HBeAg-negative chronic hepatitis B: cost-effectiveness of peginterferon alfa-2a compared to lamivudine in Taiwan

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 assessed the cost-effectiveness of peginterferon alpha-2a (PEG), compared with lamivudine, for the treatment of hepatitis B e antigen-negative chronic hepatitis B in a hypothetical cohort of 40-year-old patients in Taiwan. The authors concluded that 48 weeks of PEG was a cost-effective strategy from the perspective of the Taiwan Bureau of National Health Insurance. The quality of the study methodology was good and the authors’ conclusions are robust.

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

Study objective
The objective of the study was to assess the cost-effectiveness of peginterferon alpha-2a (PEG) in comparison with lamivudine (LAM) for the treatment of hepatitis B e antigen (HBeAg)-negative chronic hepatitis B (CHB) in a hypothetical cohort of 40-year-old patients in Taiwan.

Interventions
The two strategies under examination were PEG monotherapy versus LAM monotherapy. Both treatments were administered for 48 weeks. PEG was given at a dosage of 180 mg/day and LAM at a dosage of 100 mg/day.

Location/setting
Taiwan/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a Markov model that was developed to simulate the natural history of CHB and its possible consequences (compensated cirrhosis, hepatocellular carcinoma, liver transplantation, death). The time horizon of the analysis was a patient’s lifetime. The authors stated that the perspective of the Taiwan Bureau of National Health Insurance was adopted.

Effectiveness data:
Transition probabilities used in the model were identified through a systematic review of the literature, treatment guidelines and consensus statements. These data were supplemented by inputs from a panel of 8 hepatologists in Taiwan. Among the published evidence, preference was given to studies that enrolled Taiwanese patients. Treatment response rate and patients’ characteristics were derived from a Phase III clinical trial that directly compared LAM with PEG. Follow-up data (response rate after the end of the clinical trial) were taken from selected published sources. Disease progression was similarly based on several sources, including expert opinion. The background risk of death was based on age-specific standard life tables.

Monetary benefit and utility valuations:
Quality-of-life values were derived from published studies. One of these sources used the time trade-off approach in both Taiwanese patients and hepatologists. Another study was carried out among experts who assessed their own utilities using both the standard gamble and the time trade-off methods. This second source was used in the base-case according to expert opinion.
Measure of benefit:
The summary benefit measures were the life-years (LYs) and quality-adjusted life-years (QALYs). These were estimated using the decision model. The benefits were discounted at an annual rate of 3%.

Cost data:
The analysis of the costs considered the medical services associated with treating the disease. The costs were presented as macro-categories for specific health conditions. The unit costs were derived from the Fee Schedule for Medical Services and Reference List for Drugs. Resource consumption was determined in a survey of local hepatologists. The costs, which were in new Taiwan dollars (NTD), were converted into US dollars ($) at the rate of $1 = NTD 31.96. The long-term costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
A one-way sensitivity analysis was carried out on all model inputs. Ranges of clinical estimates were presumably based on published sources. The cost estimates were varied by +/- 25% of the base value. In addition, a probabilistic sensitivity analysis was also undertaken by assigning probabilistic distributions to model inputs. Thus, 95% confidence intervals (CIs) were generated for cost-effectiveness ratios, and cost-effectiveness acceptability curves were presented.

Results
The expected total costs were NTD 389,375 with PEG and NTD 232,382 with LAM (difference NTD 156,992).

The expected LYs were 11.45 with PEG and 11.07 with LAM (difference 0.38).

The QALYs were 10.57 with PEG and 10.12 with LAM (differences 0.45).

The incremental cost per LY gained with PEG was NTD 413,770.

The incremental cost per QALY gained with PEG was NTD 346,868 (95% CI: 228,000 to 566,000), or $10,900 (95% CI: 7,100 to 17,700).

The deterministic sensitivity analysis showed that the most influential model inputs were the relapse rate after PEG was stopped, the probability of developing compensated cirrhosis from CHB, and the relapse rate after LAM treatment was stopped. Nevertheless, the incremental cost per QALY did not exceed the value of NTD 448,000, regardless of the variations performed in the analysis.

The probabilistic sensitivity analysis showed that the value put on a QALY should have been less than NTD 350,000 ($11,100) before the probability of PEG being cost-effective fell below 50%.

Authors' conclusions
The authors concluded that 48 weeks of PEG in HBeAg-negative CHB was a cost-effective alternative to LAM from the perspective of the Taiwan Bureau of National Health Insurance. It was pointed out that future studies should investigate the long-term disease and treatment outcomes in HBeAg-negative CHB.

CRD commentary
Interventions:
The choice of the comparators was appropriate in that they are the relevant strategies in the authors’ setting. Dosages and treatment duration were based on a recent clinical trial.

Effectiveness/benefits:
Different sources were used to derive clinical inputs for the model. All of them appear to have been appropriate. The systematic review of the literature ensured that the most relevant and recent evidence was identified. The selection of a randomised clinical trial represents a valid source of treatment effectiveness, owing to the strengths of its design. The opinions of local experts are useful in terms of putting foreign data into the authors’ context. Furthermore, the authors stated that conservative assumptions were made when different estimates were available from the literature. When
uncertain estimates were used in the model, extensive sensitivity analyses were undertaken to overcome this potential limitation. The derivation of the benefit measures was described clearly.

**Costs:**
A breakdown of the cost items was not given as the costs were presented as macro-categories. This presentation of aggregated costs for health conditions is quite common in CHB, although it reduces the possibility of replicating the analysis in other settings. Nevertheless, the authors explained the approach used to derive some cost categories. The sources of the costs and other details of the analysis (e.g., price year, use of discounting and statistical tests) were reported.

**Analysis and results:**
The synthesis of the costs and benefits was appropriate. The issue of uncertainty was extensively addressed in the sensitivity analysis, the results of which were presented clearly. Patterns of transition among health states were described in detail, together with other features of the decision model. The authors noted some limitations of the analysis such as the unclear progression of disease in patients with HBeAg-negative hepatitis B virus. However, the conservative nature of some assumptions, which should have favoured LAM, ensures the robustness of the study results.

**Concluding remarks:**
The study appears robust in terms of the sources used to derive the clinical and economic data and the transparent presentation of the results. The sensitivity analysis enhances the validity of the authors’ conclusions.

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**Bibliographic details**

**Other publications of related interest**


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