Technology Guidance

High-strength insulin glargine

for treating type 1 and 2 diabetes mellitus

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has not recommended listing insulin glargine 300 units/ml on the Standard Drug List (SDL) for treating type 1 and 2 diabetes mellitus in view of unfavourable cost-effectiveness compared with insulin glargine 100 units/ml at the price proposed by the manufacturer, and low clinical need.

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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 high-strength insulin glargine 300 units/ml for treating type 1 and 2 diabetes mellitus. The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for insulin glargine 300 units/ml was considered in line with its registered indication.

1.2. 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.

1.3. Additional factors, including social and value judgments, may also inform the Committee's subsidy considerations.

Clinical need

2.1. In local clinical practice, insulin glargine 100 units/ml, which is listed on the SDL, is the most commonly used basal insulin treatment for diabetes. The Committee acknowledged that high-strength insulin glargine 300 units/ml reduces the injection burden for patients who require larger doses.

2.2. While some local clinical experts considered that insulin glargine 300 units/ml reduced the risk of severe or nocturnal hypoglycaemia compared with insulin glargine 100 units/ml, the Committee noted that hypoglycaemia rates were generally low with both strengths in clinical practice and only a small proportion of patients may benefit from using insulin glargine 300 units/ml. Thus, the Committee considered that there was a low clinical need to consider it for subsidy.

Clinical effectiveness and safety

3.1. The Committee reviewed the available clinical evidence from seven open-label, head-to-head randomised controlled trials (RCTs) which compared insulin glargine 300 units/ml with insulin glargine 100 units/ml in patients with type 1 or type 2 diabetes mellitus. All trials showed that insulin glargine 300 units/ml was non-inferior to insulin

glargine 100 units/ml in glycaemic control, based on the mean change in HbA1c from baseline to week 24 or 26. Insulin glargine 300 units/ml was generally well-tolerated.

3.2. The Committee noted that results of hypoglycaemia outcomes reported in the trials were inconsistent. All three trials in people with type 1 diabetes (EDITION 4, EDITION JP1 and EDITION JUNIOR) showed that there were no significant differences in hypoglycaemia outcomes between insulin glargine 300 units/ml and insulin glargine 100 units/ml. Among the trials in people with type 2 diabetes (EDITION 1, EDITION 2, EDITION 3, EDITION JP2), while three of the four trials showed that insulin glargine 300 units/ml resulted in a statistically significant reduction in the proportion of patients with ≥1 severe or confirmed nocturnal hypoglycaemia event, none of the trials showed significant differences between treatments in severe hypoglycaemia, or confirmed or severe hypoglycaemia at any time of the day.

3.3. The Committee noted results of a post-hoc meta-analysis of EDITION 1, 2 and 3 which showed that insulin glargine 300 units/ml was associated with a statistically significant reduction in confirmed or severe nocturnal hypoglycaemia events compared with insulin glargine 100 units/ml, but considered that the magnitude of reduction (~ 1 event per person per year) may not be clinically significant. Furthermore, as insulin glargine was injected in the evening in these trials, the risk of nocturnal hypoglycaemia could be mitigated in clinical practice by administering in the morning instead.

3.4. Based on the available evidence, the Committee considered insulin glargine 300 units/ml to be non-inferior in effectiveness and safety to insulin glargine 100 units/ml.

Cost effectiveness

4.1. The Committee agreed that a cost-minimisation approach was appropriate to assess the cost-effectiveness of insulin glargine 300 units/ml, in view of its comparable effectiveness and safety to insulin glargine 100 units/ml.

4.2. The manufacturer of insulin glargine 300 units/ml was invited to submit their value-based pricing (VBP) proposal for subsidy consideration. At the proposed price, insulin glargine 300 units/ml was not cost-effective compared with insulin glargine 100 units/ml on a cost-minimisation basis.

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 insulin glargine 300 units/ml on the SDL.

Recommendations

6.1. Based on available evidence, the Committee recommended not listing insulin glargine 300 units/ml on the SDL, in view of unfavourable cost-effectiveness compared with insulin glargine 100 units/ml at the price proposed by the manufacturer, and low clinical need.

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 26 November 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.

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