Dear Mr Boysen

NICE TAs on sofosbuvir and simeprevir

Thank you for asking for my comments on the NHS England application for a deferral of implementation of the NICE Technology Appraisals (TA) for simeprevir and sofosbuvir. The CRG HCV subgroup has discussed this request at some length. While there is some variation in detail of opinion, not one of the clinicians on the group supports the request for a delay in either TA.

It is important when considering these NICE TAs to remember that they deal almost entirely with interferon-based therapy. Adding sofosbuvir or simeprevir to pegylated interferon is certainly a step forward, but it is not the paradigm change that all-oral regimens have brought to treatment in some other countries. A significant proportion of patients who are eligible for treatment under these two NICE TAs may well opt instead to wait for more effective and more tolerable regimens, and the demand is unlikely to be as high as has been suggested.

Simeprevir

Simeprevir is perhaps the more straightforward of the two drugs to deal with. Simeprevir plus pegylated interferon and ribavirin (Sim/P/R) is a regimen whose time has largely come and gone. There are relatively few patients (perhaps a few hundred across the country) for whom this treatment is still appropriate (although some of the expert clinicians on the subgroup do not believe that it has any application at all now). These are patients with relatively mild disease due to genotype 1 or 4 virus, who have made an informed decision not to wait for more tolerable and effective oral treatments. The HCV subgroup submitted an interim policy document to NHS England in May 2014 recommending the use of Sim/P/R (at which point uptake may have been greater); this interim policy has now finally been approved by NHS England and should be implemented soon. The policy allows use of Sim/P/R in patients with genotype 1 (not genotype 4) infection, in accordance with the simeprevir licence. It is therefore similar to the NICE TA, except for the g4 indication.

The main argument from NHS England for an extension of the NICE implementation period from 90 to 180 days is that it will take this time for systems to be put in place to deliver Sim/P/R treatment. Given that uptake for this regimen is likely to be low, and for those patients in whom it is used it will be a direct replacement for telaprevir/P/R or boceprevir/P/R (both of which have longer courses and more side effects than Sim/P/R) we do not envision any difficulty for current providers in delivering the new treatment immediately. NHS England have already approved a policy very similar to the NICE TA, to be delivered through existing systems, so it is puzzling that they do not think that the NICE TA can be delivered through the same route.

The HCV subgroup was not unduly concerned about the clinical impact of a delay in implementation of the simeprevir TA because of the NHS England interim policy allowing its use (and the view of some members that it should not be used at all). However for a small group of patients with genotype 4 infection (almost exclusively Egyptian) a deferral would mean further delay in access to therapy. Genotype 1 patients (largely Caucasian) would be eligible for treatment now, while the genotype 4 patients would face a wait of several months.

Sofosbuvir

The arguments around sofosbuvir and pegylated interferon (plus or minus ribavirin) – Sof/P/R – are more complex. As with Sim/P/R many patients, especially those with mild disease, may choose to wait until all-oral regimens are available. However patients with stable cirrhosis, who are at risk of decompensation or hepatocellular carcinoma, may decide (after discussion with their clinicians) that it is better to have treatment now than delay. This is especially true for those with genotype 3 infection. There is therefore more urgency to get availability for this combination, and there is currently no interim policy to supply it through NHS England (apart from the highly restricted early access programme for sofosbuvir plus ledipasvir in decompensated liver disease). It is difficult to predict the number of patients who will opt for treatment with Sof/P/R rather than waiting, but it will not be nearly as many as the 15 000 quoted by NHS England (this figure was based on an estimate of the number that might come forward for all-oral treatment).

NHS England have requested a delay in implementation on the ground that it will be impossible to get a delivery system for Sof/P/R in place within 90 days of the NICE TA publication, but it will be possible in 180 days. This proposed delivery system is based on the idea of a centrally-commissioned service run through networks of specialist providers. The majority of the clinicians on the HCV subgroup remain of the opinion that the best way to deliver hepatitis C services in England is indeed through this network model. However this is not the only model of delivery, and is certainly not an absolute requirement for getting treatment to patients. The members of the HCV subgroup believe that current resources and delivery systems are adequate to provide safe and effective treatment for those patients who will opt for treatment with Sof/P/R.

The HCV subgroup submitted a completed proposal for a HCV Service Specification to NHS England (including the establishment of the network model) in December 2013. This specification remains under consideration by NHS England, and has yet to be approved. The HCV subgroup has asked why, if it is thought to be essential for service delivery, this specification has not been approved and adopted already.

Sof/P/R is a regimen that will have limited appeal to many patients, who will wish to wait for all oral treatment. It may however be life-saving for some people who have cirrhosis, and are at risk of rapid disease progression without treatment. A further 3 month delay may have a significant effect on the outcome for a small group of patients. This is amplified by the fact that many clinicians have held off treating some of these patients for many months already in anticipation of NICE approval of the new drugs. Given that the clinicians on the HCV subgroup can see no practical difficulty in delivering the treatment straight away (accepting that the current model is not the one that most would ideally like to see in place), and that there is no guarantee from NHS England that a better system will be put in place in the near future, there is a strong argument for making these drugs available as soon as possible, and not delaying further.

In summary, the unanimous view of the clinicians on the HCV subgroup (made up of representatives from the HPB and ID CRGs) is that:

- Sof/P/R is an important new therapeutic choice, and may be life-saving for a small number of patients;

- Sim/P/R may be useful in a minority of patients with mild disease;
- Current services will be able to deliver these treatments safely and effectively to the number of patients likely to opt for the new interferon-based regimens;
- There are no grounds (under the terms of the Health and Social Care Act 2013) for NICE to delay implementation of its guidance beyond the 90 day period specified.

Yours sincerely

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