated premature deaths.
Health events	RSV MA-LRTIs including outpatient visits, emergency department visits, hospitalisations, ICU admissions. RSV-associated deaths
Incidence of health events	• Per patient risk of primary care visit, ED visit, hospitalisation and ICU admission was stratified by the infant's age, in months, at the time of infection. • Per patient risk of hospitalisation, ICU admission was further stratified by infant subpopulation
Clinical effectiveness	• All infant population: ○ RRR for MA RSV-LRTI at 180 days post-hoc analysis requiring ≥ 2 indicators of LRTI/severity (CLEVER): 87.2%¹ ○ RRR for RSV hospitalisations at 180 days post-hoc analysis requiring ≥ 2 indicators of LRTI/severity (CLEVER): 87.2% Efficacy inputs were applied for the first 6 months, followed by efficacy waning linearly from the 7 th to the 10 th month.
Health-related quality of life	• Disutility for hospitalisation and ICU admission: 0.016974675 (Hutton et al., 2024) • Disutility for outpatient visit: 0.008487337 (Hutton et al., 2024) • Disutility for ED visit: 0.013415469 (Hutton et al., 2024) • Age-specific utility weights mapped from Singapore EQ-5D-5L adult norms and the Singapore Department of Statistics life table were used to derive the QALY loss due to RSV-associated premature death.
Types of healthcare resources included	• Drug cost • Disease management cost

Abbreviation: CHD, congenital heart disease; CLD, chronic lung disease; ED, emergency department; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; LRTI, lower respiratory tract infection; MA, medically attended; QALY, quality-adjusted life year; RRR, relative risk reduction; RSV, respiratory syncytial virus; wGA, weeks' gestational age.

¹ These estimates differ from those reported in paragraph 3.2 because they were based on a post-hoc analyses using the CLEVER case definition and a 180-day follow-up period, whereas paragraph 3.2 reported the prespecified outcomes at 150 days.

- 4.2. The base-case incremental cost-effectiveness ratio (ICER) in the submission was between SG\$105,000 and SG\$135,000 per quality-adjusted life year (QALY) gained for clesrovimab compared with no immunisation in the all-infant population. However, the Committee considered the ICER to be highly uncertain and likely underestimated given:
- There was a lack of comparative evidence to support the submission's assumption that clesrovimab's efficacy versus no immunisation for high-risk infants is equivalent to that in healthy infants.
 - The use of efficacy estimates from post-hoc analyses of the CLEVER trial was subject to potential bias and likely overestimated the efficacy of clesrovimab.
 - The incidence rates for RSV-related hospitalisation and outpatient health events were likely overestimated and highly uncertain.
 - Hospitalisation rates were derived from RSV case counts that included both inpatient and outpatient cases.
 - Outpatient rates in the submission were higher than reported local estimates without adequate justification.
 - ICU admission rates were uncertain, as the same rate was assumed across multiple gestational age groups based on data derived from a small sample size, without adequate justification for their applicability to Singapore.
 - RSV hospitalisation and MA RSV-LRTI disutility values were derived from hospitalised preterm infants despite most RSV-associated health events occurring in otherwise healthy children.
 - The submission applied inaccurate immunisation cost and administration charges for clesrovimab.
- 4.3. The Committee considered the revised base case, which addressed several uncertainties in the company's model, including restricting the analysis to healthy infants only, updating costs, and using pre-specified CLEVER trial efficacy estimates, local incidence rates and disutility values for healthy term infants. These changes increased the ICER to between SG\$165,000 and SG\$205,000 per QALY gained. The ICER remained unacceptably high across sensitivity analyses and was most sensitive to the timing of clesrovimab administration. Delaying administration by six months increased the ICER to more than SG\$365,000 per QALY gained.
- 4.4 The Committee noted that the submission also presented CUAs that compared clesrovimab to RSVpreF, nirsevimab and palivizumab. However, given the uncertain comparative efficacy and safety data in the available clinical evidence, revised base cases for these comparisons were not conducted.

- 4.5 Overall, the Committee considered that, at the price proposed by the company, clesrovimab did not represent a cost-effective use of healthcare resources for prevention of RSV-associated LRTD in infants during their first RSV season.

Estimated annual technology cost

- 5.2 Using an epidemiological approach, the submission estimated that the annual cost impact to the healthcare system (including PHIs and Community Health Assist Scheme [CHAS] clinics) would be between SG\$1 million and SG\$3 million in the first year, and between SG\$5 million and SG\$10 million in the fifth year of listing clesrovimab on the MOH Subsidised Vaccine List for prevention of RSV-associated LRTD in infants during their first RSV season.
- 5.2 The Committee considered that the submission estimates were uncertain, due to the inclusion of non-resident births and exclusion of the neonatal mortality rate. A further source of uncertainty was the overly optimistic assumption for the proportion of infants receiving clesrovimab in PHIs or CHAS clinics when listed, given that about half of all births are in private hospitals. Based on the revised budget impact model, the annual cost impact to the healthcare system was estimated to be between SG\$3 million and SG\$5 million over the first five years of listing clesrovimab on the MOH Subsidised Vaccine List for the prevention of RSV-associated LRTD in infants during their first RSV season.

Recommendations

- 6.1 Based on available evidence, the Committee recommended not listing clesrovimab on the MOH Subsidised Vaccine List for prevention of RSV-associated LRTD in infants during their first RSV season. The decision was based on the unfavourable cost effectiveness of clesrovimab compared with no immunisation.

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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 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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