NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Sofosbuvir for treating chronic hepatitis C

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Michael Jacobs

Name of your organisation: Royal College of Physicians

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
- ~~a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?~~
- ~~an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?~~
- ~~other? (please specify)~~

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What is the expected place of the technology in current practice?

Patients with chronic hepatitis C virus (HCV) infection are currently treated with pegylated interferon and ribavirin, with the addition of a first generation direct acting antiviral agent (DAA), either telaprevir of boceprevir, in cases of genotype 1 infection. These treatment regimens have been approved in previous NICE single technology appraisals, and this guidance is widely followed.

The primary aim of treatment is to achieve a sustained virological response (SVR), defined as undetectable serum HCV RNA using a sensitive PCR either 12 (SVR12) or 24 (SVR24) weeks after stopping treatment. This essentially equates to cure from HCV infection. SVR rates following treatment have progressively improved over the last 20 years as new treatments have become available, but 30-50% patients still do not attain an SVR in clinical practice and therefore remain infected with HCV. Furthermore, treatment is prolonged (either 6 or 12 months) and arduous due to multiple adverse effects.

Chronic HCV infection is usually slowly progressive over many years. Treatment at all stages of liver disease has been determined to be cost effective and therefore all patients with HCV are potential candidates for treatment. Unfortunately patients with advanced liver disease, who most urgently require virological cure, are least likely to succeed with current standard of care treatment. Not only is treatment least likely to result in SVR in this group of patients, but also they are at greatest risk of severe adverse effects from treatment. These adverse effects may be life threatening (such as hepatic decompensation and sepsis), and in many individuals who most need treatment the risks are currently too great to proceed. Many other patients with less advanced liver disease have chosen to defer antiviral treatment due to the potential adverse effects of current treatment, and in particular long duration treatment with interferon.

Sofosbuvir is a first-in-class DAA, a nucleotide inhibitor of HCV RNA polymerase (NS5B). The key registration trials demonstrate an improved SVR rate when sofosbuvir is combined with pegylated interferon and ribavirin, including the highest SVR rates achieved in large trials for patients with cirrhosis. Furthermore, the adverse effect profile of sofosbuvir-based treatment appears much more favourable, both because sofosbuvir itself is well tolerated and also because total treatment duration is usually 12 weeks, reducing the adverse effects attributable to interferon and ribavirin. In addition to interferon-sparing regimes, there are also data that support the use of interferon-free regimes using sofosbuvir and ribavirin alone. This is the first opportunity effectively to treat patients who are ineligible or intolerant of interferon, including those with the most advanced liver disease. The inclusion of sofosbuvir in treatment regimes, both with and without interferon, therefore clearly meets a large unmet need for patients with chronic HCV infection.

Hepatitis C treatment is currently provided almost exclusively in specialist centres, under the supervision of Hepatitis Specialist Nurses. Interferon-free regimes in particular are likely to reduce the need for monitoring during treatment, increase the applicability of treatment outside specialist centres, and ultimately increase the

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proportion of prevalent patients with chronic HCV infection who are successfully treated – which is essential if treatment is going to have a significant impact on incidence of HCV infection and serious complications of infection.

Sofosbuvir was approved by the EMA through an accelerated assessment process for medicines of major public health interest. Economic considerations permitting, UK patients will benefit from this very significant therapeutic advance. The great majority of patients would gain from improved SVR and/or significantly fewer side effects using sofosbuvir-based treatment when compared with current standard of care. It is likely that in the short-term sofosbuvir would be very widely used if cost-effectiveness were demonstrated, and current standard of care regimes would become obsolete. The place of sofosbuvir in HCV treatment in the medium term is more complicated because several other new DAAs will be licensed and appraised. We still have much to learn about the optimal regimes and combinations of drugs for particular patient groups as more therapeutic options become available.

The advantages and disadvantages of the technology

The impressive SVR rates in large clinical trials using both interferon-sparing and interferon-free regimes, with a safety profile that is as good or better than current standard of care, implies that patients would benefit from widespread use of sofosbuvir. For most patients, sofosbuvir-based regimes are shorter and simpler than current standard of care and will require less intensive monitoring. Fewer laboratory tests and hospital visits will be needed. A proportion of patients currently treated using standard of care require supportive therapy with erythropoietin (for anaemia) or G-CSF (for neutropaenia), and this is less likely to be needed using sofosbuvir-based regimes. Regimens that include interferon remain unsuitable for patients who are interferon intolerant or ineligible, including some patients with advanced liver disease who most urgently require treatment.

The clinical trials have in the main included the types of patients who are treated in the UK. Further data are awaited for some particular groups of patients, such as renal dialysis patients. The trials have largely used SVR12 (see above) as the primary end-point, which is now a widely accepted surrogate for “cure” from HCV infection.

Equality and Diversity

Chronic hepatitis C is prevalent in deprived minority groups who are poorly represented on health care commissioning groups. These groups include ethnic minorities, injecting drug users and the homeless. Substantial numbers of patients with hepatitis C are derived from disadvantaged patients, ethnic minority groups, immigrant populations, the prison population, the homeless and those attending drug and alcohol services. The complexity and duration of current treatment regimes is a substantial barrier to treating many patients. Simplification of treatment by increasing application of new DAAs such as sofosbuvir is an essential next step for delivering effective treatment to these patients, and thereby treating a sufficient proportion of prevalent cases to reduce the incidence of infection and serious complications.

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Any additional sources of evidence
High quality and relevant evidence is widely available. The published trials of sofosbuvir contain important data on efficacy and safety.

Implementation issues

As described above, introduction of sofosbuvir would tend to simplify treatment regimes for chronic HCV infection. Centres with experience in managing patients with hepatitis C will be able to deliver this intervention without additional training. There is a need to improve accessibility of HCV treatment (see above) and simpler treatment regimes are an important component of this.