Cost-effectiveness analysis of lamivudine and adefovir dipivoxil in the treatment of patients with HBeAg-negative chronic hepatitis B

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
The study compared lamivudine and adefovir dipivoxil in the treatment of patients with hepatitis B 'e' antigen (HbeAg)-negative chronic hepatitis B (CHB). Both drugs involved a daily oral dose of 100 mg.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with chronic HbeAg-negative CHB. No further details of the study population were provided.

Setting
A specific setting was not specified in the study, but it appears to have been secondary care. The economic study was carried out in Spain.

Dates to which data relate
The effectiveness data were derived from studies published between 1999 and 2005. The dates for the resource use data were not stated. The costs were presented for the year 2003.

Source of effectiveness data
The effectiveness data were derived from a review of published work and from expert opinion.

Modelling
A decision tree was created in which a treatment decision was made at the beginning of each year for 4 years. Every year the patients would either respond or not respond to treatment, or the patient would resist or not resist treatment. The probabilities of response and resistance changed each year. A graphical representation of the tree with the probabilities was presented in the paper.

Outcomes assessed in the review
The outcomes assessed were the probability of response, the probability of resistance, and the probability of non-response for each strategy in each of the 4 years.
Study designs and other criteria for inclusion in the review
Clinical studies were chosen for inclusion in the review if they used the same treatment regimen as the two drugs being evaluated for 4 years.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Approximately 9 studies were included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
All the clinical probabilities used in the decision analysis were reported in the paper, but they were too numerous to report here.

Methods used to derive estimates of effectiveness
A panel of experts was used to derive some of the estimates of effectiveness. No further details were given.

Estimates of effectiveness and key assumptions
There were too many estimates based on expert opinion to be reported here. Please see the original paper.

Measure of benefits used in the economic analysis
The measure of benefit used was the virological response at the end of year 4.

Direct costs
The unit costs and the resource quantities were reported separately. The direct costs of the public health system were included. These covered the costs of drug acquisition, visits, and diagnostic or laboratory tests to determine virological response and HBV drug resistance. The costs were obtained from published sources, while a panel of hepatologists estimated the quantities. The costs were presented for the year 2003. A discount rate of 3% was applied to the costs.

Statistical analysis of costs
No statistical analysis of the costs was reported.
**Indirect Costs**
The indirect costs were not included.

**Currency**
Euros (EUR).

**Sensitivity analysis**
A sensitivity analysis was performed on the variables assumed to be sensitive. These included:

- not applying a discount rate to the costs;
- increasing the dosage of lamivudine from 100 to 150 mg/day;
- considering decompensation costs to be zero;
- increasing from two to four times per year the number of visits and laboratory tests investigating adefovir resistance in patients treated with lamivudine;
- reducing by half the cost of the diagnostic test of HBV resistance; and
- adjusting the lamivudine arm response rate at year 4 with the intention of achieving the threshold value.

**Estimated benefits used in the economic analysis**
The virological response at year 4 was 40.4% for the lamivudine arm and 78.0% for the adefovir dipivoxil arm.

**Cost results**
The estimated total costs for 4 years of treatment for lamivudine and adefovir dipivoxil arms as initial treatment, with a 3% discount rate, were EUR 11,457 (lamivudine) and EUR 21,939 (adefovir dipivoxil), respectively.

**Synthesis of costs and benefits**
The costs and benefits were combined by calculating a cost-effectiveness ratio (the average cost per patient with successful therapy response at year 4) and an incremental cost-effectiveness ratio (ICER; the cost per additional patient responding to adefovir dipivoxil). The ICER is the important statistic.

The cost-effectiveness ratio was EUR 28,375 for the lamivudine arm and EUR 28,132 for the adefovir dipivoxil arm.

The ICER of adefovir dipivoxil versus lamivudine was EUR 27,872.

The sensitivity analysis found that only two variables significantly impacted on the results. These were the virological response rate to adefovir dipivoxil and the virological response rate to lamivudine. If the proportion of the lamivudine arm responding at year 4 increased to above 40.7%, there was a favourable impact on the average cost-effectiveness analysis for the lamivudine strategy.

**Authors’ conclusions**
Long-term treatment with adefovir dipivoxil is a cost-effective strategy in patients with hepatitis B ‘e’ antigen (HbeAg)-negative chronic hepatitis B (CHB).
The reason for the choice of the comparator was clear. It was chosen because it represented the treatment provided for patients with HBeAg-negative chronic hepatitis B. You should consider whether this is a widely used technology in your own setting.

**Validity of estimate of measure of effectiveness**

The authors did not state that a systematic review of the literature had been undertaken. It was not stated how the studies were identified and selected for inclusion, other than that they were concerned with the same treatment regimen as the present study. Therefore, some relevant studies might not have been included, thus biasing the estimation of the effectiveness parameters. No details of how the studies were combined were provided. Only one of the effectiveness measures was subjected to a sensitivity analysis. A panel of experts was used to derive some estimates of effectiveness. However, no details of who the experts were, or how they were selected, were given.

**Validity of estimate of measure of benefit**

The estimation of benefits was modelled. The instrument used to derive a measure of health benefit (decision analysis model) was appropriate.

**Validity of estimate of costs**

All the categories of costs relevant to the perspective adopted were included in the analysis. The costs and the quantities were reported separately, which enhances the generalisability of the study findings. A sensitivity analysis of the quantities was conducted, using ranges that appear to have been appropriate. A sensitivity analysis of some of the prices was also conducted. Appropriate discounting was performed and the price year was identified.

**Other issues**

The authors acknowledged that their study is the first cost-effectiveness analysis to examine the long-term therapy of adefovir dipivoxil as first-line treatment for HBeAg-negative patients. The issue of generalisability to other settings was partially addressed by performing sensitivity analysis on some of the costs and quantities included in the analysis. The authors did not present their results selectively.

**Implications of the study**

The authors suggested that, from an economic point of view, adefovir dipivoxil is a cost-effective strategy in first-line treatment with oral antiviral drugs.

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