A cost-utility analysis of cinacalcet in secondary hyperparathyroidism in five European countries

Iannazzo S, Carsi M, Chirolí S

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The study examined the cost-effectiveness of cinacalcet for the treatment of secondary hyperparathyroidism in haemodialysis patients with chronic kidney disease in five European countries. The authors concluded that cinacalcet might be considered as a cost-effective strategy compared with standard treatment from the perspective of national health care systems in all five countries when dialysis costs were excluded. The analysis used conventional and transparent methods that enhance the robustness of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The study examined the cost-effectiveness of cinacalcet (calcimimetic agent) for the treatment of secondary hyperparathyroidism in haemodialysis patients with chronic kidney disease in five European countries.

Interventions
Standard treatment alone (vitamin D sterols and phosphate binders) was compared to cinacalcet plus standard care for the treatment of chronic kidney disease haemodialysis patients with poorly controlled secondary hyperparathyroidism.

Location/setting
Italy, Spain, Portugal, Switzerland, and Czech Republic/Secondary care.

Methods
Analytical approach:
The analysis was based on a probabilistic, patient-level simulation Markov model. A lifetime horizon was considered. The authors stated that the perspective of the national health care system was adopted for each European country.

Effectiveness data:
Clinical inputs and patient characteristics were mainly based on the OPTIMA (Open-Label, Randomized Study Using Cinacalcet to Improve Achievement of KDOQI Targets in Patients with End-Stage Renal Disease) study, a European, multi-centre, open-label, 23-week, randomised trial that involved 552 haemodialysis patients with poorly controlled secondary hyperparathyroidism (Messa, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details). Country-specific registries and databases were used for epidemiological data. The relative risk of death for cinacalcet plus standard therapy versus standard therapy alone was a key input of the model; this was calculated as a function of sex, age, and the concentrations of plasma parathyroid hormone, serum calcium, and phosphorus.

Monetary benefit and utility valuations:
Utility valuations came from publications of international relevance, such as a previous health technology assessment report by the UK National Institute for Health and Clinical Excellence (NICE), a Dutch cohort study, and other reference sources. Various instruments were used in each publication. Health utility estimates were taken from patients or the general population.

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were used as the summary benefit measures. An annual discount
rate of 3.5% was applied.

**Cost data:**
Direct medical costs included those for cinacalcet and standard treatment drugs and for the treatment of cardiovascular events, fractures, parathyroidectomy, haemodialysis, and peritoneal dialysis. Event rates and dosages mainly came from the OPTIMA study. Unit costs were based on local prices (drugs) and tariffs (hospitalisations) such as Diagnosis Related Groups, except for the Czech Republic (as Diagnosis Related Groups were not available), where costs were based on national databases. Costs were discounted at an annual rate of 3.5%. The currency was given in Euros (EUR) using currency conversions for Switzerland and the Czech Republic. The price year was 2010.

**Analysis of uncertainty:**
A probabilistic sensitivity analysis was carried out using published ranges of values and standard deviation estimates, supplemented by authors’ assumed values. Cost-effectiveness acceptability curves were constructed to identify the optimal treatment. One-way sensitivity analyses were performed for all inputs using ranges of 10% above and below baseline values. An alternative scenario including future costs of dialysis was also considered.

**Results**
For cinacalcet, the expected life years were 9.15 in Italy, 7.41 in Spain, 9.44 in Portugal, 9.05 in Switzerland, and 7.21 in the Czech Republic. The expected QALYS were 5.84 in Italy, 4.72 in Spain, 5.98 in Portugal, 5.70 in Switzerland, and 4.58 in the Czech Republic.

For standard treatment, the expected life years were 7.95 in Italy, 6.31 in Spain, 8.26 in Portugal, 7.65 in Switzerland, and 6.11 in the Czech Republic. The expected QALYS were 4.95 in Italy, 3.91 in Spain, 5.09 in Portugal, 4.69 in Switzerland, and 3.78 in the Czech Republic.

Costs without dialysis for cinacalcet were EUR 51,756 in Italy, EUR 43,264 in Spain, EUR 52,819 in Portugal, EUR 68,883 in Switzerland, and EUR 51,120 in the Czech Republic. Costs without dialysis for standard treatment were EUR 23,595 in Italy, EUR 19,387 in Spain, EUR 24,888 in Portugal, EUR 34,253 in Switzerland, and EUR 18,369 in the Czech Republic. Far higher costs were observed when dialysis costs were included, especially for cinacalcet where a longer life expectancy was found.

Excluding dialysis costs, the incremental cost per life year gained with cinacalcet over standard treatment was EUR 23,473 in Italy, EUR 21,789 in Spain, EUR 23,680 in Portugal, EUR 24,682 in Switzerland, and EUR 29,726 in the Czech Republic. The corresponding incremental cost per QALY was EUR 31,600 in Italy, EUR 29,300 in Spain, EUR 31,200 in Portugal, EUR 34,200 in Switzerland, and EUR 40,800 in the Czech Republic. Including dialysis costs, the incremental cost per life year ranged from EUR 42,800 to EUR 82,800, while the incremental cost per QALY ranged from EUR 57,500 to EUR 114,700.

At a willingness-to-pay threshold of EUR 40,000 per QALY, the probability of cinacalcet being cost-effective was 88% to 98% in all countries except in the Czech Republic, where this rate was only 51%.

Base case results were robust to variation in model inputs, with initial age and unit costs of cinacalcet being the main drivers.

**Authors' conclusions**
The authors concluded that cinacalcet might be considered as a cost-effective strategy compared with standard treatment from the perspective of national health care systems in all five countries when dialysis costs were excluded.

**CRD commentary**
**Interventions:**
The comparators were appropriately selected as the proposed treatment was compared with the standard pattern of care for this specific patient population.

**Effectiveness/benefits:**
A selective approach was used to identify relevant sources of evidence. Most data came from a pivotal clinical trial,
whose methodological aspects such as randomised and multi-country design should have ensured the validity of the clinical inputs. Additional epidemiological data came from appropriate country-specific databases. It was not clear how short-term results of the clinical trial were extrapolated to the long-term. Extensive sensitivity analyses were conducted on all clinical parameters. Both life years and QALYs were appropriate benefit measures to capture the impact of the disease on patients’ health. Key information on the derivation of utility valuations was reported and, in general, appropriate sources of data appear to have been used.

Costs:
The analysis was conducted from the perspective of the health care system in all five countries; the cost categories included reflected this viewpoint. Costs associated with cardiovascular events, fractures and other events were reported for each country, while other costs were not provided. In general, appropriate sources appear to have been used for hospitalisations and drug costs, although few details were provided. A key model driver was the inclusion of future costs of dialysis; the authors stated that a consensus on the inclusion or exclusion of these costs was not reached. Other details for price year and discount rate were provided. No justification on the adoption of the same discount rate for each country was given.

Analysis and results:
Uncertainty was satisfactorily investigated using deterministic and probabilistic sensitivity analyses, whose methodological aspects and key findings were reported. The study was conducted in five European countries; similar results were found, so it was likely that these findings would be transferable to other European countries. The authors acknowledged that the main issue of the analysis was related to the question about the inclusion of dialysis costs. The expected costs and benefits were clearly presented for scenarios with and without dialysis costs. An incremental approach was appropriately used to synthesise the costs and benefits of the two treatments.

Concluding remarks:
The analysis used conventional and transparent methods that enhance the robustness of the authors’ conclusions.

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