Cost-effectiveness of peginterferon alpha-2a compared with lamivudine treatment in patients with HBe-antigen-positive chronic hepatitis B in the United Kingdom


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 two treatment strategies for chronic hepatitis B (CHB) infection. The treatments were peginterferon (pegIFN) alpha-2a (40 kDa) 180 microg monotherapy and lamivudine 100 mg monotherapy. An additional scenario was evaluated in which adefovir salvage treatment was used for lamivudine-resistant patients.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis

Study population
The population comprised patients with CHB virus infection. The study took its main data and results from several clinical studies.

Setting
The setting for the study was outpatient and inpatient care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data used in the model came from studies published between 1988 and 2006. The cost data were from 2005. The price year was 2005.

Modelling
A Markov state transition model was used to simulate the natural history of HBeAg-positive CHB. The health states were reported and a number of modelling assumptions were fully justified. In the base-case, a 4-year intervention horizon was assumed for lamivudine. Transition probabilities and their sources were reported. The model was analysed using the Monte Carlo technique.

Study designs and other criteria for inclusion in the review
The parameters used in the model included natural history estimates considering the course of CHB infection, disease progression, virological response and viral resistance, as well as treatment efficacy estimates, treatment durability and the effect of treatment-related adverse events. Utilities for different health states were also incorporated.

Sources searched to identify primary studies
Sources included meta-analyses, randomised clinical trials, observational studies and other studies of varied design (van Nunen et al. 2003, Lau et al. 2005, Crowley et al. 2000, Wong et al. 1995, Bennett et al. 1997, see 'Other Publications of Related Interest' below for bibliographic details). UK life tables were used to estimate all-cause mortality rates for patients without disease-attributable mortality risks.

Methods used to derive estimates of effectiveness
The process used to identify the data was not reported. No inclusion criteria were specified for any parameters. The method used to select the estimates was neither reported nor discussed.
Measure of benefits used in the economic analysis
The authors used life-years (LYs) and quality-adjusted life-years (QALYs) as the measures of benefit. The utility weights associated with CHB disease states were estimated from published economic evaluations in which utilities were obtained from an average of the standard gamble and time trade-off methods (Wong et al. 1995, Bennett et al. 1997). Utility weights were age-adjusted. For those patients who seroconverted, UK population-based age-specific quality-of-life weights were applied. An absolute decrease rate in utility was applied to pegIFN alpha-2a (40 kDa) treatment compared with lamivudine to account for symptoms during therapy. The benefits were discounted but the annual rate used was not reported.

Direct costs
Health-related direct costs included drug acquisition costs and health state costs. The health state costs were obtained from a review of hepatitis B treatments in the UK based on treatment protocols developed with expert advisors (National Institute for Health and Clinical Excellence (NICE), UK), published cost estimates for the progressive stages of liver disease, an observational study on mild hepatitis C in the UK, a study of the costs of liver transplantation in the UK, and authors' opinions. The drug costs were taken from the British National Formulary. The costs were discounted but the annual rate used was not reported. The price year was 2005.

Statistical analysis of costs
The total annual costs of each health state were reported, along with their corresponding standard deviations and source (Bennett et al. 1997), but no statistical analysis of the costs was carried out.

Indirect Costs
No productivity costs were reported.

Currency
UK pounds sterling (£).

Sensitivity analysis
The authors stated that sensitivity analyses were performed on each model input in order to determine the impact of parameter uncertainty on the estimated incremental cost-effectiveness ratios (ICERs). They also conducted a probabilistic sensitivity analysis and generated a cost-effectiveness acceptability curve. An additional scenario was evaluated in which adefovir salvage treatment was used for lamivudine-resistant patients.

Estimated benefits used in the economic analysis
The estimated benefits were 22.60 discounted LYs and 18.55 discounted QALYs for the lamivudine strategy and 22.99 discounted LYs and 18.85 discounted QALYs for the pegIFN alpha-2a (40 kDa) strategy.

Compared with lamivudine monotherapy, pegIFN alpha-2a (40 kDa) monotherapy increased life expectancy by 0.60 years, discounted LYs by 0.39 and discounted QALYs by 0.30.

The difference still favoured pegIFN alpha-2a (40 kDa) when compared with adefovir salvage therapy (increase of 0.33 LYs and 0.14 discounted QALYs).

Cost results
The total discounted cost was £14,877 per patient for pegIFN alpha-2a (40 kDa) versus £11,777 for lamivudine, a difference of £3,100.

This difference persisted against pegIFN alpha-2a (40 kDa) when compared with adefovir salvage therapy (£875).

Synthesis of costs and benefits
The ICERs were £7,977 per discounted LY gained and £10,444 per discounted QALY gained for pegIFN alpha-2a (40 kDa) in comparison with lamivudine.
The ICER of pegIFN alpha-2a (40 kDa) was £6,100 per discounted QALY gained in comparison with adefovir salvage therapy.

The ICERs were most sensitive to variation in the probability of developing compensated cirrhosis from CHB, pegIFN alpha-2a (40 kDa) seroconversion rate, lamivudine treatment durability, and the probability of developing compensated cirrhosis from seroconversion.

The cost-effectiveness acceptability curve indicated that there was a greater than 95% probability that pegIFN alpha-2a (40 kDa) was cost-effective in comparison with lamivudine at the £30,000 per QALY threshold.

Authors’ conclusions
The authors stated that the use of peginterferon (pegIFN) alpha-2a (40 kDa) as first-line treatment for patients with chronic hepatitis B (CHB) was highly likely to be cost-effective, compared with lamivudine, given certain assumptions about disease progression and the efficacy and cost of therapy.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used: mainly it was a treatment available in the study setting. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors combined data from existing models with data from several published studies of varying designs. No systematic search for data was reported, which could be an important limitation. The inclusion and exclusion criteria were not reported. The authors also made some assumptions that were justified with reference to the medical literature. The sources of effectiveness evidence were derived from meta-analyses and randomised clinical trials, which represent adequate sources for estimating effectiveness.

Validity of estimate of measure of benefit
The estimation of the health benefits (QALYs) was modelled using a Markov model. The methods used to estimate the utility weights were not described as they were taken from published studies (Wong et al. 1995 and Bennett et al. 1997). Survival analysis (LYs) results were also reported.

Validity of estimate of costs
A health system perspective (UK National Health Service) was reported, but only the total annual costs of each health state with their corresponding standard deviations and source were reported. The resource quantities and the unit costs were not reported separately, which would make it difficult to rework the analysis in other settings. The price year and the sources of resource use and unit costs were adequately reported. The costs were discounted but the annual rate used was not reported. Discounting would appear to have been appropriate as the time horizon was greater than 1 year. Sensitivity analyses were conducted to assess the robustness of the cost estimates used.

Other issues
The authors compared their findings with those from other studies and found their results were in agreement. The results of the study appear to have been adequately presented. The authors’ conclusions appear to reflect the scope of their analysis. However, the authors reported some limitations to their study. First, the inherent uncertainties in models projecting long-term outcomes. Second, the assumption that all the patients in the CHB health state followed the same clinical course and that rates of progression followed the natural history of CHB disease. Third, HBsAg seroconversion was not included in the analysis. Finally, sequential therapy other than adefovir salvage treatment was not included.

Implications of the study
The difference with other studies and the NICE analysis highlights the challenge of modelling long-term treatment and outcomes in CHB and the need for longer-term controlled trials. The authors also stated that other important factors, such as budget impact and equity, should be taken into account since cost-effectiveness information is only one of them.

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**Other publications of related interest**


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