

Re: Entecavir for the treatment of chronic hepatitis B: Appraisal consultation document

Dear Dr Feinmann,

Thank you for providing us with the opportunity to review the above mentioned document.

We agree with the comments made by the appraisal committee and provide the following comments and observations for your consideration:

1. As noted by the committee we agree that the assumptions made in the manufacturer's model regarding the duration of therapy do not reflect clinical practice:
 - The majority of HBeAg positive patients would spend significantly longer on antiviral therapy than the two years suggested in the model. If a patient has achieved HBeAg seroconversion at 2 years they would receive a further 6-12 months of consolidation therapy and those who hadn't seroconverted would continue on treatment until failure (when another antiviral would be used).
 - In the model the manufacturer assumes that patients who achieve HBeAg seroconversion in year 1 would not receive therapy in year two, again in reality patients would receive consolidation therapy for at least 6-12 months.
 - The assumption that HBeAg negative patients receive only 5 years of antiviral treatment is incorrect. In clinical practice patients will remain on therapy until HBsAg loss/Seroconversion or treatment failure.
2. The analysis in LAM-refractory patients omitted adefovir monotherapy, which is a key comparator and is less costly than entecavir.
3. The analysis in LAM-refractory patients used an overly pessimistic estimate of the efficacy of adefovir plus lamivudine. Trials on adefovir plus lamivudine in patients with more severe disease show adefovir salvage therapy to produce substantial benefits, which are considerably higher than those assumed.¹
4. With the exception of commercial in confidence data, it would have been useful to be able to view the appendices of the submission in order to assess whether the inclusion criteria used, studies identified and statistical methods employed were appropriate.

We look forward to the distribution of the Final Appraisal Determination.

Yours sincerely,

 – Gilead

1. Lampertico P, et al. 42nd EASL, 2007; Barcelona, Spain; Poster #502.