Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Sofosbuvir for treating chronic hepatitis C

Draft scope (pre-referral)

Draft 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. Infected needles used for injecting drugs are currently the most common route of transmission. Symptoms of chronic HCV 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 chronic hepatitis 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 are also at increased risk of developing hepatocellular carcinoma. Liver transplantation may be needed for people with decompensated cirrhosis or hepatocellular carcinoma.

The true incidence 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 individuals are chronically infected with HCV in the UK, and that most of this infection (~90%) is genotype 1 and genotype 3. However, about 5 out of every 6 chronic hepatitis patients are unaware of their infection.

The aim of treatment is to prevent liver disease progression, hepatocellular carcinoma development, and HCV transmission. The HCV genotype influences treatment decisions and response. People with 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. For those with mild HCV, a 'watchful waiting' approach may be agreed, on an individual basis, between the patient and clinician. NICE guidance (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 (TA200) 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) is a uridine nucleoside analogue that inhibits HCV polymerase, preventing viral replication. Sofosbuvir is administered orally.

Sofosbuvir does not have a UK marketing authorisation. Sofosbuvir has been studied in a range of clinical trials which have included patients infected with HCV of all genotypes (1-6), treatment naive and treatment experienced patients, and patients who are also co-infected with HIV. Sofosbuvir has been investigated with or without ribavirin (in addition to, or without peginterferon) and compared to peginterferon and ribavirin, placebo and no treatment.

Intervention(s)	Sofosbuvir in combination with ribavirin (with or without peginterferon)
Population(s)	Adults with genotype 1, 4, 5 and 6 chronic hepatitis C • who have not been previously treated Adults with genotype 2 and 3 chronic hepatitis C • who have not been previously treated • who have previously been treated
Comparators	Adults with genotype 1, 4, 5, 6 chronic hepatitis C: • Peginterferon alfa, with or without 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) Adults with genotype 2 and 3 chronic hepatitis C: • Peginterferon alfa (with or without ribavirin)
Outcomes	The outcome measures to be considered include: • sustained virological response • degree of 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: • Presence or absence of HIV • Response to previous treatment (non-response, partial response, relapsed) • Presence or absence of IL28b polymorphism Guidance will only be issued in accordance with the marketing authorisation. *Subject to referral by the Department of Health, the invite for participation in this technology appraisal is anticipated for after January 2014, when new arrangements for the pricing of pharmaceuticals are expected to be in place. Consequences for this appraisal will be explored through further consultation on the scope pre invitation.*

Related NICE recommendations	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 July 2013. Technology appraisal No. 106, Aug 2006, 'Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C' Review Proposal Date July 2013 (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 July 2013 (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

Questions for consultation

Have the most appropriate comparators for sofosbuvir for treating hepatitis C been included in the scope? Are the comparators listed routinely used in clinical practice?

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

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular

protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which sofosbuvir will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits

Where do you consider sofosbuvir will fit into the existing NICE pathway; Hepatitis B and C testing?

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)