A cost-effectiveness analysis of levodopa/carbidopa intestinal gel compared to standard care in late stage Parkinson's disease in the UK


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
This study examined the cost-effectiveness of levodopa carbidopa intestinal gel, compared with standard care, for the treatment of advanced Parkinson's disease. The authors concluded that the gel was effective and was cost-effective for patients for whom no other treatment was effective or suitable, but further research was needed. The methods were valid, but the limitations of the key inputs might affect the validity of the authors’ conclusions and, as they stated, further research is needed.

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

Study objective
This study examined the cost-effectiveness of levodopa carbidopa intestinal gel, compared with standard care, for advanced Parkinson's disease, which was defined by a Hoehn and Yahr scale stage of three or more and treatment not working for more than half of every day.

Interventions
Five years of treatment with the gel was compared against standard care, which was the medically determined best available oral treatment, for patients with advanced Parkinson's disease for whom other treatments were not working or were not recommended.

Location/setting
UK/secondary care.

Methods
Analytical approach:
The analysis was based on a published Markov model, with a lifetime horizon. The authors stated that it was conducted from the perspective of the UK NHS and Personal Social Services.

Effectiveness data:
The clinical data were from a selection of relevant studies. The efficacy of treatment was estimated by the improvement in Hoehn and Yahr scale stage and the reduction in time when treatment was not working; this was the key input for the model. The short-term treatment effect was from a pooled analysis of two clinical studies of 30 patients in total. No additional effect was assumed in subsequent cycles (after 6 months). The effects on time spent in OFF state were from a subgroup of eight patients enrolled in a clinical trial, for whom treatment was not working for more than half of every day. The data on adverse events were from a long-term safety study. Expert opinion and assumptions were needed.

Monetary benefit and utility valuations:
The utility values were from an interim analysis of an ongoing unpublished study, called the Duodopa in Advanced Parkinson's: Health outcomes and Net Economic Impact (DAPHNE) study, that used the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years were used as the summary benefit measures and were discounted at
an annual rate of 3.5%.

Cost data:
The analysis included the costs of drugs (administration and follow-up) and disease (depending on the health state), including hospitalisations, consultations and tests, institutional care, professional caregivers, and respite care. The costs of drugs were from a previous study, in which the resource use was based on clinical data and assumptions, which were validated by an advanced Parkinson's disease clinician. The costs of disease management were from an observational study of advanced Parkinson disease that was conducted by neurologists and geriatricians in hospitals across the UK. The unit costs were from UK official sources, such as the British National Formulary and NHS Reference Costs. The mean health state costs were calculated, using an ordinary least-squares regression. All costs were in UK pounds sterling (£), at 2007 to 2008 prices. A 3.5% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out to assess the uncertainty in the eligibility for drug treatment, the treatment effect, the drop-out and adverse event rates, the treatment duration, the health state costs, the discount rates, and the time horizon. Alternative assumptions were based on the literature or authors' opinions.

Results
Compared with standard care, the levodopa carbidopa intestinal gel generated an additional 1.10 QALYs, 0.77 life-years, and £39,644. The incremental cost per QALY gained was £36,024 and the incremental cost per life-year gained was £51,741.

The most influential inputs were the duration of treatment, the health state at the start of treatment, and the long-term benefit. Changes in these inputs resulted in cost-utility ratios that ranged from £32,127 to £66,421. The highest ratio was produced by the assumption of lifetime treatment duration.

Authors’ conclusions
The authors concluded that the levodopa carbidopa intestinal gel was effective for the treatment of advanced Parkinson’s disease, and was cost-effective for patients with no other effective treatment options, but further research was needed.

CRD commentary
Interventions:
The selection of the comparators appears to have been appropriate for the patients. The levodopa carbidopa intestinal gel had orphan drug status in several countries, as it was a last resort treatment for advanced Parkinson's disease.

Effectiveness/benefits:
The clinical data were generally from studies with few patients or small subgroups of patients from larger clinical trials. This was due to the specific condition that could benefit from the gel and the orphan nature of the gel. The authors acknowledged this key limitation and conducted sensitivity analysis on the main clinical parameters. QALYs and life-years were appropriate benefit measures, which captured the impact of the disease on patients' health and allow cross-disease comparisons. The derivation of the health-related quality of life estimates was reported and a validated instrument was used to elicit the patient preferences.

Costs:
The economic analysis was transparently presented, with extensive information on the unit costs, resource quantities, and data sources. Most of the data were from official UK sources, consistent with the perspective adopted. The resource use for some health states was based on a very low number of observations and regression analyses were performed. The impact of variations in the key cost inputs was tested in the sensitivity analyses. Details, such as the price year and discount rate, were provided.

Analysis and results:
The results were extensively presented. The costs and benefits were combined, using an incremental approach. A deterministic approach was used in the sensitivity analysis, which focused on selected inputs and assumptions. It was stated that a probabilistic analysis would have been difficult to perform, as the definition of distributions for the
parameters would have been complicated. The authors pointed out the importance of restricting the analysis to patients eligible for last resort treatment. They highlighted that their findings should be considered in the context of the limited data available. They did not discuss the transferability of their results.

Concluding remarks:
The methods were valid, but the limitations of the key inputs might affect the validity of the authors' conclusions and, as they stated, further research is needed.

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