Economic evaluation of lamivudine compared with interferon-alpha in the treatment of chronic hepatitis B in the United States

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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.

Health technology
Lamivudine was compared with interferon-alpha in the treatment of chronic hepatitis B in the USA.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients suffering from chronic hepatitis B. No inclusion or exclusion criteria were reported.

Setting
The setting was a hospital. The economic analysis was carried out in the USA.

Dates to which data relate
Effectiveness and resource use data were collected from studies published between 1998 and 2000. Cost data were from 1999. The price year was 1999.

Source of effectiveness data
Effectiveness estimates were taken from a review of completed studies.

Modelling
A one-year decision analytic model was used to determine the cost-effectiveness of the two drug treatments for chronic hepatitis B.

Outcomes assessed in the review
The review assessed the HBeAg seroconversion rate and the rate of progression to cirrhosis.

Study designs and other criteria for inclusion in the review
Effectiveness estimates were taken from three randomised controlled trials.
Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
Three primary studies were included in the review.

Methods of combining primary studies
The HBeAg seroconversion rate for treated patients was obtained from a randomised controlled trial of lamivudine versus IFN-alpha and the HBeAg seroconversion rate for untreated patients was obtained from pooling estimates from two, placebo-controlled trials. The rate of progression to cirrhosis, for those who did not seroconvert, was obtained by pooling estimates. For lamivudine these estimates were from the two placebo controlled trials and the lamivudine versus IFN-alpha trial. The estimates for placebo and IFN-alpha was assumed to be the same weighted average due to the absence of a statistically significant difference and the small sample.

Investigation of differences between primary studies
Not stated.

Results of the review
The HBeAg seroconversion rate was 17.5% for patients treated with lamivudine and 18.8% for patients treated with interferon-alpha.

The HBeAg seroconversion rate for untreated patients was 5%.

The rate of progression to cirrhosis was 2.2% for patients treated with lamivudine, and 8.7% for patients treated with interferon-alpha and for untreated patients.

Measure of benefits used in the economic analysis
The measures of benefits used in the economic analysis were the number of HBeAg seroconversions and the number of cirrhosis cases.

Direct costs
Direct costs were not discounted due to the short time horizon of the study (less than one year). Quantities and unit costs were reported separately for the drugs. Direct costs were the costs of drugs and hospitalisation due to chronic hepatitis B. The quantity/cost boundary adopted was that of a third-party payer. Medication costs were based on average wholesale prices. The price year was 1999. Cost estimates were updated to 1999 US dollars using the consumer price index for US medical care services. It was assumed that the fixed annual drug budget contained funds sufficient for the treatment of 100 patients with interferon-alpha. Within this budget of $558,910, it would be possible to treat 353 patients with a standard 12-month course of lamivudine therapy.

Statistical analysis of costs
No statistical analysis of costs was reported.

**Indirect Costs**
Indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were reported on the cost of lamivudine and on the seroconversion rate.

**Estimated benefits used in the economic analysis**
Among the 353 patients treated with lamivudine, 62 would achieve HBeAg seroconversions and 6 would progress to cirrhosis. If 100 patients were treated with interferon-alpha and the remaining 253 patients were left untreated, 32 patients would seroconvert (19 treated, 13 untreated) and 28 patients would progress to cirrhosis (7 treated, 21 untreated).

**Cost results**
Given that 22 fewer patients receiving lamivudine would progress to cirrhosis, treatment with lamivudine would result in hospital cost savings of $309,386. These cost savings offset the drug costs of lamivudine therapy by 55%.

**Synthesis of costs and benefits**
Lamivudine therapy had a cost per additional HBeAg seroconversion obtained of $12,703 compared with no treatment. The cost per additional HBeAg seroconversion obtained for interferon-alpha in comparison to no treatment was $39,922. For lamivudine not to be cost-effective compared to interferon-alpha, the cost of a one-year course with lamivudine would have to increase by 250% or the one-year seroconversion rate obtained with lamivudine would need to decrease by 50%.

**Authors' conclusions**
The authors argued that, from the perspective of a third party payer within a fixed drugs budget, lamivudine is a more cost-effective therapy than interferon-alpha for the treatment of chronic hepatitis B.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the choice of comparator, namely that they were currently available drug treatments. You, as a user of the database, should decide if these health technologies are relevant to 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. More details about the sources searched, search strategies employed and inclusion criteria for studies to be selected could have been provided. Adequate details about the methods of combining primary effectiveness estimates were provided. As the authors stated, effectiveness estimates were taken from a small number of primary studies. Effectiveness estimates for both treatments were taken at 12 months after initiation of therapy, although the treatment duration varied across treatments.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis. The effect of the two drug treatments
on quality of life was not considered, which makes it difficult to compare the results with those from studies that report on similar health technologies. The authors suggested that, if these factors were not accounted for, the cost-effectiveness of lamivudine would increase. However, in terms of seroconversion rate, it must be remembered that IFN-alpha is better than lamivudine, by 0.05%. The authors also made assumptions about the rate of progression to cirrhosis, such that the rate for IFN-alpha was much higher.

Validity of estimate of costs
Good features of the cost analysis were that the perspective was explicit and therefore only drug costs were included, and that the price year was reported. However, the authors made some assumptions, which should be questioned. Firstly, the size of the budget was arbitrarily calculated based on treating 100 patients with IFN-alpha. Secondly, it was assumed that the incidence of chronic hepatitis B (or number eligible for treatment) was equal to the number of patients who could be treated with lamivudine within this arbitrary budget. Indeed, it can be shown that, if the incidence was at least as big as the number who could be treated within a fixed drug budget, taking no other costs into account, this method is correct. However, if the budget is actually big enough to treat all incident cases with IFN-alpha, then, if other health outcomes are not considered (i.e. only the seroconversion rate), then all would be treated with IFN-alpha. Where the budget is not limited to treatment with just these drugs, for example a hospital budget, then the question of whether either drug were cost-effective would require a comparison with the incremental costs and benefits of other therapies. However, the authors performed sensitivity analyses on the cost of lamivudine and reported hospital cost savings due to fewer cases of cirrhosis with lamivudine. Treatment costs and indirect costs were not considered.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, but did not address the issue of generalisability to other settings. The authors do not seem to have presented their results selectively. The study considered patients suffering from chronic hepatitis B and this was reflected in the authors’ conclusions. The authors acknowledged that they did not investigate combination treatment options such as lamivudine plus interferon-alpha. Rather than determining the cost-effectiveness of lamivudine and interferon-alpha in two patient samples, the authors used a fixed budget. This determined the sample size. In particular, it implied that 253 patients in the interferon-alpha group were left untreated. The cost-effectiveness of interferon-alpha should thus be based on the 100 patients who were actually treated and not, as in this case, on the total sample of 353 patients.

Implications of the study
The authors stated that, given a fixed drug budget, lamivudine allows a greater number of patients to achieve HBeAg seroconversion, reduces the rate of progression to cirrhosis and provides additional histological benefits to patients, regardless of whether seroconversion occurs. These conclusions should, however, be viewed in the light of the limited perspective, assumptions regarding numbers eligible to be treated, and other issues described above.

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