

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Sofosbuvir-ledipasvir for treating genotype 1 chronic hepatitis C

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of sofosbuvir-ledipasvir within its licensed indication for treating genotype 1 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 infected blood. Contaminated needles used to inject drugs are currently the most common route of transmission. Symptoms of chronic hepatitis C are typically mild and non-specific, including fatigue, flu-like symptoms, anorexia, depression, sleep disturbance, pain, itching and nausea. Often, people with hepatitis C 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 C which can be life-long.

Chronic hepatitis C is categorised according to the extent of liver damage, as mild, moderate, or severe (where severe refers to cirrhosis). About 30% of people with chronic hepatitis C 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. Liver transplantation may be needed for people with decompensated cirrhosis or hepatocellular carcinoma.

The true prevalence of HCV infection 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 varies geographically. People can be infected with more than 1 genotype. The most recent national estimates (2012) suggest that around 215,000 people are chronically infected with HCV in the UK and that approximately 90% of these people are infected with is genotype 1 or genotype 3. However, more than half of people with chronic hepatitis C are unaware of their infection.

The aim of treatment is to cure the HCV infection, and prevent liver disease progression, hepatocellular carcinoma development, and HCV transmission. The HCV genotype influences treatment decisions and response. For those with mild hepatitis C, a 'watchful waiting' approach may be agreed between the patient and clinician on an individual basis. NICE guidance on hepatitis C (technology appraisals 75 and 106) recommend combination therapy with ribavirin and peginterferon alfa-2a or peginterferon alfa-2b for people with chronic hepatitis C regardless of disease severity or genotype. Monotherapy

with peginterferon alfa-2a or peginterferon alfa-2b is recommended for people who are unable to tolerate ribavirin or for whom ribavirin is contraindicated. NICE technology appraisal 200 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 patients depending on their genotype and their initial response to treatment.

For people with genotype 1 chronic hepatitis C, who have or have not been previously treated, NICE guidance also recommend telaprevir in combination with peginterferon alfa and ribavirin (NICE technology appraisal guidance 252) or boceprevir in combination with peginterferon alfa and ribavirin (NICE technology appraisal guidance 253).

The technology

Sofosbuvir-ledipasvir (brand name unknown, Gilead Sciences) is a fixed-dose combination product. Sofosbuvir is a uridine nucleotide analogue that inhibits HCV polymerase, and ledipasvir is a macrocyclic antiviral agent and a protease inhibitor. They both act to inhibit viral replication. Sofosbuvir-ledipasvir is administered orally.

Sofosbuvir-ledipasvir does not have a UK marketing authorisation for treating genotype 1 chronic hepatitis C. It has been studied in combination with and without ribavirin in adults with genotype 1 chronic hepatitis C (without HIV) who have or have not received previous treatment.

Intervention(s)	Sofosbuvir-ledipasvir with or without ribavirin
Population(s)	<p>Adults with genotype 1 chronic hepatitis C</p> <ul style="list-style-type: none"> • who have not been previously treated • in whom previous treatment has not resulted in a sustained virological response
Comparators	<ul style="list-style-type: none"> • Peginterferon alfa with ribavirin • Telaprevir in combination with peginterferon alfa and ribavirin • Boceprevir in combination with peginterferon alfa and ribavirin

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • sustained virological response • rapid virological response (leading to shortened treatment duration) • development of resistance to sofosbuvir- ledipasvir • 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 evidence allows the following subgroups will be considered:</p> <ul style="list-style-type: none"> • Response to previous treatment (non-response, partial response, relapsed) <p>Guidance will only be issued in accordance with the marketing authorisation.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>Technology appraisal No. 300, 'Peginterferon alfa and ribavirin for the treatment of chronic hepatitis C in children and young people'. Review Proposal Date September 2016.</p> <p>Technology appraisal No. 253, Apr 2012, 'Boceprevir for the treatment of genotype 1 chronic hepatitis C'. Review Proposal Date April 2015.</p> <p>Technology appraisal No. 252, Apr 2012, 'Telaprevir for the treatment of genotype 1 chronic hepatitis C'. Review Proposal Date April 2015.</p> <p>Technology appraisal No. 200, Sep 2010, 'Peginterferon alfa and ribavirin for the treatment of chronic hepatitis C'. Guidance added to static list Dec</p>

	<p>2013.</p> <p>Technology appraisal No. 106, Aug 2006, 'Peginterferon alfa and ribavirin for the treatment of mild chronic hepatitis C (partially updated in TA200)'. Guidance added to static list Dec 2013</p> <p>Technology appraisal No. 75, Jan 2004, 'Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of chronic hepatitis C (partially updated in TA200)'. Guidance added to static list Dec 2013</p> <p>Technology appraisal in preparation, 'Sofosbuvir for treating chronic hepatitis C'. Earliest anticipated date of publication October 2014.</p> <p>Technology appraisal in preparation, 'Simeprevir in combination with peginterferon alfa and ribavirin for treating genotype 1 or 4 chronic hepatitis C'. Earliest anticipated date of publication January 2015.</p> <p>Proposed technology appraisal, 'ABT-450/ritonavir/ABT-267 in combination with ABT-333 for treating genotype 1 chronic hepatitis C'. Publication TBC.</p> <p>Proposed technology appraisal, 'Faldaprevir for treating genotype 1 chronic hepatitis C', Earliest anticipated date of publication TBC.</p> <p>Related Guidelines:</p> <p>Clinical Guideline in Preparation, 'Hepatitis C' Earliest anticipated date of publication TBC.</p> <p>Related Public Health Guidance/Guidelines:</p> <p>Public Health Guidance No. 18, Feb 2009, 'Needle and syringe programmes'</p> <p>Related Quality Standards:</p> <p>Quality Standard No. 23, Nov 2012, 'Quality standard for drug use disorders' Review Proposal Date Nov 2017.</p> <p>Related NICE Pathways:</p> <p>NICE Pathway 'Hepatitis B and C'. Pathway created: Dec 2012</p> <p>http://pathways.nice.org.uk/</p>
<p>Related national Policy</p>	<p>Department of Health Hepatitis C Action Plan for England (Jul 2004).</p> <p>http://www.nhs.uk/hepatitisc/SiteCollectionDocuments/pdf/hepatitis-c-action-plan-for-england.pdf</p>

Questions for consultation

Have all relevant comparators for sofosbuvir-ledipasvir been included in the scope? Which treatments are considered to be established clinical practice in the NHS for genotype 1 chronic hepatitis C?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom sofosbuvir-ledipasvir 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-ledipasvir 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 sofosbuvir-ledipasvir 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 sofosbuvir-ledipasvir 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.

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)