Long-term costs and clinical outcomes associated with metformin-glibenclamide combination tablets (Glucovance) in patients with type 2 diabetes sub-optimally controlled by metformin: a modelling study in the French setting


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 investigated the cost-effectiveness of treatment with a single-tablet metformin-glibenclamide combination in patients with type 2 diabetes becoming hyperglycaemic on metformin monotherapy. The analysis showed that the combination tablet was a cost-effective strategy from the perspective of the French third-party payer. The analysis was based on a validated model and, despite somewhat limited reporting of the economic data, the authors’ conclusions appear to be robust.

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

Study objective
The objective was to assess the cost-effectiveness of treatment with a single-tablet metformin-glibenclamide combination in patients, with type 2 diabetes, becoming hyperglycaemic on metformin monotherapy.

Interventions
The three strategies considered for patients with inadequate glycaemic control on metformin therapy were to, increase metformin dosage, switch to glibenclamide monotherapy (5mg), or switch to metformin-glibenclamide combination therapy (500mg/2.5 mg or 500mg/5mg, depending on the previous metformin dosage).

Location/setting
France/primary care.

Methods
Analytical approach:
A published decision analytic model was developed to predict the long-term clinical and economic outcomes associated with the three strategies. A long-term horizon (35 years) was considered. The authors stated that the perspective of the third-party payer was adopted.

Effectiveness data:
The key short-term clinical estimates for the effectiveness of combination therapy compared with monotherapies were derived from a 16-week, randomised controlled trial that enrolled 411 patients with inadequate glycaemic control. The long-term data on the clinical management of diabetes and its risk of complications were derived from the published decision model (the CORE Diabetes Model). Other clinical inputs came from the ECODIA study, a descriptive cross sectional survey of the clinical characteristics and medical management of type 2 diabetic patients in France in 1999. The key clinical outcome was the improvement in glycaemic control with consequential improvement in risk of cardiovascular, renal and other microvascular diseases.

Monetary benefit and utility valuations:
The utility valuations were based on the published model, the details of which were not reported.

Measure of benefit:
Life-years (LYs) and Quality-adjusted LYs (QALYs) were used as the summary benefit measures. Both were
discounted at an annual rate of 3%.

Cost data:
The authors stated that the economic analysis included the costs related to treatment, complications, and medications. A breakdown of cost items was not provided. The costs and quantities were derived from published sources, the details of which were not given. Drug dosages reflected the trial data. Medical management of type 2 French patients was obtained by means of a questionnaire completed by primary care and specialist practitioners. The costs were in Euros (EUR) and the price year was 2005. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
A deterministic, univariate, sensitivity analysis was performed on key model inputs as well as on the time horizon and the discount rate. A non-parametric bootstrapping approach was also used to derive mean and standard deviations of life expectancy, QALYs, and costs.

Results
For metformin 500mg, the expected LYs gained were 10.89, QALYs were 7.81, and costs were EUR 30,841.

For glibenclamide 5mg, the LYs were 10.876, QALYs were 7.798, and costs were EUR 30,607.

For combination therapy 500mg/2.5mg the LYs were 11.31, QALYs were 8.26, and costs were EUR 27,510.

For combination therapy 500mg/5mg the LYs were 11.15, QALYs were 8.08, and costs were EUR 28,814.

The incremental analysis revealed that each combination therapy dominated (was both more effective and less expensive than) both metformin alone and glibenclamide alone.

The sensitivity analysis indicated that the most influential model inputs were changes in glycosylated haemoglobin A\textsubscript{1c} and the time horizon, but changes in these inputs did not alter the conclusions of the base-case analysis, and combination therapy remained dominant.

Authors’ conclusions
The authors concluded that a single-tablet metformin-glibenclamide combination in patients with type 2 diabetes becoming hyperglycaemic on metformin monotherapy, was a cost-effective strategy from the perspective of the French third-party payer.

CRD commentary
Interventions:
The selection of the comparators was appropriate in that they reflected the strategies of the clinical trial.

Effectiveness/benefits:
The derivation of the clinical data was based on two studies which were selected by the authors, and which reflected treatment patterns in the authors’ setting. The other epidemiological and clinical estimates related to diabetes care were already included in the published model, which is a well-known simulation of diabetes complications. The use of a large clinical trial should have ensured the validity of these clinical inputs. Key values were varied in the sensitivity analysis. The derivation of the benefit measure was based on data incorporated in the previous model, thus little information on the utility values was provided. QALYs are a validated benefit measure, which capture the impact of the interventions on patients’ health and are also comparable with the benefits of other health care interventions.

Costs:
The analysis of costs was only partially presented. The authors only reported the costs as macro-categories and did not describe the sources used to derive these data. Only drug dosages were reported in detail. Some cost results were reported only in graphical format. This partially reduces the transparency of the economic analysis. Other aspects of the analysis such as the price year and use of discounting were reported.
Analysis and results:
The costs and benefits were clearly presented. They were not synthesised, which was appropriate, given the dominance of combination therapy. The issue of uncertainty was partially addressed by focusing on individual model inputs and assumptions. The authors stated that the decision model was validated in 66 published analyses, and this reinforces the validity of this analysis.

Concluding remarks:
The analysis was based on a validated model and a clear presentation of the sources of clinical evidence on treatment effectiveness was given. The authors’ conclusions appear to be robust despite the somewhat limited reporting of the economic data.

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Bibliographic details

Other publications of related interest


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