HEALTH TECHNOLOGY APPRAISAL on Interferon Alfa and Ribavirin for the treatment of mild chronic Hepatitis C Comment on Appraisal Consultation Document (ACD)	
To: NICE	**FROM: NHS Quality Improvement Scotland**

Reviewer 1

Whether all the relevant evidence has been taken into account?

I believe that all the relevant evidence has been taken into account and the interpretation of this by the Appraisal Committee is correct. There are 2 typographical errors in the evidence in section 3.3, the dose of peg Interferon Alfa 2b should 1.5mcg/kg and not 180 mcg as stated. The error is repeated twice in that section.

Whether the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate?

I believe the Appraisal Committee have produced good summaries of the clinical and cost effectiveness of these medications and therapies and the work there is commissioned on the cost effectiveness of these therapies is appropriate for the applications to the NHS.

Whether the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

I feel that the recommendations of the Appraisal Committee are sound and constitute a suitable basis for guidance to the NHS and indeed, they reflect what is largely current practice in many units throughout Scotland and the rest of the United Kingdom

Reviewer 2

Whether all the relevant evidence has been taken into account?

It is not possible to determine what evidence has been examined as no references have been given. However, I would judge the evidence is complete.

Whether the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate?

I would raise three issues:

A. Section 3.3. There is a mistake in the dose of peginterferon alfa-2b which should read 1.5 micrograms/kg rather than 180 micrograms.

B. Sections 3.2 and 3.3. The statements that patients with genotypes 1, 4, 5 and 6 may be eligible for shorter duration (at least 24 weeks) of combination therapy if the viral load is low are premature. No definition of low viral load is given and individual manufacturers assays are variable and not standardised.

The latest manufacturers summary of product characteristics refer to this area as follows:

Viraferonpeg - For patients who exhibit virological response at week 12, treatment should be continued for another nine month period (i.e., a total of 48 weeks). In the subset of patients with genotype 1 infection and low viral load (< 600,000 IU/ml) who become HCV-RNA negative at treatment week 4 and remain HCV-RNA negative at week 24, the treatment could either be stopped after this 24 week treatment course or pursued for an additional 24 weeks (i.e. overall 48 weeks treatment duration). However, an overall 24 weeks treatment duration may be associated with a higher risk of relapse than a 48 weeks treatment duration.

Pegasys – patients infected with genotype 1 regardless of viral load should receive 48 weeks of therapy.

C. Sections 1.4 and 7.3.4. There is increasing literature on the possibility of treating patients with genotypes 2 and 3 infection with shorter courses of therapy (12, 14 and 16 weeks) provided there is an EVR at 4 weeks (Hepatology 2004;40:1260-5; Gastroenterology 2005;129:522-7; NEJM 2005;352:2609-17).
Perhaps the committee should consider this area as patients with mild disease are more likely to respond readily.

Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

Suitable for guidance in Scotland.

Reviewer 3

I am not sure if the papers looking at early viral response to therapy have been looked at. There is evidence that some patients with genotype 1 virus with a low load may only require 24 weeks of treatment if there are signs that they are responding to treatment.
Patients with genotype 2 and 3 who are responding to treatment with suppression of their viral load may only require between 12 and 16 weeks of treatment

If the above were to be considered then the cost effectiveness may be more evident

I agree with the recommendations to treat patients (with all genotypes) with mild disease but the duration of therapy may be shortened in some instances (see above). This should be referred to in the final document.

Reviewer 4

This is, as usual, a comprehensive and thoughtful review of the use of antiviral therapy for mild and moderate hepatitis C infection, and the conclusions reached are well supported by the evidence. I know of no other significant evidence not considered, and would expect the conclusions to be as valid in Scotland as in England.

9 March 2006