Reviewer's report

Title: Cost-effectiveness analysis of different rescue therapies in patients with lamivudine-resistant chronic hepatitis B

Version: 1 Date: 26 July 2012

Reviewer: Jonathan Minton

Reviewer's report:

MAJOR COMPULSORY REVISIONS
None identified.

MINOR ESSENTIAL REVISIONS
1) Start of results paragraph: statement: "...TDF Monotherapy and combination therapy provide the best health benefits". The phrase 'best health benefits' is a bit ambiguous and subjective. Instead just summarise the results, with something like: both options were on the efficiency frontier for both positive and negative populations.

2) End of 1st methods paragraph: reference needed to support why 3% discount rate was adopted.

3) Reference needed to support the claim that "serum HBV DNA level is an ideal surrogate marker for antiviral therapies because of its independent predictive ability for CHB disease progression."

4) 1st paragraph of model overview section: "Patients could transition between two health states in each annual cycle, as indicated by arrows in the figure." Firstly, this is a bit ambiguous as it implies the cycle length might be 6 months not 12 months, when instead it seems to mean that there were two other states an individual could move to from the initial state... Secondly, the authors need to say which figure (rather than just 'the figure').

5) The paper needs to state what the basis is for the ranges listed in tables 1-3. Are they 95% CIs or something else?

6) Table 4 needs to be reorganised to be clearer. I think the + and - populations should be grouped together (i.e. currently higher tier is therapy type, lower tier is population type. It should be the other way around). The clinical outcomes should be grouped together (cumulative incidence of compensated cirhosis, death, etc), then the total costs and total QALYs. It should be clearer what the comparison for the ICERs is, and ICERs using the next best option (as in the full incremental analysis) should be described separately, and in preference to, ICERs using the same 'no treatment' baseline.

7) Clarification needed as to why not all health states are linked to death states, as shown in figure 1. Does the model not have a 'probability of death from other causes' parameter for people in the initial state? If not why not?
DISCRETIONARY REVISIONS

1) Analysis section: I think "cost-effectiveness acceptability range" should be "cost-effectiveness acceptability curve" evaluated over the range X to Y.

2) Last para of results - base case analysis" - "In the ... positive cohort, ADV and ... were both dominated because their incremental costs per QALY gained were ... and ... respectively." I think this is unclear on its own but clear enough when combined with the figure. (Hence only being discretionary change.) A distinction should be made between simple and extended dominance.

3) I think there should be a justification for why CEACs and not CEAFs were used.

4) End of paragraph before discussion: the term 'preferred rescue therapies' is a little too subjective.

5) Use of terms 'constrained economic situation' (near end of discussion) and 'health care systems with limited health resources' both imply that there are some health care systems with unlimited health resources! Suggest making these terms tighter so they refer, perhaps to countries with significantly less per capita healthcare spending than most developed world nations.

6) Reporting the joint costs and QALYs for each point on figs 2a and 2b might make this more informative.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests