Cost-effectiveness of add-on lamotrigine therapy in clinical practice

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.

Health technology
Patients with epilepsy that were either not controlled or were suffering from intolerable side effects from medication were given lamotrigine (LTG) as an add-on therapy.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The patients were at least 18 years old. All patients were receiving add-on LTG therapy because of uncontrolled epilepsy or intolerable side effects from conventional AEDs or vigibatrin, and were under the care of neurologists in the hospital.

Setting
The setting was secondary and tertiary care. The economic study was carried out in the Netherlands.

Dates to which data relate
The dates to which the effectiveness and resource evidence referred were not given. The price year was 2004.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The same patients provided both the effectiveness and the cost data. The whole study was carried out retrospectively.

Study sample
No power calculations were reported. All patients meeting the inclusion criteria were included in the study. A total of 165 patients were included in the study, for one year they received conventional AEDs and for one year they received LTG.

Study design
This was a multi-centre (35 centres) before-and-after study. The patients were studied for 2 years in total. There was no follow-up after those 2 years.
Analysis of effectiveness
As the same patients were studied for both treatments, they were comparable. If LTG was prescribed for inadequate seizure control, then LTG therapy was considered effective if there was a reduction in mean seizure frequency of at least 50% during the year after starting LTG and no other AED had been added to the patient's medication. If LTG was prescribed for intolerable adverse effects of AEDs, then LTG was considered effective if there was no clinically relevant increase in mean seizure frequency in the year following the introduction of LTG and no other AED had to be added to the patient's medication.

Effectiveness results
Overall, LTG was effective in 78 of the 165 patients (47%).

In the group receiving LTG because of inadequate seizure control, effectiveness was 40.2% and 14% of patients became seizure free.

In the group receiving LTG because of intolerable side effects of other AEDs, effectiveness was 62.3%. Twenty-six percent of patients were seizure free before LTG therapy and 25% were seizure free afterwards.

Clinical conclusions
LTG add-on therapy improved outcomes for the class of patients studied.

Measure of benefits used in the economic analysis
The measure of benefits used was the percentage of patients treated effectively.

Direct costs
Discounting was not carried out as the costs were incurred during less than 2 years. The costs included were for outpatient department visits, emergency room visits, hospital admissions, diagnostic investigations (radiology, EEG and laboratory tests) and anti-epileptic medication. The resource data were obtained from the hospital, while the price data were taken from a published source. The price year was 2004.

Statistical analysis of costs
A bootstrap analysis was conducted to produce a joint distribution of costs and effectiveness.

Indirect Costs
No indirect costs were measured.

Currency
Euros (EUR).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
The effectiveness of LTG was 47%. It was assumed that the effectiveness would have been zero without LTG since LTG was given to patients for whom treatment had previously failed.
Cost results
The average costs were EUR 1,266.3 in the year preceding LTG use and EUR 1,719.0 in the year following its introduction.

The costs of adverse effects would have been taken into consideration in the costing.

Synthesis of costs and benefits
The incremental cost-effectiveness ratio (ICER), that is, the cost of obtaining one successfully treated patient, was EUR 954.

The ICER for patients who started LTG because of inadequate seizure control was EUR 849, while that for patients who started LTG because of adverse effects was EUR 1,094.

Authors’ conclusions
Lamotrigine (LTG) therapy can be effective for patients who cannot tolerate conventional anti-epileptic drugs (AEDs) or for whom they are ineffective, but this benefit costs on average EUR 452.80.

CRD COMMENTARY - Selection of comparators
The choice of the comparator, conventional AEDs, was justified by it representing current practice in many settings. You should decide whether the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The source of the effectiveness data was a single study. The study design, a before-and-after study that observed patients before and after the introduction of a treatment, was not the most appropriate design for the study question. This is because the condition of the patients at the beginning of the first and second years might not have been the same. Also, the authors were studying two types of patients, those for whom conventional therapy was ineffective and those for whom it produced intolerable side effects. It would have been better to have had one type of patient, particularly as the authors did not measure the effectiveness of the LTG therapy in terms of side effects. The study sample was representative of the study population, as it included all adult patients being given LTG because of the ineffectiveness of AEDs or their intolerable side effects. Since the patients were the same in the intervention and comparator groups there was no need to show comparability, unless they had changed in some way during the first year of the study. The analysis of effectiveness was generally handled credibly, with the exception that there were no data for side effects. There were no other sources of effectiveness data.

Validity of estimate of measure of benefit
The estimation of benefits, the percentage of patients treated effectively, was obtained directly from the effectiveness analysis.

Validity of estimate of costs
From the cost perspective adopted (i.e. the hospital system), all the relevant categories of cost appear to have been included. The authors acknowledged that it would have been better to have included the direct costs borne by the patients and families as well as the indirect costs. Their inclusion would have meant that the cost-advantage for conventional AEDs would have been much less. The costs and the quantities were reported separately. The resource use quantities were taken from a single study and no other sources, while the prices were taken from published sources and a source that was not clear (described as tariffs). No statistical or sensitivity analyses of either the quantities or prices were performed. The price year was reported.

Other issues
The authors made appropriate comparisons of their results with the findings from other studies. The issue of generalisability to other settings was not addressed. The authors did not present their results selectively. For the reasons given above, it was unclear whether the authors' conclusions reflected entirely the scope of the analysis. The authors reported some limitations of their study. The patients were not blinded and not controlled. We do not know what the outcomes would have been for patients who stayed with conventional AEDs for 2 years; they might have been switched to LTG because they were in a particularly bad period of their disease, which might have improved with their existing medication.

**Implications of the study**

The authors regarded this study as supporting the use of LTG for patients who have problems with conventional AEDs. They used an analysis of quality-adjusted life-years (QALYs) in their discussion to argue that the extra cost of LTG therapy is worthwhile when comparisons are made with other costs in health care that are considered acceptable. However, they did not give sufficient information to enable an assessment of their QALY analysis.

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