

Systematic review and economic evaluation of a long-acting insulin analogue, insulin glargine

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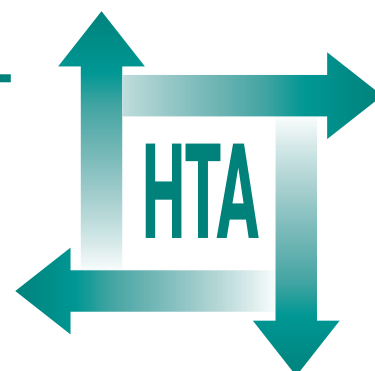
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Executive summary

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Executive summary

Objectives

The aim of this review was to evaluate the use of insulin glargine in its licensed basal-bolus indication in terms of both clinical and cost-effectiveness.

Methods

A systematic review of the literature, involving a range of databases, was performed to identify all papers relating to insulin glargine.

Results

Number and quality of studies

Nineteen studies met the inclusion criteria but full reports were available for only six.

Clinical effectiveness

For type 1 diabetes patients, insulin glargine appears to be more effective than neutral protamine Hagedorn (NPH) in reducing fasting blood glucose (FBG) but not in reducing glycosylated haemoglobin (HbA_{1c}) and there is some evidence that both insulins are as effective as each other in both FBG and HbA_{1c} control. For type 2 patients for whom oral antidiabetic agents provide inadequate glycaemic control, there is no evidence that insulin glargine is more effective than NPH in reducing either FBG or HbA_{1c} and some evidence that both insulins are as effective as each other in both FBG and HbA_{1c} control.

Evidence for control of hypoglycaemia is equivocal. In studies where insulin glargine is demonstrated to be superior to NPH in controlling nocturnal hypoglycaemia, this may be only apparent when compared with once-daily NPH and not twice-daily NPH. Further, this superiority of glargine over NPH in the control of

nocturnal hypoglycaemia may relate to one formulation of insulin glargine (HOE901[80]) and not another (HOE901[30]). There is no conclusive evidence that insulin glargine is superior to NPH in controlling symptomatic hypoglycaemia and severe hypoglycaemia. Insufficient data are available to conclude whether insulin glargine is different from each of the commonly used NPH dosing regimens: once daily and more than once daily.

Health economics

There are no published economic studies on insulin glargine or indeed NPH insulin. An economic evaluation of insulin glargine has been provided in the Aventis submission. Given the lack of a published evidence base for the cost-effectiveness of insulin glargine, the economic review concentrates on a review of the industry submission and an amended ScHARR model. Three economic models are provided in the submission, two relating to type 1 diabetes (previously on other basal-bolus regimes or previously on premix therapies) and one relating to type 2 diabetes. All three models compare the cost-utility of insulin glargine against NPH insulin. In general, the structures of the models are poor. In all three models, mistakes relating to assumptions and calculations have been made. The industry submission concludes that insulin glargine is highly cost-effective in all three models. The incremental cost per quality-adjusted life year (QALY) ratios generated by the company models are presented in the first table.

Based on the evidence presented, there appears to be no rationale for the two separate models within type 1 diabetes. No evidence has been presented that suggests type 1 patients previously receiving premix therapies would experience better glycaemic control on insulin glargine than patients previously treated by other basal-bolus regimes.

Cost per QALY results provided in the Aventis submission

Model	Base-case cost per QALY (£)	Cost per QALY range (£)
Type 1 (other basal-bolus)	1,148–1,292	792–45,853
Type 1 (premix)	Dominant	Dominant–9,509
Type 2	4,552–7,169	3,887–308,105

Cost per QALY results estimated by ScHARR

Patient group	Base-case cost per QALY ^a (£)	Cost per QALY range (£)
Type 1	3,496–4,978	954–554,411
Type 2	32,508–43,411	6,168–10,214,864
^a Cost per QALY ratio depends on the method on administration (vial, cartridge or insulin pen).		

An evaluation of the industry model was made and a separate model was constructed. The assessment team believe that the cost per QALY estimates generated by the Aventis model may be an underestimate for several reasons:

Information from the Aventis submission was submitted in confidence to NICE. This information was made available to the NICE Appraisals Committee but has been removed from this version of the report.

The incremental cost per QALY ratios generated from the assessment team models are presented in the second table.

The cost-effectiveness of insulin glargine in both type 1 and type 2 diabetes is highly sensitive to the amount of utility associated with reducing the fear of hypoglycaemia. The industry submission explores this issue through a number of analyses and the claimed base case is based on the most favourable of these analyses. By changing this assumption, the cost per QALY ranges from cost-effective to not cost-effective.

Conclusions

The evidence suggests that, compared with NPH insulin, insulin glargine is effective in reducing the

number of nocturnal hypoglycaemic episodes, especially when compared with once-daily NPH. There appears to be no improvement in long-term glycaemic control and therefore insulin glargine is unlikely to reduce the incidence of the long-term microvascular and cardiovascular complications of diabetes.

Recommendations for further research

Further research into insulin glargine is needed in these key areas:

- Quality of life associated with fear of hypoglycaemia.
- Economic impact of balance of HbA_{1c} control and incidence of hypoglycaemia achieved in practice. Studies examining the economic evidence on insulin glargine should be published.

Publication

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NHS R&D HTA Programme

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The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, consumer groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including consumers) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or designing a trial to produce new evidence where none currently exists.

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

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