NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Sofosbuvir for treating chronic hepatitis C

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of sofosbuvir within its licensed indication for treating chronic hepatitis C.

Background

The hepatitis C virus (HCV) causes inflammation of the liver and affects the liver's ability to function. HCV is a blood-borne virus, meaning that it is spread by exposure to contaminated blood. Contaminated needles used for injecting drugs are currently the most common route of transmission. Symptoms of chronic HCV infection are typically mild and non-specific, including fatigue, flu-like symptoms, anorexia, depression, sleep disturbance, pain, itching and nausea. Often, people with HCV do not have any symptoms, and 15 to 20% of infected people naturally clear their infections within 6 months. However, the remainder develop chronic hepatitis which can be life-long.

Chronic hepatitis is categorised according to the extent of liver damage, as mild, moderate, or severe (where severe refers to cirrhosis). About 30% of people infected with HCV will develop cirrhosis; the time for progression to cirrhosis varies, but takes 40 years on average. Cirrhosis can progress to become 'decompensated', where the remaining liver can no longer compensate for the loss of function. A small percentage of people with chronic hepatitis and cirrhosis also develop hepatocellular carcinoma. Liver transplantation may be needed for people with decompensated cirrhosis or hepatocellular carcinoma.

The true prevalence of HCV is difficult to establish and likely to be underestimated because many people do not have symptoms. There are 6 major genotypes and several subtypes of HCV, the prevalence of each vary geographically. People can be infected with more than one genotype. The most recent national estimates (2012) suggest that around 216,000 people are chronically infected with HCV in the UK, and that most of this infection (approximately 90%) is genotype 1 and genotype 3. However, more than half of people with chronic hepatitis C are unaware of their infection.

The aim of treatment is to cure hepatitis C, and prevent liver disease progression, hepatocellular carcinoma development, and HCV transmission. The HCV genotype influences treatment decisions and response. People with HCV genotype 1 or 4 and a specific change in one of their genes (called IL28b polymorphism) are likely to have a better response to treatment than those who do not. People with HCV genotype 2 or 3 respond better to peginteferon with ribavirin treatment than people infected with the other HCV

genotypes. For those with mild hepatitis C, a 'watchful waiting' approach may be agreed, on an individual basis, between the patient and clinician. NICE guidance on hepatitis C (TA75, TA106) recommends that standard treatment for the majority of people with chronic hepatitis C, regardless of disease severity, is combination therapy with ribavirin and either peginterferon alfa-2a or peginterferon alfa-2b. Monotherapy with peginterferon alfa-2a or peginterferon alfa-2b is recommended for patients who are unable to tolerate ribavirin or for whom ribavirin is contraindicated. NICE guidance on hepatitis C (TA200) also recommends that people who have been previously treated with peginterferon alfa and ribavirin or with peginterferon alfa monotherapy have an option to receive further courses of peginterferon alfa and ribavirin. Shortened courses of combination therapy are also recommended as an option for certain patient subgroups. For people with genotype 1 chronic hepatitis C, who have not been previously treated or who have been previously treated, NICE guidance also recommends telaprevir in combination with peginterferon alfa and ribavirin (TA252) or boceprevir in combination with peginterferon alfa and ribavirin (TA253).

The technology

Sofosbuvir (brand name unknown, Gilead Sciences) is a uridine nucleotide analogue that inhibits HCV polymerase, preventing viral replication. Sofosbuvir is administered orally.

Sofosbuvir has a UK marketing authorisation 'in combination with other medicinal products for treating chronic hepatitis C in adults'. It has been studied in a range of clinical trials which have included patients infected with HCV of all genotypes (1-6), as well as in patients who were co-infected with HIV. For people with chronic hepatitis C genotype 1, 4, 5 or 6, sofosbuvir was only studied in those who had not previously received treatment, while in people with chronic hepatitis C genotype 2 or 3, it was studied in those who had either previously received treatment or who were treatment naive. Sofosbuvir has been investigated with ribavirin in people with chronic hepatitis C genotype 1, 4, 5, or 6 (in addition to peginterferon alfa), with or without ribavirin in people with chronic hepatitis C genotype 2 or 3 (in addition to, or without peginterferon alfa) and compared to peginterferon and ribavirin, placebo and no treatment.

Intervention(s)	• Sofosbuvir in combination with peginterferon alfa and ribavirin • Sofosbuvir in combination with ribavirin
Population(s)	Adults with chronic hepatitis C
Comparators	• Peginterferon alfa with ribavirin • Telaprevir in combination with peginterferon alfa and ribavirin (for genotype 1 only) • Boceprevir in combination with peginterferon alfa and ribavirin (for genotype 1 only) • Best supportive care (including treatments to manage the liver disease without a treatment for the hepatitis C)
Outcomes	The outcome measures to be considered include: • sustained virological response • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If evidence allows the following subgroups will be considered: • Co-infection with HIV • Response to previous treatment (non-response, partial response, relapsed) Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations and NICE pathways	Related Technology Appraisals: Technology appraisal No. 253, Apr 2012, 'Boceprevir for the treatment of genotype 1 chronic hepatitis C' Review Proposal Date April 2015. Technology appraisal No. 252, Apr 2012, 'Telaprevir for the treatment of genotype 1 chronic hepatitis C' Review Proposal Date April 2015. Technology appraisal No. 200, Sep 2010, 'Peginterferon alfa and ribavirin for the treatment of chronic hepatitis C' Review Proposal Date tbc. Technology appraisal No. 106, Aug 2006, 'Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C' Review Proposal Date tbc (partially updated in TA200). Technology appraisal No. 75, Jan 2004, 'Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C' Review Proposal Date tbc (partially updated in TA200). Related Guidelines: Clinical Guideline in Preparation, 'Hepatitis C' Earliest anticipated date of publication tbc. Related Public Health Guidance/Guidelines: Public Health Guidance No. 18, Feb 2009, 'Needle and syringe programmes' Related Quality Standards: Quality Standard No. 23, Nov 2012, 'Quality standard for drug use disorders' Review Proposal Date Nov 2017. Related NICE Pathways: Nice Pathway: Hepatitis B and C testing, Pathway created: Dec 2012
Related NHS England Policy	None.