Comparative clinical- and cost-effectiveness of candesartan and losartan in the management of hypertension and heart failure: a systematic review, meta- and cost-utility analysis

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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 compared the clinical efficacy and cost-effectiveness of branded candesartan and generic losartan in the treatment of hypertension and heart failure. The authors concluded that branded candesartan was not cost-effective compared with generic losartan, for the treatment of hypertension, from the perspective of the UK NHS. The cost-effectiveness framework was conventional and the clinical analysis was very well conducted. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to compare the clinical efficacy and cost-effectiveness of two angiotensin II receptor blockers, namely branded candesartan and generic losartan, in the treatment of hypertension and heart failure.

Interventions
Generic losartan was compared with branded candesartan. The highest doses for both drugs (100mg per day for losartan and 32mg per day for candesartan) were considered.

Location/setting
UK/primary care.

Methods
Analytical approach:
The economic analysis was based on a Markov model, with a 10-year time horizon. The authors stated that the analysis was carried out from the perspective of the UK NHS.

Effectiveness data:
The clinical data were identified by a systematic review of the literature in MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL), which contained the Hypertension and Heart Group's specialist register. The reference lists of retrieved articles were handsearched. Two searches were carried out; one for hypertension and one for heart failure. Head-to-head randomised, double-blind, active-controlled trials of adult patients were included. The key endpoint was the mean change from baseline to 24 hours after the dose, in diastolic blood pressure and systolic blood pressure, for the hypertension trials, and a composite of cardiovascular death and hospital admission for the management of heart failure, for the heart failure trials. A random-effects model was used to calculate the weighted mean differences. Heterogeneity between the pooled studies was investigated. Framingham equations were used to estimate the long-term impact of short-term changes in blood pressure. All-cause mortality was based on UK life tables.

Monetary benefit and utility valuations:
The utility values were derived from a National Institute for Health and Clinical Excellence (NICE) guideline. A similar utility loss, due to adverse treatment effects, was assumed for both treatment arms.

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

Cost data:
The economic analysis included the costs of drug acquisition and of managing initial non-fatal stroke and coronary heart disease events, as well as those for ongoing management. The drug costs were based on their official prices (except for generic losartan, which was based on expert opinion), while other costs were from a NICE guideline. All costs were in UK pounds sterling (£). The price year was 2009 and a 3.5% annual discount rate was applied.

Analysis of uncertainty:
Four alternative scenarios were considered, as one-way sensitivity analyses, by changing the baseline risk (increasing the cohort pre-treatment systolic blood pressure to a range of 140 to 180 mmHg), varying the hypertensive effectiveness, reducing the price of generic losartan, and varying the cohort starting age.

Results
For the treatment of hypertension, depending on the baseline risk, the incremental cost per QALY gained with candesartan over generic losartan ranged from £41,469 to £52,644 in men and from £41,591 to £85,244 in women. These figures were above the commonly used cost-effectiveness threshold of £40,000 per QALY.

The cost-effectiveness of candesartan decreased as the baseline risk lowered, but it remained almost always above £40,000 per QALY. Candesartan became increasingly unfavourable, when the acquisition cost of generic losartan dropped, or in younger cohorts. Generic losartan could save approximately £200 million per year in drug costs for the NHS.

For heart failure, no head-to-head trials were found and an economic evaluation was not carried out.

Authors’ conclusions
The authors concluded that branded candesartan was not cost-effective compared with generic losartan for the treatment of hypertension from the perspective of the UK NHS. Generic losartan could save £200 million per annum in drug costs.

CRD commentary
Interventions:
A justification for the selection of the comparators was given. Losartan was the first angiotensin II receptor blocker to receive a marketing authorisation for the management of hypertension, while candesartan was the market leader in the authors’ setting. The introduction of generic losartan made the cost-effectiveness comparison more interesting.

Effectiveness/benefits:
The selection of the clinical data was well carried out, with the relevant sources identified by a systematic search of the literature. A detailed list of the inclusion and exclusion criteria was given. Two reviewers carried out the search, and any disagreements were discussed with a third investigator. All analyses were based on intention-to-treat, as recommended. The inclusion of head-to-head randomised trials ensured the validity of the clinical inputs. A validated approach was used for the meta-analysis that pooled evidence from multiple sources. Standard equations were used to estimate the long-term impact of changes in blood pressure. Limited details of the utility valuations were given, but they were from a NICE guideline, which was likely to have followed high-quality methods. QALYs were an appropriate benefit measure because the disease has a substantial impact on both survival and quality of life.

Costs:
The cost categories were consistent with the perspective and the data sources reflected the UK NHS setting, but a breakdown of cost items was not given, except for drug prices, with other costs presented as category totals. The price year and discounting were clearly reported. The cost estimates were treated deterministically and only the price of losartan was varied in the sensitivity analyses. No information on the patterns of resource consumption was given.

Analysis and results:
An appropriate incremental approach was used to synthesise the costs and benefits of the alternative strategies. The projected costs and benefits were not presented; only the incremental cost-utility ratios were given. Limited information on the structure and assumptions of the decision model was given. The uncertainty was partly investigated, using a deterministic approach, which considered variations in the model inputs singly and focused on selected parameters. The results might be transferable to settings with a similar cost structure.

Concluding remarks:
The cost-effectiveness framework was conventional and the clinical analysis was very well conducted. The authors’ conclusions appear to be robust.

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