Cost effectiveness of duloxetine in the treatment of diabetic peripheral neuropathic pain in the UK

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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 investigated the six-month costs and health benefits of using duloxetine as an additional treatment to the recommended current practice, in the UK, in diabetic patients experiencing peripheral neuropathic pain. The authors concluded that second-line duloxetine created potential cost-savings to the health system while also yielding important improvements to the numbers of responders and QALYs gained. The study methods were transparent, thorough and appropriate and the authors’ conclusions reflect the analysis undertaken.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study estimated the cost-effectiveness of duloxetine for peripheral neuropathic pain in patients with diabetes mellitus. A hypothetical cohort of 1,000 adults were assumed to have symmetrical diabetic peripheral neuropathy (DPN), with daily glycaemic control and daily pain, present for at least six months.

Interventions
Duloxetine, a five-hydroxytryptamine and norepinephrine uptake inhibitor, at a dose of 60mg per day, was compared with the current treatment for DPN, in the UK. This was based on clinical practice guidelines and was first-line treatment with a tricyclic antidepressant (amitriptyline, 75mg), followed by an anticonvulsant (gabapentin, 1,800mg), and then an opioid-related therapy (tramadol, 300mg). Duloxetine was considered in addition to the above sequence of treatments as first-, second-, third- and fourth-line therapy.

Location/setting
UK/out-patient care.

Methods
Analytical approach:
A decision analytic model was used to evaluate the costs and effects over six months of treatment. The efficacy data were derived from published studies. The authors stated that the perspective was that of the UK National Health Service (NHS).

Effectiveness data:
The effectiveness data, for the treatment response from baseline pain severity, were categorised into three levels; no response (under 30% improvement), partial response (30 to 49% improvement), or full response (30% improvement or more, or 50% improvement or more). A structured literature review of the published clinical data, using Medline and internet databases, was used to obtain the data on the relative risk and proportion of treatment responses for the five drugs. The sources included two randomised controlled trials (RCTs) of duloxetine and placebo (Goldstein, et al. 2005, and Raskin, et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details) and seven RCTs for the remaining drugs. Clinical opinion was used for the time to treatment switch due to a lack of efficacy or adverse events, but no further details of how and from whom this opinion was derived, were given.

Monetary benefit and utility valuations:
The UK utility weights were taken from a pivotal study (McCrink, et al. 2006, see ‘Other Publications of Related
Interest’ below for bibliographic details), which derived the weights using the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
The measures of benefit were quality-adjusted life-years (QALYs) and the numbers of additional full and partial responders.

Cost data:
The resources, included in the cost analyses, were drugs, out-patient visits (endocrinology) and general practitioner (GP) visits, and treatment switching. Drug doses were obtained from clinical studies and the unit drug costs were obtained from the British National Formulary. Out-patient visits were valued using the NHS National Reference Costs 2004 and GP visits, using community and hospital care costs published by the Personal Social Services Research Unit 2004. All costs were reported in UK pounds sterling (£).

Analysis of uncertainty:
One-way and threshold analyses were performed, in which the values of all the major parameters were altered. Probabilistic sensitivity analyses were also undertaken, using 5,000 iterations. The details of the distribution types, mean, and upper and lower values were presented in full. Cost-effectiveness acceptability curves, incremental cost-effectiveness scatter plots, and tornado diagrams were used to present the results of the uncertainty analyses.

Results
The treatment cost, per 1,000 patients, was £306,148 at baseline without duloxetine, £271,358 for first-line treatment with duloxetine, £229,077 for second-line treatment, £310,487 for third-line treatment, and £309,607 for fourth-line treatment.

The additional QALYs gained, per 1,000 patients, were 1.6 for third- and fourth-line, 1.9 for second-line, and 2.5 for first-line treatment with duloxetine compared with baseline.

Duloxetine produced higher QALYs and lower costs than (i.e. dominated) the baseline treatment option, when used for first- and second-line treatments. The incremental cost per QALY was £2,698 for third-line, and £2,109 for fourth-line duloxetine treatment over baseline.

The sensitivity analyses showed that second-line duloxetine remained dominant across a wide range of different parameter values. The base-case incremental costs were most sensitive to gabapentin and duloxetine drug costs and the incremental costs per QALY were strongly influenced by the response rates. The results of the probabilistic sensitivity analyses suggested a 94% probability that second-line duloxetine treatment would be cost-saving and produce additional QALYs.

Authors’ conclusions
The authors concluded that the inclusion of duloxetine was a cost-effective strategy, when used as a second-line treatment prior to the use of an anticonvulsant, as this would provide additional benefits and reduced health care costs, for patients with diabetic peripheral neuropathic pain, in the UK.

CRD commentary
Interventions:
The interventions were clearly reported and the usual treatment group reflected the recommended clinical practice in the UK. The substitution of pregabalin for gabapentin did not alter the overall findings.

Effectiveness/benefits:
The effectiveness data were derived from a structured literature review of published studies. The sources included 10 RCTs that are likely to provide high quality evidence on drug efficacy. The quality of life data were derived from one pivotal study, which used the most common and acceptable preference-based generic quality of life tool (EQ-5D). However, as the analysis relied on the quality of these sources and extensive details were not provided, the primary studies should be consulted for an assessment of their validity and relevance.
Costs:
The types of costs appeared appropriate for a health provider (UK NHS) perspective. The sources of these costs were clearly reported. Discounting was not applied, but this was appropriate given the short six-month time horizon.

Analysis and results:
The costs and effects were combined into incremental cost-effectiveness ratios and all results were clearly reported and illustrated. The sensitivity analyses were transparent and comprehensive, thus enabling the reader to capture the impact on the base-case results of the uncertainty around the input parameters. The authors discussed a number of limitations to their study, including a lack of evidence for the assumption that pregabalin was equivalent to gabapentin, and the fact that the clinical efficacy of treatment was independent of its place in the treatment sequence.

Concluding remarks:
The methodological quality of the study appears to have been robust and was explicitly and clearly reported. The authors' conclusions seem to be sound.

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Other publications of related interest


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