Response to Sofosbuvir ACD ID 654 on behalf of NHS England Specialised Commissioning

This response has been prepared on behalf of NHS England Specialised Commissioning. It has been written by the Commissioning Advisory Group (CAG) on Hepatitis C, representing the Infectious Diseases and HPB Clinical Reference Groups, and has been reviewed by all members of the group including the accountable commissioners.

Members of the CAG are familiar with sofosbuvir, having participated in clinical trials in the UK with this drug, and we are aware of the very considerable pressure from patients and clinicians for access to this valuable therapeutic option. There are clearly concerns that the drug may prove to be 'unaffordable' and NHS England commissioners are working closely with the clinical experts on the Advisory Group to ensure that, if NICE approved, the drug can be commissioned as part of a stratified approach to treating hepatitis C, making the most cost effective use of the new drug. The Advisory Group has recommended that clinical networks be established with regular MDT meetings to discuss patients and ensure that the most appropriate therapies are provided. This structure will ensure that only those patients who will get significant benefit from the addition of sofosbuvir will be offered treatment. It will also ensure that extended duration treatment with sofosbuvir will only be used when strictly appropriate. We note that the ICER for Genotype 1 patients who are 'intolerant' of Pegylated interferon and ribavirin was £49,249 per QALY. A network approach to HCV commissioning will ensure that only patients who are truly 'intolerant' of pegylated interferon and ribavirin will be considered for this option: specialist centres identify only a small proportion of patients as falling into this category (perhaps 5 - 10%). The same reasoning applies to patients with genotypes 2 and 3 HCV where for most patients 24 weeks of interferon free sofosbuvir is a 'second best' option limited to those who are genuinely intolerant of interferon.

In the ACD ICERs are divided by the presence or absence of cirrhosis. While we recognize the merit in so doing it does raise several significant concerns:

- Non-invasive methods of assessment are not entirely reliable in clinical practice (as opposed to clinical trials), they are not useful in some patients (e.g. the obese, where fibroscan is unreliable), and the division into cirrhosis and non-cirrhosis will inevitably lead to a return to a policy of liver biopsies for many patients. This will deter patients from therapy and render some vulnerable sub groups (e.g. prisoners where a biopsy is logistically very difficult) ineligible for sofosbuvir.

- The greatest potential benefit of treating hepatitis C is seen in patients in the immediately pre-cirrhotic stage, in whom effective treatment may avert the development of cirrhosis and avoid a lifetime risk of hepatocellular carcinoma (with all the screening resources that this requires). Even liver biopsy is an unreliable test in this group. The

potential benefits of treating this (not insignificant) sub group of patients are not accounted for in the simple 'cirrhotic/non-cirrhotic' model.

- We are also concerned that the extensive literature relating to the extra-hepatic manifestations of hepatitis C (EHMs), such as specifically neuro-cognitive dysfunction, have not been adequately reviewed and considered. Many patients with hepatitis C complain of severe fatigue and excluding patients with mild hepatitis C and disabling fatigue from sofosbuvir and permitting only those with cirrhosis (who may be asymptomatic) to access the drug (or vice versa) will be clinically difficult to implement. Other rare but potentially devastating EHMs such as cryoglobulinaemia and non-Hodkins lymphoma are also unrelated to the degree of liver damage.

- There is emerging evidence, largely but not exclusively based on modeling, demonstrating the benefits of treating active injecting drug users with effective anti-viral therapy and thereby reducing onward transmission; this has not been considered in the ACD.

In clinical practice virtually the only clinical group who are truly 'Interferon intolerant' are patients with advanced, decompensated cirrhosis. NHS England has already commissioned an urgent therapeutic program for such patients (they will receive 12 weeks of funded sofosbuvir plus 'free' daclatasvir/ledipasvir as part of an expanded access program) and we anticipate that about 500 such patients will be treated in this scheme. For patients who present after the discontinuation of this scheme 24 weeks of sofosbuvir is likely to be a highly effective treatment option and data presented at International Liver Meetings (EASL and AASLD) indicate that treated patients may re-compensate and avoid liver transplantation or death. It would be helpful if NICE were able to review the cost-effectiveness of therapy in this group. We would be very concerned if patients with end stage liver disease due to HCV were unable to access life saving therapy and we suggest that NICE review the cost effectiveness of this intervention.

We were surprised by the cost effectiveness analysis with telaprevir – as experienced users of this drug we find that the side effect profile (profound anaemia, rashes and malaise) necessitate frequent out-patient visits and a number of patients require hospital admissions for blood transfusions and other serious adverse events. Real world experience has shown a much higher frequency of significant adverse events with both first generation protease inhibitors than suggested by clinical trials, and we are concerned that these additional NHS costs have not been adequately examined.

Sofosbuvir is an important new drug with significant clinical advantages over current agents. The commissioning arrangements that we have recommended will allow physicians to use the drug in the most clinically and cost effective manner and thereby ensure maximum benefits to patients and the wider community. We request that the NICE committee include the evidence and

expert opinions presented in this consultation response when making their final decision on sofosbuvir.

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