Evaluating the cost-effectiveness of reduced mild hypoglycaemia in subjects with type 1 diabetes treated with insulin detemir or NPH insulin in Denmark, Sweden, Finland and the Netherlands

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Record Status
This is an economic evaluation that meets the criteria for inclusion on NHS EED.

CRD summary
The study examined the cost-effectiveness of insulin detemir (insulin analogue) versus neutral protamine Hagedorn (human) insulin in four European countries based on the incidence of mild hypoglycaemia in patients with type 1 diabetes. The authors concluded that insulin detemir was a very cost-effective alternative to neutral protamine Hagedorn insulin in Denmark, Sweden, Finland and the Netherlands. The analysis used valid and transparent methods that reported data sources and investigated uncertainty. The authors' conclusions appear robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The study estimated the short-term cost-effectiveness of insulin detemir versus neutral protamine Hagedorn insulin in four European countries based on the incidence of mild hypoglycaemia in patients with type 1 diabetes.

Interventions
Insulin detemir (insulin analogue) was compared with neutral protamine Hagedorn (human) insulin. A daily dose of 40 international units (IU) was assumed for both medications in the base case analysis.

Location/setting
Denmark, Sweden, Finland, and the Netherlands/primary care.

Methods
Analytical approach:
The analysis was based on a simple decision tree with a one-year time horizon. The authors stated that the perspective of the health care payer was adopted.

Effectiveness data:
Clinical inputs came from published sources that were selectively identified by the authors. Evidence of baseline rates for mild hypoglycaemic events with neutral protamine Hagedorn insulin was taken from a UK study that was conducted over nine to 12 months in secondary care diabetes centres. The relative risk of events for insulin detemir compared with neutral protamine Hagedorn insulin was supplemented by data from a health technology assessment performed by the Canadian Agency for Drugs and Technology in Health (CADTH) published in 2008. In this study, a meta-analysis of clinical trials was conducted to assess the reduction in hypoglycaemic events for insulin detemir with neutral protamine Hagedorn insulin (without a distinction between mild and severe events).

Monetary benefit and utility valuations:
Health utility valuations for mild hypoglycaemic events were taken from a published study that used validated health states and a time trade-off model in Canadian and UK individuals with and without diabetes.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure.

Cost data:
Pharmacy costs included those for both types of insulin under examination plus that of a single self-monitoring of
Analysis of uncertainty:
A probabilistic sensitivity analysis was performed to generate cost-effectiveness acceptability curves. One-way sensitivity analyses were carried out by varying base case values of model inputs for alternative published sources and using a probabilistic approach.

Results
In comparison with neutral protamine Hagedorn insulin, insulin detemir increased QALYs by 0.019 in all countries, and increased costs by EUR 238.72 in Denmark, EUR 238.47 in Sweden, EUR 308.51 in Finland, and EUR 223.01 in the Netherlands.

The incremental cost per QALY gained with insulin detemir over neutral protamine Hagedorn insulin was EUR 12,644 in Denmark, EUR 12,612 in Sweden, EUR 16,568 in Finland, and EUR 12,216 in the Netherlands.

Using the WHO recommendations for willingness-to-pay thresholds based on gross domestic product, insulin detemir was highly cost-effective (below the gross domestic product per capita) in all countries. At a willingness-to-pay threshold of EUR 50,000 per QALY, the probability of insulin detemir being cost-effective was above 86% in all countries.

Using an alternative source of hypoglycaemia rate based on a clinical trial, more favourable cost-utility ratios were achieved. In general, even when using higher pharmacy costs or different daily dosages, insulin detemir remained a very cost-effective strategy.

Authors' conclusions
The authors concluded that insulin detemir was a very cost-effective alternative to neutral protamine Hagedorn insulin for patients with type 1 diabetes in Denmark, Sweden, Finland and the Netherlands.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as the analysis compared two available long-acting insulin drugs.

Effectiveness/benefits:
The treatment effect for insulin detemir versus neutral protamine Hagedorn insulin was taken from a meta-analysis of clinical trials that should ensure high internal validity. Relative risk was found for all hypoglycaemic events instead of just for mild episodes; the authors stated that the value used should be considered conservative given the strongest impact of insulin detemir on mild events. Baseline events were based on a UK study (given the lack of country-specific data). Extensive sensitivity analyses were conducted on clinical parameters. The use of QALYs was appropriate given the impact of the disease on health-related quality of life. The authors justified the selection of utility values among those available in the literature and provided details on the instruments used. Alternative sources of data were used in the sensitivity analyses.

Costs:
The cost analysis was limited to the costs of drugs according to the short-term time horizon and the third-party payer perspective. Details on unit costs and daily dosages were reported for both drugs; typical sources for each country were used. Some resource use was varied in the sensitivity analysis. The price year was reported, which would allow reflection exercises. The authors stated that the real-life daily dosages for the two medications represented an important model driver.

Analysis and results:
An incremental approach was appropriately used to synthesise costs and benefits of both treatments. Valid approaches were used to analyse the potential uncertainty associated with variations in clinical and economic inputs. The methods
and results of the probabilistic analysis were clearly illustrated. The authors stated that previous long-term models had shown the cost-effectiveness of insulin detemir but were based on several assumptions; the objective of this model was to conduct a simple analysis based on short-term evidence. The results were clearly presented. Study findings were likely to be valid for other developed countries with similar drug costs.

Concluding remarks:
The analysis used valid and transparent methods that reported data sources and investigated uncertainty. The authors’ conclusions appear robust.

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