OBJECTIVES: Two billion people worldwide have been infected with hepatitis B virus and approximately 400 million present chronic disease. Part of chronically infected patients with HBV develop cirrhosis and liver failure. Two strategies are adopted for treatment of chronic hepatitis B: a) use of interferon (conventional and pegylated) for a limited timeframe and b) use of nucleoside/tide analogs for a determined period. This analysis aims to assess the incremental cost-utility ratio for peginterferon-alfa-2a (40 KD) versus lamivudine, in treatment of HBAg-positive and HBBeAg-negative patients with hepatitis B, from the perspective of the National Health Service. METHODS: A Markov model was used to estimate the clinical and economic impact of the incorporation of peginterferon-alfa-2a (40 KD). Clinical stages were based on liver histology, cirrhotic decompensation, liver cancer and liver transplantation. Costs were estimated based on resource utilization described in a Delphi panel with experts. Response and seroconversion rates with peginterferon alfa-2a (40 KD) were 36% for HBAg-negative, and 32% for HBBeAg-positive patients. For lamivudine, rates were 23% and 19%, respectively. Data concerning the quality-of-life were extracted from the international literature, due to the lack of local data. A lifetime horizon was assumed. RESULTS: The ICER (peginterferon-alfa-2a vs. lamivudine) was R$20,192 HBAg-negative patients, and R$33,749 for HBBeAg-positive patients, assuming a discount rate of 3%. A probabilistic sensitivity analysis was conducted using second-order Monte Carlo simulation. Tested parameters were costs per stage, treatment costs, discount rate, and responsiveness to treatment. The 95% confidence interval for the ICER ranged from R$12,275 to R$35,048 for HBAg-negative patients, and R$17,771 to R$67,430 for HBBeAg-positive patients. CONCLUSION: The study suggests that therapy with peginterferon-alfa-2a (40 KD) has a robust and favorable cost-utility ratio in the Brazilian public health system for both serological profiles.