The cost effectiveness of rufinamide in the treatment of Lennox-Gastaut syndrome 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
The aim was to estimate the costs and clinical effectiveness of rufinamide as an additional therapy for children with Lennox-Gastaut syndrome (LGS). The authors concluded that rufinamide was cost-effective in increasing the successful treatment of patients with LGS. The reporting was not sufficiently clear to assess whether or not the conclusions are appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to estimate the costs and clinical effectiveness of rufinamide as an adjunctive therapy for children with Lennox-Gastaut syndrome (LGS).

Interventions
Rufinamide as the first addition to treatment was followed by standard antiepileptic drug therapy. This was compared with topiramate as the first addition, followed by standard therapy; lamotrigine as the first addition, followed by standard therapy; and standard therapy alone.

Location/setting
UK/secondary care.

Methods
Analytical approach:
The study used a state-transition model to synthesise the data from key clinical trials that compared the three treatments against placebo. The time horizon was three years, and the authors stated that the perspective was that of the UK NHS.

Effectiveness data:
The estimates of clinical effectiveness were from three placebo-controlled clinical trials of rufinamide, lamotrigine, and topiramate. These data were combined using mixed-treatment comparison models. The mean ages of patients in the three trials were 10, 11, and 14 years. The main clinical effectiveness outcome was the proportion of successfully treated patients, which were defined as patients with at least a 50% reduction in seizure frequency.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The primary measure of benefit was a one percent increase in the number of successfully treated patients.

Cost data:
The costs included those of the drugs, diagnostics, accident and emergency visits, and social services. The resource use data were from a survey of five physicians, and the prices were from NHS Reference Costs and the Personal Social Services Research Unit. All costs were in UK pounds sterling (£) at 2006 prices and discounted at a rate of 3.5% per year.
Analysis of uncertainty:
A one-way sensitivity analysis was performed by varying the hospitalisation rates, the discount rate, the costs, and the time horizon. The authors presented the results in a cost-effectiveness acceptability curve.

Results
Over the three-year time horizon, the rates of successful treatment, for tonic-atonic seizures (drop attacks), were 11.3% for rufinamide, 7.2% for topiramate, 5.2% for lamotrigine, and 3.3% for standard care.

The total discounted cost of rufinamide was £50,985, compared with £50,728 for topiramate, £50,975 for lamotrigine, and £51,437 for standard care.

The incremental cost for a 1% increase in the number of successfully treated patients, in terms of drop attacks, was £62 for rufinamide, compared with topiramate, and £2 for rufinamide, compared with lamotrigine. Rufinamide was dominant, as it was less costly and more effective, compared with standard care.

At a willingness-to-pay of £250 for a 1% increase in the number of successfully treated patients (drop attacks), the likelihood of rufinamide being the most cost-effective option was over 80%.

Authors' conclusions
The authors concluded that rufinamide was cost-effective in increasing the successful treatment of patients with LGS.

CRD commentary
Interventions:
The interventions were adequately described apart from standard care. Standard care appears to have been a mixture of antiepileptic drugs, such as valproate and benzodiazepines, without each of the three additional treatments, but some patients in the placebo arm of the rufinamide trial were receiving lamotrigine, topiramate, or both.

Effectiveness/benefits:
The effectiveness data were from trials with good designs and they were combined using appropriate methods. The key results from each trial were described well. The authors reported the proportion of treatment-limiting adverse events, but did not separate out these adverse events, which was required as only specific adverse-event costs were included. The distinction between drop attacks and total seizures was not made clear in the paper. The authors justified not using utility values to assess quality of life, as there were no suitable published values for children with LGS, but an economic evaluation published in the same year as this study, with one co-author (Verdian, et al. 2010, see 'Other Publications of Related Interest' below for bibliographic details), did use utility values that were previously estimated by that co-author.

Costs:
Those costs relevant to the perspective appear to have been included. The measurement of resource data was from a small survey of physicians, which might not have been the best source of evidence. The prices for these resources and their sources were reported and can be checked, but the annual costs of topiramate, lamotrigine, and rufinamide reported in table III did not match those reported in the text. The authors reported the price year and the discount rate.

Analysis and results:
The model structure was not completely clear. The text stated that patients could continue without their seizures controlled or switch to a new treatment, but patients who did not respond to the additional treatment were switched back to standard therapy. The authors did not explain why the total costs per treatment differed between the analyses with different outcomes (drop attacks or total seizures); the costs of the strategies should be independent of the choice of clinical outcome. The incremental analysis was appropriate for comparing the costs and outcomes of the treatment strategies. The three-year time horizon might not have been sufficient to fully capture the differences in costs and outcomes between treatments, but the authors discussed this and explained why they selected it. They justified some key decisions and discussed the strengths and limitations of the study. The authors conducted a sensitivity analysis on two values for the probability of hospitalisation given a drop attack, but it would have been useful to assess the probability of hospitalisation at which rufinamide was no longer cost saving compared with standard care.
Concluding remarks:
The reporting was not sufficiently clear to assess whether or not the conclusions are appropriate.

Funding
Funding received from Eisai Ltd, manufacturer of rufinamide.

Bibliographic details

PubMedID
20151724

DOI
10.2165/11313640-000000000-00000

Original Paper URL

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Anticonvulsants /economics /therapeutic use; Child; Child, Preschool; Computer Simulation; Cost-Benefit Analysis /statistics & numerical data; Epilepsy, Absence /drug therapy /economics; Fructose /analogs & derivatives /economics /therapeutic use; Great Britain; Health Care Costs /statistics & numerical data; Humans; Infant; Intellectual Disability /drug therapy /economics; Models, Economic; Randomized Controlled Trials as Topic; Syndrome; Time Factors; Treatment Outcome; Triazines /economics /therapeutic use; Triazoles /economics /therapeutic use

AccessionNumber
22010000759

Date bibliographic record published
10/11/2010

Date abstract record published
06/07/2011