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Dear Sir or Madam

Re: Sofosbuvir for treating chronic hepatitis C [ID654] - Consultation on the decision to amend the deferred funding

The Royal College of Physicians (RCP) plays a leading role in the delivery of high quality patient care by setting standards of medical practice and promoting clinical excellence. We provide physicians in the United Kingdom and overseas with education, training and support throughout their careers. As an independent body representing over 30,000 Fellows and Members worldwide, we advise and work with government, the public, patients and other professions to improve health and healthcare.

The RCP is grateful for the opportunity to respond to the above consultation. In doing so, we have liaised with our experts in gastroenterology, hepatology, infectious diseases and genito-urinary medicine. We would like to make the following general and specific points as well as endorsing the submission of the British Society of Gastroenterology (BSG).

General comments (also submitted to the similar request regarding simeprevir in combination with peginterferon alfa and ribavirin for treating genotypes 1 and 4 chronic hepatitis C [ID 668])

We believe that a range of contributory factors means that NHS England Specialised Commissioning is facing huge financial issues and is therefore not able to afford the services it has taken on. Hepatitis C presents a particular problem. New treatments are available which are highly effective, demonstrably cost-effective yet unaffordable - the introduction of sofosbuvir, simeprevir, and daclatasvir has already caused significant issues in the US.

It is our opinion that NICE is likely to recommend the use of these drugs as:

- the treatments are highly cost effective (preventing the development of very costly liver disease)
- 'affordability' does not fall under NICE remit.

However, the NICE consultation on sofosbuvir has already been extended twice and there have been very significant changes made between the first and the second ACD. The final TA has still not been published (the original date was September).

A waiver has now been requested on the implementation period for the NICE guidance for sofosbuvir and for simeprevir - increasing it to 180 days from publication. This request has been made on the grounds that

the introduction of the new therapies is not clinically possible without the establishment of formal clinical networks defined by a national service specification. Our experts do not agree with this stance for several reasons:

Simeprevir - the case of simeprevir is the more straightforward than sofosbuvir. NHSE has approved (and indeed has fast-tracked) a policy for the use of simeprevir, which will be in place by late December 2014. This policy essentially allows the same use of simeprevir as the NICE TA, with the exception of use in genotype 4 virus (which makes up a tiny fraction of cases in England). If this policy can be introduced immediately without the need for a service specification then we see no reason why the NICE TA should be delayed. We are aware that NHSE have had the proposed service specification since December 2013. The specification has not been approved to date, and we do not feel it any more likely to be in place at 180 days than it is at 90 days. If the specification is considered essential for the development of new treatments we wonder why this has not been given greater priority?

Sofosbuvir - The situation with the sofosbuvir TA is more complicated, yet many of the same points above apply. Overall, we are unaware of any expert clinical opinion that says that the NICE TA could not be implemented immediately, using available resource. We therefore do not see this as a valid reason for delaying the implementation of NICE guidance on these drugs.

It is important to set these issues in the context that we are already lagging behind much of the developed world in our treatment of HCV. The disputed NICE TAs are still for interferon-based combinations, which have been in widespread use in the US for at least 6 months. NICE will not be reporting on interferon-free regimens (which are the standard of care in many countries) until the middle of next year.

Specific comments

The introduction of sofosbuvir does mark a significant advance in the treatment of chronic hepatitis C infection. However, the current NICE consultation relates to treatment with sofosbuvir in combination with pegylated interferon (with a few exceptions for subgroups of genotype 2 and 3 disease where it is recommended without interferon). This is very different from the paradigm shift in treatment seen in the United States and a number of other European countries, where for some time treatment has been available using sofosbuvir in combination with other potent oral anti-viral drugs such as simeprevir and daclatasvir. These all-oral treatments are better tolerated, simpler to administer, and have generally better success rates than regimens that still rely on sofosbuvir in combination with interferon.

The estimate of 15 000 patients being treated annually quoted by NHS England is made in the context of all-oral therapy being available, and is likely to be a significant over-estimate if the only treatment available still includes interferon. (Many physicians and patients will choose not to take up treatment with Sofosbuvir as part of an interferon-containing regimen, and will choose to wait for all oral therapy). The true figure is difficult to estimate, but is probably 6 -8 000 patients per year (compared with a historical rate of about 5 000 per year). Course length for sofosbuvir-containing regimens is shorter than for previous treatments (with pegylated interferon/ribavirin +/- 1st generation protease inhibitors), and side effects are dramatically reduced. The amount of clinical input for each patient will therefore be significantly reduced, and it is likely that existing treatment services will in general be able to cope with the predicted level of treatment demand that would follow implementation of the Sofosbuvir NICE TA.

One particular group of patient will gain significant benefit from treatment under this NICE TA: patients with advanced liver damage due to hepatitis C genotype 3 infection. Published and ongoing studies demonstrate that the addition of Sofosbuvir to interferon and ribavirin, including treatment of patients who have failed prior dual therapy with interferon and ribavirin, will result in a high cure rate for patients with established cirrhosis. Successful treatment will prevent liver failure, reduce the risk for liver cancer, and substantially reduce the need for liver transplantation in this population. Delaying treatment by contrast will result in avoidable harm to a proportion of these patients. The availability of sofosbuvir for treatment of hepatitis C genotype 3 infection represents the first improvement in treatment for the last 15 years.

The best way of delivering a high quality service for patients with hepatitis C infection is through managed networks based around specialist centres. The formal proposal for a Service Specification based on this principle was submitted to NHS England in December 2013, and remains under consideration. The request for deferral by NHS England is in part predicated on the assumption that this Service Specification is accepted and prioritised by CPAG, and that specialised centres will be commissioned and functioning by August 2015. In fact, there is no certainty that it will be approved by the Specialised Commissioning Oversight Group (SCOG). Even if the Service Specification is eventually approved it is unlikely to be done in time for the 2015-16 commissioning round, and NHS England have made it clear that new services will only be commissioned 'in year' in exceptional circumstances. The request for deferral of sofosbuvir treatment on the grounds that a reliable and functioning new delivery structure will be in place by August 2015 is therefore based on a series of assumptions and aspirations rather than by fact.

NICE will judge the request for deferral on four specific criteria. The responses to these are as follows:

a. The health technology cannot be appropriately administered until training is in place;

All the centres likely to be using sofosbuvir plus pegylated interferon have been treating patients with pegylated interferon in combination with ribavirin, boceprevir, and telaprevir for some considerable time. They therefore already have staff trained and experienced in the use and monitoring of interferon and ribavirin. Sofosbuvir has very few significant side effects or drug-drug interactions (certainly fewer than the 1st generation protease inhibitors), and many of the centres will already be using sofosbuvir under the early access programme. For those centres that do not have previous experience of sofosbuvir the additional training required will be minimal.

b. The health technology cannot be appropriately administered until certain health service infrastructure requirements including goods, materials or other facilities are in place;

As discussed above, all treatment for hepatitis C infection would be better managed through clinical networks. This would allow for universal quality standards, equity of access, and better data collection. However, there is no absolute requirement for these networks, and there is as yet no guarantee from NHS England that it will commission them anyway. Some informal networks already exist, the current system of treatment delivery is adequate (at least in the short term), and the absence of universal clinical networks should not prevent the most urgent patients from receiving treatment as soon as possible.

c. The health technology cannot be appropriately administered until other appropriate health services resources, including staff, are in place;

Given the estimated level of demand for the treatment regimens covered by the NICE TA (i.e. predominantly sofosbuvir in combination with pegylated interferon), the shorter courses of these regimens compared with first generation protease inhibitors, and the relative simplicity of monitoring patients on sofosbuvir compared with other drugs, the current levels of human resource and facilities should be adequate to deliver the proposed treatments. Approximately 5 000 patients per year are being treated successfully with far more complex and lengthy drug regimes, and there is no reason to think that a moderate increase in numbers being treated will be unmanageable.

d. The health technology is not yet available in England.

This criterion is not relevant to the current consultation.

Overall, the facts do not support the NHS England case for an increase to the implementation period for this NICE TA.

Yours faithfully

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