Pulmonary surfactant

for treating respiratory distress syndrome in premature infants

Technology Guidance from the MOH Drug Advisory Committee

Guidance recommendations

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

- ✓ Calfactant 105 mg/3 ml and 210 mg/6 ml and poractant alfa 120 mg/1.5 ml intratracheal suspension vials for treating respiratory distress syndrome in premature infants.

Subsidy status

Calfactant 105 mg/3 ml and 210 mg/6 ml, and poractant alfa 120 mg/1.5 ml intratracheal suspension vials are recommended for inclusion on the MOH Standard Drug List (SDL) for the abovementioned indication.

SDL **does not** apply to beractant 200 mg/8 ml vial.

Poractant alfa does not have regulatory approval with the Health Sciences Authority (HSA). The responsibility of prescribing an unregistered product to patients lies with the treating clinician. Before poractant alfa is administered, it is important to consider the availability of other suitable registered alternatives and inform the parent(s) or carer of the infant that the product is unregistered.

Updated on 1 September 2020

Factors considered to inform the recommendations for subsidy

Technology evaluation

1.1 The MOH Drug Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of pulmonary surfactant (beractant and calfactant) for treating respiratory distress syndrome (RDS) in premature infants in October 2019. The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from public healthcare institutions. Published clinical and economic evidence were considered in line with the registered indications for each pulmonary surfactant.

1.2 Poractant alfa, which does not have regulatory approval from the Health Sciences Authority (HSA) for use in Singapore, was subsequently considered in March 2020, as part of a review of unregistered (exemption) items for conditions with high clinical need.

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 subsidy considerations.

1.5 Subsidy may be considered for an unregistered product if it is:

- An additional strength or dosage formulation of an existing subsidised drug preparation that is required for populations in whom the subsidised preparation is unsuitable;
- Intended to replace an existing subsidised drug preparation which has been permanently discontinued, but was the sole source registered with HSA;
- A drug or formulation/strength that is standard of care for a specific subgroup of patients (e.g. paediatric or geriatric patients) that do not have suitable treatment alternatives; or
- A drug or supplement that is standard of care for a rare disease.

Clinical need

2.1 In local clinical practice, animal-derived intratracheal pulmonary surfactants are the standard of care for treating RDS in premature infants, in line with international clinical guidelines. No other pharmacological alternatives are available. The Committee acknowledged the high clinical need to subsidise a pulmonary surfactant to address a therapeutic gap in the MOH List of Subsidised Drugs.

Clinical effectiveness and safety

3.1 The Committee reviewed the available clinical evidence and noted that all pulmonary surfactants significantly reduced neonatal mortality and morbidity outcomes such as air leak syndromes, pneumothorax, and pulmonary interstitial emphysema compared with placebo in premature infants with RDS. All surfactants were well tolerated with favourable safety profiles.

3.2 A systematic review comparing calfactant and beractant to each other did not report any significant differences between the agents in terms of mortality, need for oxygen requirements, air leak syndromes or other secondary morbidity outcomes.

3.3 Clinical trials comparing beractant and poractant alfa reported that both products were superior to placebo in reducing neonatal mortality, air leak syndromes, pneumothorax and pulmonary interstitial emphysema. Poractant alfa was found to be superior to beractant in reducing mortality prior to discharge, and patent ductus arteriosus requiring treatment. It also led to a significant improvement in the composite outcome of death or oxygen requirement at 36 weeks' postmenstrual age. No comparison of poractant with calfactant was available.

3.4 Subgroup analyses comparing different doses of poractant alfa versus beractant reported that only patients receiving a higher dose of poractant alfa (>100 mg/kg) had significantly improved outcomes.

Cost effectiveness

4.1 No published local or overseas cost-effectiveness studies of pulmonary surfactants were available. The Committee considered that, as a class, pulmonary surfactants were likely to be cost-effective compared to placebo, in view of their relatively low cost per treatment episode and their significant impact on reducing mortality rates.

4.2 At the October 2019 meeting, the Committee agreed that a cost-minimisation approach was appropriate to select the lowest priced pulmonary surfactant for subsidy consideration in view of comparable efficacy and safety between beractant and calfactant. It noted that the manufacturer of calfactant offered the lowest price as part of their value-based pricing (VBP) proposal.

4.3 In March 2020, the Committee considered that the price of poractant alfa was acceptable, in view of the high clinical need to provide an alternative subsidised pulmonary surfactant for patients.

Estimated annual technology cost

5.1 The Committee noted that the annual cost impact was estimated to be less than SG$500,000 in the first year of listing calfactant and poractant alfa on the SDL.

Recommendation

6.1 Based on available evidence considered during two committee meetings, the Committee recommended calfactant 105 mg/3 ml and 210 mg/6 ml, and poractant alfa 120 mg/1.5 ml intratracheal suspension vials be listed on the SDL for treating RDS in premature infants, in view of acceptable clinical and cost-effectiveness, reasonable budget impact and the high clinical need for these treatments to ensure appropriate patient care.

6.2 The Committee advised that clinicians are expected to take full responsibility when prescribing poractant alfa, and should inform the parent(s) or carer of the infant that the product is unregistered, before treatment is administered.

VERSION HISTORY

Guidance on pulmonary surfactant for treating respiratory distress syndrome in premature infants

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 1 Apr 2020

2. **Guidance updated to include subsidy of poractant 120 mg/1.5 ml intratracheal suspension**
   Date of Publication 1 Sep 2020

About the Agency

The Agency for Care Effectiveness (ACE) is the national health technology assessment agency in Singapore residing within the Ministry of Health. It conducts evaluations to inform the subsidy of treatments, and produces guidance on the appropriate use of treatments for public hospitals and institutions in Singapore. The guidance is based on the evidence available to the Committee on 7 October 2019 and 20 March 2020. This 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

Principal Head (HTA)
Agency for Care Effectiveness
Email: ACE_HTA@moh.gov.sg