

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Albinterferon alfa-2b for the treatment of hepatitis C

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of albinterferon alfa-2b within its licensed indication for the treatment of adults with hepatitis C who have compensated liver disease and previously untreated with interferon alfa.

Background

Hepatitis C is a disease of the liver caused by infection with the hepatitis C virus (HCV). Generally the virus is transmitted parenterally, but the natural history of the disease is not completely understood. The virus is primarily acquired through percutaneous exposure to contaminated blood. Since the viral inactivation programme was implemented in the mid-1980s and blood donor screening started in 1991, the transmission of HCV in the UK, via transfusion of blood, blood products or organ transplantation, has all but ceased. However, injecting drug use, cosmetic and other practices involving percutaneous exposure remain common routes of transmission. HCV prevalence is correlated with markers of sexual activity, but HCV incidence in monogamous heterosexual partners of infected people is extremely low. There is a transmission rate of about 6% from mother to child if the mother is an HCV carrier. Concomitant HIV infection increases the risk of transmission.

Estimates from the Health Protection Agency suggest that approximately 142,000 people between the ages of 15-59 years were infected with chronic HCV in England and Wales in 2003; a prevalence rate of 0.44% in this age group. More than 90% of all newly diagnosed infections in the UK occur in people who inject drugs.

People infected with HCV are often asymptomatic, but about 20% will develop acute hepatitis and will experience non-specific symptoms including malaise, weakness and anorexia. About 80% of those exposed go on to develop chronic hepatitis. The rate of progression of the disease is slow but variable, usually taking about 20–50 years from the time of infection. About 30% of those who are infected develop cirrhosis within 20–30 years, and a small percentage of these people are at a high risk of developing hepatocellular carcinoma. A third may never progress to cirrhosis or will not progress for at least 50 years. Some people with end-stage liver disease or hepatocellular carcinoma may require liver transplantation.

There are 6 major genotypes and several sub-types of HCV, the prevalence of which varies geographically. Genotype 1 is the most common in the UK, accounting for about 40–50% of cases. Genotypes 2 and 3 contribute another

40–50%; and genotypes 4, 5 and 6 constitute the remainder, about 5%. Genotype is a key predictor of the effectiveness of anti-viral treatment and patients with genotypes 2 and 3 generally respond better to treatment than those with genotypes 1, 4, 5 and 6.

A person is classified as having mild, moderate or severe chronic hepatitis C based on the extent of liver damage. The main indicator of liver damage is the degree of fibrosis, although the degree of necroinflammation also contributes to the diagnosis.

For the majority of people with hepatitis C (regardless of disease severity), the standard treatment is combination therapy with ribavirin and either peginterferon alfa-2a or peginterferon alfa-2b. Monotherapy with peginterferon alfa is used only for people unable to tolerate ribavirin (in line with NICE guidance TA75 and TA106).

Second or subsequent courses of treatment are not recommended for people who have been treated with a first course of either combination therapy or monotherapy with peginterferon alfa if they have not had an early response (as indicated by reduction in viral load at 12 weeks). NICE guidance on treatment for hepatitis C is currently being partly updated for chronic disease.

The technology

Albinterferon alfa-2b (Joulferon, Novartis) is a recombinant albumin and alfa-IFN fusion protein which has direct antiviral activity and immune-modulating effects. Albinterferon alfa-2b is administered by subcutaneous (SC) injection.

Albinterferon alfa-2b does not have a UK marketing authorisation. It has been studied in clinical trials in combination with ribavirin compared with peginterferon alfa-2a or peginterferon alfa-2b both in combination with ribavirin in adults with chronic hepatitis C virus infection who have compensated liver disease and who have not been previously treated with interferon alfa.

Intervention(s)	Albinterferon alfa-2b in combination with ribavirin
Population(s)	People with chronic hepatitis C with compensated liver disease and who have had no prior treatment with interferon alfa.
Comparators	<ul style="list-style-type: none"> • Ribavirin and peginterferon alfa-2a • Ribavirin and peginterferon alfa-2b
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • virological response to treatment • sustained virological response • biochemical response (e.g. ALT)

	<ul style="list-style-type: none"> • histological improvement (inflammation and fibrosis) • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
Other considerations	<p>If the evidence allows subgroups will be considered. These may include factors associated with a sustained virological response (for example, genotype).</p> <p>Guidance will only be issued in accordance with the marketing authorisation.</p>
Related NICE recommendations	<p>Related Technology Appraisals:</p> <p>Technology Appraisal TA106. August 2006. Peginterferon alfa and ribavirin for the treatment of mild hepatitis. Currently being reviewed as a part-review of TA75 and TA106. Expected issue date October 2010</p> <p>Technology Appraisal TA75. January 2004. Hepatitis C - pegylated interferons, ribavirin and alfa interferon. - Part review of existing guidance no.14. Currently being reviewed as a part-review of TA75 and TA106. Expected issue date October 2010</p> <p>Technology Appraisal in preparation review MTA of TA106 and 75.</p>

Questions for consultation

Have the most appropriate comparators for the treatment of albinferon alfa-2b been included in the scope? Are the comparators listed routinely used in clinical practice?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)