From: [redacted] [mailto:[redacted]@soton.ac.uk]
Sent: 16 June 2010 10:51
To: TA Comm B
Cc: Jeremy Powell
Subject: RE: NICE MTA - Hepatitis C - peginterferon alfa and ribavirin - Appraisal Consultation Document comments

Hi Jeremy,

On behalf of SHTAC, please find our comments on the Hepatitis C ACD below:

We feel that the caveats in our report around the fact that SVRs for shortened treatment duration came from relatively small subgroups of the RCTs should be mentioned. The best place would be following on from the last sentence in para 4.1.3, something like "in many of the trials the sustained virological response rates were based on sub-groups of randomised patients who achieved a rapid viral response. It was not reported whether these sub-groups were statistically powered to detect a significant difference between trial arms".

Para 4.1.10 - sentence about halfway down "...but these did not meet the inclusion criteria for the review as they featured an active treatment comparator" suggest adding "...but these did not meet the inclusion criteria for the review (based on the decision problem) as they featured an active treatment comparator".

4.1.12 - we feel the 1st sentence which reads "...shortening the duration of treatment of peginterferon alfa plus ribavirin to 16 weeks (HCV genotype 2 or 3) or 24 weeks (HCV genotype 1) may be associated with a slight reduction in sustained virological response" is misleading as in some trials shortened treatment was associated with increased SVRs. We would ask that this is removed and replaced with something like "....there are no statistically significant differences between shortened and standard durations of treatment". This same point applies to section 4.3.2 and we would ask that this is similarly amended.

Para 4.2.5 - sentence about halfway down "For people whose hepatitis C did not respond or relapsed on previous peginterferon therapy, data on sustained virological response rates were taken from clinical trials" change to "...data on sustained virological response rates were taken from two clinical trials".

Section 4.2.9 - 3rd sentence "Although appropriate probability distributions appear to have been used for the probabilistic sensitivity analyses, the Assessment Group noted that **limiting the distributions for some inputs** does not appear to make best use of data reported in the submission." The bit in bold doesn't actually make any sense and we would suggest changing it to what was said in the report, which was that "...the parameterisation of the distributions used for some inputs does not appear to make best use of data reported in the submission."

4.2.21 - the 1st sentence "Data on sustained virological response rates were extracted from clinical trials included in the clinical-effectiveness review and used in the model..." is not quite true. The clinical effectiveness review only supplied SVRs for the shortened treatment duration subgroup of patients. SVRs for the re-treatment and the HCV/HIV subgroups were taken from active comparator RCTs (not systematically reviewed by us).

Para 4.3.9 - a cross-reference to section 4.2.22 is given, but should this not be 4.2.23?

If you have any queries or need clarification of any of these comments, please do not hesitate to contact me.

Kind regards,

[redacted]

[redacted]

[redacted]

Southampton Health Technology Assessments Centre (SHTAC)

University of Southampton

First Floor, Epsilon House

Enterprise Road

Southampton Science Park

Southampton

SO16 7NS

Tel: [redacted]
Fax: [redacted]
E-mail: [redacted]@soton.ac.uk