The cost-effectiveness analysis of entecavir in the treatment of chronic hepatitis B (CHB) patients in Poland


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
This study evaluated the use of entecavir for the treatment patients with chronic hepatitis B. The authors concluded that entecavir was the preferred treatment, compared with lamivudine, for nucleoside-naive patients who were hepatitis B e antigen positive or negative and, compared with adefovir, for lamivudine-refractory patients. Despite some limitations in the effectiveness data, the methods of the analysis were generally sound and the authors' conclusions appear to be appropriate.

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

Study objective
This study compared the cost-effectiveness of entecavir versus lamivudine and versus adefovir for the management of patients with chronic hepatitis B.

Interventions
Two cohorts of patients were considered. For patients who were nucleoside-naive and either hepatitis B e antigen positive or negative, two years of treatment with entecavir (0.5mg per day) was compared with lamivudine (100mg per day). If resistance to lamivudine developed, adefovir dipivoxil was given as a salvage treatment. For patients who were refractory to lamivudine, 10 years of treatment with entecavir (1mg per day) was compared with adefovir (10mg per day).

Location/setting
Poland/secondary care.

Methods
Analytical approach:
A decision analytic model with a 10-year time horizon was used to synthesise the cost and effectiveness data from a variety of sources. The authors reported that the health care payer perspective was used.

Effectiveness data:
The effectiveness data were from published literature. The treatment efficacy estimates were from international randomised controlled trials. The estimates for liver complications were from a 13-year prospective, population-based cohort study. The life expectancy was estimated from national statistics. The primary clinical outcomes were the number of cases of hepatocellular carcinoma, decompensated cirrhosis, and compensated cirrhosis.

Monetary benefit and utility valuations:
The utility values were from a published study. They were derived from a British population, using the standard gamble technique.

Measure of benefit:
Life-years saved (LYS) and quality-adjusted life-years (QALYs) were the summary measures of benefit. They were discounted at an annual rate of 5%.
Cost data:
The direct costs were those for the acquisition of the antiviral drugs and the treatment of compensated and
decompensated cirrhosis, and hepatocellular carcinoma. Medication resource use was derived from clinical trials and
the treatment costs for chronic hepatitis B were from a Polish costing study. All costs were expressed in Polish zlotych
(PLN) and inflated, where necessary, using the consumer price index. The price year was 2006 and the costs were
discounted at an annual rate of 5%.

Analysis of uncertainty:
The parameter uncertainty was investigated in a deterministic one-way sensitivity analysis on a number of parameters
that included: the health state utilities for compensated and decompensated cirrhosis, and hepatocellular carcinoma; the
age at the start of treatment; the duration of treatment; the discount rate; and the treatment costs in each health state.

Results
An incremental analysis was performed and the results were presented separately for men and for women.

For patients who were nucleoside naive and hepatitis B e antigen positive, two years of treatment with entecavir
compared with lamivudine saved PLN 2,062,796 per 100 patients in drug acquisition costs and PLN 369,676 per 100
men and PLN 373,701 per 100 women in chronic hepatitis B complication costs. It resulted in an increase in LYS of 30
per 100 men and 32 per 100 women; and an increase of 28 QALYs per 100 men and 30 QALYs per 100 women.

For patients who were nucleoside naïve and hepatitis B e antigen negative, two years of treatment with entecavir
compared with lamivudine saved PLN 2,084,739 per 100 patients in drug acquisition costs and PLN 185,066 per 100
men and PLN 187,564 per 100 women in chronic hepatitis B complication costs. It resulted in an increase in LYS of 14
per 100 men and 16 per 100 women; and an increase of 13 QALYs per 100 men and 15 QALYs per 100 women.

For patients who were lamivudine refractory, 10 years of treatment with entecavir compared with adefovir saved PLN
424,383 per 100 men and PLN 429,007 per 100 women in chronic hepatitis B complication costs, with equal drug
costs. It resulted in an increase in LYS of 27 per 100 men and 30 per 100 women; and an increase of 26 QALYs per
100 men and 29 QALYs per 100 women.

For all patient populations entecavir was dominant, which means it was more effective and less costly than the
alternative. These results were robust in most of the variations tested in the sensitivity analyses.

Authors’ conclusions
The authors concluded that entecavir was the preferred strategy as it was more effective and less costly than either
lamivudine (with adefovir as a salvage treatment) in nucleoside-naive patients who were hepatitis B e antigen positive or
negative, or adefovir in lamivudine-refractory patients.

CRD commentary
Interventions:
The rationale for the choice of the interventions was clearly stated. The interventions were chosen on the basis of their
availability and use in the authors’ setting (Poland).

Effectiveness/benefits:
The clinical estimates were derived from selected published studies, but no systematic review of the literature was
reported and it is not possible to determine if the best available evidence was used. The main characteristics of the
selected studies, including one trial, were briefly reported, but not sufficiently for an assessment of the validity of the
data. The utilities were derived from a published study and the details of the population and the valuation method were
reported. It was necessary to use data from a British population as there were no other data and these estimates were
tested in the sensitivity analysis. Both LYS and QALYs are benefit measures that allow cross-disease comparisons.

Costs:
The included direct costs reflected the perspective. The medication costs were clearly reported, along with number of
days on therapy. The treatment costs for the health states associated with chronic hepatitis B progression were presented
as totals, which might limit the generalisability of the analysis. Discounting and the price year were reported, facilitating future reflation exercises. Inflation adjustments were made using the consumer price index, but the medical component of this index might have been more appropriate; the impact inflation adjustments is likely to have been minimal.

**Analysis and results:**
The model structure was clearly reported, with a diagram and the modelling assumptions. An appropriate incremental approach was adopted for the synthesis and, correctly, no incremental cost-effectiveness ratios were calculated as one treatment dominated the other. One-way sensitivity analyses were conducted to assess the impact of the modelling assumptions, to some extent, but probabilistic sensitivity analysis would have more fully explored the impact of parameter uncertainty on the results. The results of the base case and the sensitivity analysis were adequately reported. The authors acknowledged a number of limitations of their study and these mainly related to the quality and availability of the effectiveness data.

**Concluding remarks:**
Despite some limitations in the effectiveness data, the methods of the analysis were generally sound and the authors’ conclusions appear to be appropriate.

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