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 objective was to examine the cost-effectiveness of pregabalin as an additional therapy in comparison with usual care in patients with refractory partial epilepsy. The authors concluded that the cost-effectiveness of pregabalin compared favourably with the published estimates of the cost-effectiveness of other add-on antiepileptic drugs. The study was well conducted and satisfactorily presented. The authors’ conclusions were valid.

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

Study objective
The objective was to examine the cost-effectiveness of pregabalin as an additional therapy in comparison with the usual care in patients with refractory partial epilepsy, which was not adequately controlled on at least one standard antiepileptic drug.

Interventions
Pregabalin (300mg per day) was compared with no additional therapy. The treatment was assumed to be given for up to one year.

Location/setting
USA/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a Markov model which simulated patient management for the two strategies, while considering the efficacy of the drugs and the impact of their side effects. The time horizon of the analysis was one year and the authors did not report the perspective.

Effectiveness data:
The clinical data appear to have been derived from a selection of known, relevant studies. The treatment effect for the study drug was taken from randomised controlled trial (RCT)s of pregabalin versus placebo. The data for patients participating in these RCTs, prior to randomisation, were used to assess the frequency of seizure-days without add-on therapy. Data from more than one RCT were pooled to create single estimates. The data on side effects were taken from a published meta-analysis of add-on therapies for patients with refractory partial epilepsy. The primary clinical outcome was the number of seizure-days with and without pregabalin.

Monetary benefit and utility valuations:
The utility values were derived from a US survey of approximately 200 patients with partial seizures using a 0 to 100 scale.

Measure of benefit:
The summary benefit measures were seizure-free days (SFDs) and quality-adjusted life-years (QALYs).

Cost data:
The economic analysis considered only the cost of pregabalin, on the assumption that all other costs were common to both strategies. The cost of pregabalin was calculated using the average wholesale prices from the Red Book. The average daily dose in clinical practice was considered. All costs were in US dollars ($) and the price year appears to have been 2006.

Analysis of uncertainty:
A comprehensive probabilistic approach was used to address the issue of uncertainty using stochastic distributions for model inputs in order to generate confidence intervals (CIs) for the cost-effectiveness results. A series of univariate sensitivity analyses was also carried out to consider variations in the model assumptions such as alternative dosages of pregabalin (150mg per day to 600mg per day) or inclusion of the costs of specialist visits for patients discontinuing pregabalin therapy. Such costs were based on Medicare payment rates. Variations in other model inputs appear to have been based on authors' opinions.

Results
The number of SFDs, over one year, was 162.2 with pregabalin, and 138.4 with usual care only, and the QALYs were 0.520 with pregabalin, and 0.507 without. The cost of pregabalin was $678 (the cost was zero for the control group).

The incremental cost per SFD gained with pregabalin was $28.45 (95% CI: 27.25, 29.44). The incremental cost per QALY gained with pregabalin was $52,893 (95% CI: 49,249, $56,983).

The sensitivity analysis showed that the utility decrements associated with a seizure-day were the most influential model input, with the incremental cost per QALY ranging from $29,980 to $300,003. Variation in other model inputs did not have a strong impact on the cost-effectiveness results.

Authors' conclusions
The authors concluded that the cost-effectiveness of pregabalin compared favourably with the published estimates of the cost-effectiveness of other add-on antiepileptic drugs.

CRD commentary
Interventions:
The authors justified their selection of the comparators. Pregabalin was the newest antiepileptic drug to be approved by the US Food and Drug Administration for use as an add-on therapy for adults with partial onset seizures. The usual care was restricted to first-line drugs without any add-on ones. Thus, the two strategies were appropriately selected.

Effectiveness/benefits:
RCTs were used to derive the bulk of the evidence on treatment efficacy. They are generally regarded as a valid source of evidence given their methodological strengths. Thus, the clinical inputs were likely to be valid. The details of the patients' characteristics, follow-up, and other methodological issues, such as how the data were pooled, were not reported. Similarly, the details on the source for safety data (i.e. the meta-analysis) were not given. The derivation of the utility valuations was based on a single survey, which might not represent the most appropriate source of evidence, but the authors pointed out that there were few publications on the quality-of-life of patients on add-on therapy. QALYs are a validated benefit measure and are comparable with the benefits of other health care interventions, and this will help to overcome the difficulties associated with a disease-specific measure such as SFDs.

Costs:
The analysis of costs was restricted to drug costs, which were calculated using typical US sources. The authors did not state the perspective adopted, but the use of Medicare costs in the sensitivity analysis suggests that the viewpoint was that of the third-party payer. The unit costs and quantities of resources used were presented separately. The price year was not explicitly reported. The authors stated that considering only drug costs led to conservative estimates for pregabalin, since the favourable impact of a more effective drug on other health care resources was not included in the model.

Analysis and results:
The costs and benefits were appropriately synthesised. The issue of uncertainty was satisfactorily addressed in the
probabilistic sensitivity analysis. The results of both the base-case and the sensitivity analyses were clearly presented. The methodology of the decision model was described. The authors noted that a potential limitation of the analysis was the use of a one-year time horizon, which required assumptions on the clinical impact of treatment, given the 12-week follow-up period in the pregabalin RCTs. Another potential drawback was the threshold of 50% reduction in seizure frequency at six months which determined treatment continuation. Such a definition of treatment response might not reflect the real-world pattern of care and might not be generalisable to other health care systems.

Concluding remarks:
The study was well conducted and satisfactorily presented. The authors’ conclusions were valid.

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MeSH
Anticonvulsants /adverse effects /economics /therapeutic use; Ataxia /chemically induced; Cost-Benefit Analysis /statistics & numerical data; Costs and Cost Analysis; DNA-Binding Proteins; Disease-Free Survival; Dizziness /chemically induced; Drug Administration Schedule; Drug Costs; Drug Therapy, Combination; Epilepsies, Partial /drug therapy /economics; Follow-Up Studies; Health Care Costs; Humans; Models, Economic; Models, Theoretical; Outcome Assessment (Health Care) /statistics & numerical data; Pregabalin; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic /statistics & numerical data; Stochastic Processes; Transcription Factors; gamma-Aminobutyric Acid /adverse effects /analogs & derivatives /economics /therapeutic use

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