19th Expert Committee on The Selection and Use of Essential Medicines

April 8-12 2013

Expert peer review on application for adding Peg Interferon

1. Assessment of efficacy
a. Have all relevant studies on efficacy been included
   NO

   Based on analysis of trial data, the guidelines recommend shortened courses of combination therapy with peginterferon alfa (2a or 2b) and ribavirin for the treatment of adults with chronic hepatitis C who have a rapid virological response to treatment at week 4 that is identified by a highly sensitive test and are considered suitable for a shortened course of treatment (mainly those with a low initial viral load). This results in comparable efficacy as the longer course with significant cost savings with some loss of QALYs.¹

2. NICE technology appraisal guidance 252. Telaprevir for the treatment of genotype 1 chronic hepatitis C. April 2012
   The committee concluded that addition of Telaprevir produced better SVR in adults with Genotype 1 chronic hepatitis C related compensated liver disease. Hence Telaprevir in combination with peginterferon and ribavirin was recommended as an option for new patients or patients needing retreatment for Genotype 1 chronic hepatitis C related compensated liver disease²

b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Combination therapy with Ribavirin and peginterferon produces a sustained virological response (SVR) in 40 - 50% of genotype 1 and upto 80% of Genotype 2 and 3 chronic hepatitis C virus infections. Higher response rates are seen with lower viral loads. Latinos and Africans have lower response rates and Asians higher response rates than whites.

c. Please provide any additional relevant information with reference

   In patients with HIV and HCV co-infection the SVR to combination therapy is lower – 29% in genotype 1 and 62% with genotype 2 and 3 infection³


2. Assessment of safety
a. Have all relevant studies on safety been included
   Yes
b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

Peg interferon combined with ribavirin has significant toxicity leading to discontinuation in 10 to 14% of patients. Interferon causes depression and anxiety in 20 to 30% of patients and anaemia and neutropenia are common.

c. Please provide any additional relevant information with reference
Peg interferon causes more bone marrow suppression than plain interferon requiring dose reduction in 20% 

It can also cause thrombocytopenia and rash. Hypothyroidism, Grave’s disease and thyroiditis are seen in 5 to 10% on interferon therapy. Flu like symptoms are seen in 80% of patients.

Interferon cannot be given in decompensated liver disease and pregnancy and worsens autoimmune conditions.


3. Assessment of cost and availability
a. Have all relevant data on cost been provided
   No

   NICE technology appraisal guidance TA200 Peginterferon alfa and ribavirin for the treatment of chronic hepatitis C September 2010

   According to this guideline, the cost of treatment with peginterferon alfa-2a plus ribavirin (Copegus) is estimated to be £3215 for 16 weeks or £4824 for 24 weeks of therapy (for people with genotypes 2 or 3), or £11,425 for 48 weeks of therapy (for people with genotypes 1 or 4). For people treated with peginterferon alfa-2b plus ribavirin (Rebetol), the cost is £5540 for 24 weeks or £11,081 for 48 weeks of therapy (for people with genotype 1) 

b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

Peg interferon is a very expensive drug costing around £11000 for a 48 week course in the UK. However biosimilars are now available in Egypt at $2000 for a 48 week course. Biosimilars are available in India as well.

NICE data 2004 reported an incremental discounted cost per QALY of £3291 for genotypes 2 or 3 with low baseline viral load.

c. Please provide any additional relevant information with reference
d. Is the product available in several low and middle income countries? Yes

4. Assessment of public health need
   a. Please provide the public health need for this product (1-2 sentences)

   The burden of disease is huge with approximately 150 million people infected worldwide with 15 – 30% going on to develop cirrhosis. Many of these are coinfected with HIV and are at high risk of hepatocellular cancer.

   b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable Yes

   NICE guidelines
   American Association for the Study of Liver Diseases

5. Are there special requirements for use or training needed for safe/effective use?
   If yes, please provide details in 1-2 sentences Yes

   Patients need to be carefully screened to rule out conditions precluding interferon use. High level laboratory facilities are required for quantitative RNA measurements and genotyping. Facilities for performing liver biopsy are required. Patients need to be monitored carefully for drug side effects

6. Is the proposed product registered by a stringent regulatory authority?
   Yes

7. Any other comments

   Telaprevir and Boceprevir have recently been approved for chronic HCV Genotype 1 related liver disease but remain prohibitively expensive.

8. What is your recommendation to the committee (please provide the rationale)

   I recommend addition of this drug to the EML for the following reasons.
   HCV infection can be cleared in a significant percentage of cases. No other treatment is available for this condition.
   Cost of drugs are coming down with the advent of biosimilars and government agreements with drug companies. Addition to the EML may encourage governments to negotiate lower prices for the drug.
   However, these drugs can only be used with adequately trained personnel and high level laboratory support.