

[GUIDANCE IS OUTDATED AND HAS BEEN WITHDRAWN ON 1 SEPTEMBER 2023.]

## Technology Guidance

# Long-acting erythropoiesis-stimulating agents for treating anaemia in chronic kidney disease

Technology Guidance from the MOH Drug Advisory Committee

## Guidance Recommendations

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

- ✓ Darbepoetin alfa 20 mcg/0.5 ml, 40 mcg/0.5 ml and 120 mcg/0.5 ml solution for injection prefilled syringes for treating anaemia in chronic kidney disease.

### Subsidy status

Darbepoetin alfa 20 mcg/0.5 ml, 40 mcg/0.5 ml and 120 mcg/0.5 ml solution for injection prefilled syringes are recommended for inclusion on the MOH Standard Drug List (SDL) for the abovementioned indication.

SDL subsidy **does not** apply to darbepoetin alfa 10 mcg/0.5 ml, 30 mcg/0.5 ml, 60 mcg/0.5 ml, 180 mcg/0.5ml solution for injection prefilled syringes or any formulations or strengths of methoxy polyethylene glycol epoetin-beta.

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## 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 long-acting erythropoiesis-stimulating agents (ESAs; darbepoetin alfa and methoxy polyethylene glycol epoetin-beta) for treating anaemia in chronic kidney disease (CKD). The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with senior healthcare professionals from the public healthcare institutions. Published clinical and economic evidence for darbepoetin alfa and methoxy polyethylene glycol epoetin-beta (MPGE) was considered in line with their registered indications.
- 1.2. The 10mcg/0.5ml, 30mcg/0.5ml, 60mcg/0.5ml and 180mcg/0.5ml strengths of darbepoetin alfa were excluded from evaluation as they are not used in local practice and no prices were proposed for subsidy consideration by the manufacturer.
- 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.

### Clinical need

- 2.1. The Committee heard that ESAs are routinely used in local practice to treat anaemia in CKD, especially in patients requiring dialysis. The Committee acknowledged that, approximately 5,000 subsidised patients were treated with ESAs for anaemia in CKD last year, based on drug utilisation data from the public healthcare institutions.
- 2.2. The Committee noted that while short-acting ESAs (erythropoietin alfa and erythropoietin beta) are already subsidised for this condition, long-acting ESAs (darbepoetin alfa and MPGE), which are not subsidised, may improve patient adherence and reduce administration costs as they are given less frequently. Although patients with CKD can claim some of the cost of ESAs under MediShield Life, those who require high-dose long-acting ESAs still incur out-of-pocket expenses. Therefore, the Committee agreed that there was a clinical need to improve the affordability of long-acting ESAs for these patients.

## Clinical effectiveness and safety

- 3.1. The Committee agreed that erythropoietin alfa and erythropoietin beta were appropriate comparators to darbepoetin alfa and MPGE. Darbepoetin alfa and MPGE were also compared with each other.
- 3.2. The Committee reviewed available evidence from a Cochrane network meta-analysis (NMA) which compared erythropoietin alfa, erythropoietin beta, darbepoetin alfa, MPGE, erythropoietin alfa biosimilar and erythropoietin beta biosimilar to one another for treating anaemia in CKD. They noted that the results showed no statistically significant differences in preventing blood transfusions among the ESAs. The frequencies of safety outcomes such as all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, hypertension and vascular access thrombosis were also similar for all ESAs. The Committee considered that the results were uncertain, noting that there were differences in the participants' characteristics between the included studies and heterogeneity in the treatment effect estimates. However, on balance, they accepted that there was insufficient evidence to suggest that any ESA formulation was superior to another. They further acknowledged that local clinical experts considered that darbepoetin alfa, MPGE, erythropoietin alfa and erythropoietin beta were clinically comparable.

## Cost effectiveness

- 4.1. The Committee agreed that a cost-minimisation approach was appropriate to assess the cost-effectiveness of the long-acting ESAs, in view of their comparable efficacy and safety to short-acting ESAs and to one another. The Committee acknowledged that erythropoietin beta was an appropriate comparator in the cost-minimisation analysis (CMA) as it had the lowest unit cost among the short-acting ESAs.
- 4.2. Based on the value-based pricing (VBP) proposals submitted by the manufacturers, the Committee agreed with the results of the CMA, which showed darbepoetin alfa to be more cost-effective than erythropoietin beta and MPGE, while MPGE was not cost-effective compared with erythropoietin beta.

## Estimated annual technology cost

- 5.1. The Committee noted that the annual cost impact was estimated to be less than SG\$1 million in the first year of listing darbepoetin alfa on the SDL.

## Additional considerations

- 6.1 In view of the low risk of misuse of darbepoetin alfa and its potential to reduce administrative costs for patients, the Committee considered that an SDL listing was appropriate.

## Recommendations

- 7.1. Based on available evidence, the Committee recommended listing darbepoetin alfa 20 mcg/0.5 ml, 40 mcg/0.5 ml and 120 mcg/0.5 ml solution for injection prefilled syringes on the SDL in view of comparable clinical effectiveness and favourable cost effectiveness compared to erythropoietin beta and MPGE at the prices proposed by the manufacturer, and the clinical need for a long-acting ESA to be subsidised to ensure appropriate patient care.
- 7.2. At the prices proposed by the manufacturer, methoxy polyethylene glycol epoetin-beta was not recommended for listing on the SDL due to unfavourable cost effectiveness compared with erythropoietin beta and darbepoetin alfa.

### 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 guidance, and education.

As the national HTA agency, ACE conducts evaluations to inform government subsidy decisions for treatments, diagnostic tests and vaccines, and produces guidance for public hospitals and institutions in Singapore.

This guidance is based on the evidence available to the MOH Drug Advisory Committee as at 18 August 2021. It 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](http://www.ace-hta.gov.sg/about)*

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