9th June 2015

Dear NICE Team,

Re: NHS England response consultation: (Hepatitis C (chronic)

- Daclatasvir[ID766].
- Ombitasvir/paritaprevir/ritonavir with or without dasabuvir [ID731]
- Ledipasvir-sofosbuvir [ID742]

As a committee member of the United Kingdom Clinical Pharmacy Association (UKCPA) Gastroenterology and Hepatology Group I would like to thank NICE for requesting us to respond to the comments made by NHSE to the ACD consultation on the new anti-virals for hepatitis C.

Due to the confidential nature of the NHSE comments the committee response is based on my overall senior opinion and discussion themes which we as a group have had since the changing paradigm of hepatitis C.

The NHSE response to the ACD consultation is robust and attempts have certainly been made to address the concerns put forward by NICE and committee members and we feel this should be acknowledged. However we believe there remains a number of points which need addressing and outline these below.

- It is our understanding that a NICE Only in Research (OIR) specification was developed to deal with interventions which may not be supported by a sufficiently robust evidence base to justify an unqualified recommendation. In the latter instance NICE would outline what further research is carried out to help realise the promise of the intervention. NICE have not outlined that their appraisal process supports an OIR scheme for the anti-virals currently available. NHSE have not outlined specifically what research they would want NICE to undertake nor has their response defined who would be responsible for funding this.

- How would a OIR specification give clarity on what treatment regimen would be 'first line' etc? This is not clear in the response from NHSE and with the current access policy being very limited we would be concerned if these restrictions on choice remained the case until a multiple technology appraisal was undertaken.

- If a regimen choice was given in a OIR access scheme how would this be done and by whom?

- The NHSE response has outlined that there are a number of drugs in the pipeline which may rival the effectiveness of the currently licensed anti-virals however surely this is the same with any drug which NICE appraise or NHSE have to consider? Uncertainties with regards a treatment can never be fully excluded and it would be unrealistic for NHSE to use this as an argument for an OIR specification.

- We appreciate that collating an abundance of real world data could facilitate more robust decision making and support this. Are we in a position where the results of the first phase of the EAP can be used – these results have been presented at the recent EASL conference and further support the benefits of some of the anti virals currently available. Have NHSE considered using filtered non UK based real world data such as HCV-Target from the States to enhance their assurance with regards treatment regimens?

- Will we need to wait for real life experience data for all of the upcoming agents including those that may not be licensed until 2016/17? How much real life data and in what time scale will be considered sufficient? As the NHSE response outlines it is challenging to predict how swiftly disease progression can take place in a non-cirrhotic patient. One could argue that an F2 patient who is of African descent, overweight, diabetic, male and 65years of age may progress faster than those with no other risk factors –will there be capacity in an OIR specification to take this into account?

- Does the existence of an OIR specification remove the ability for exceptional cases? Will there be an exceptional panel? And will this be fully supported / funded by NHSE?

- NHSE outline that they are confident that a stepwise implementation programme can be formed to substantially reduce the burden of disease however we are not convinced based on the delays we have seen in the development of a cirrhotic and advanced fibrosis policy.

- We are concerned that an NHSE promoted NICE OIR approach will remove the ability of a common sense approach and importantly clinician expertise where more than the clinical scenario with regards a patient is taken into account (e.g. previous treatment history, social and psychological factors).

- Research has shown that lifetime healthcare costs for a HCV-infected person are significantly higher than for non-infected persons. This point has not been focused on in the NHSE response and so the added value of treating and curing a less advanced patient has not been made clear.

- A recent report in the Lancet led by leaders in the field of Hepatology and Health Economics outline that viral hepatitis remains a significant issue in the UK. It stresses that hepatitis C can be prevented and details that a lack of investment in this disease area has not assisted with stemming the increase in HCV prevalence. The longer that the HCV infected population are left untreated the greater the risk of potential transmission. We acknowledge that anti-viral treatment is but one aspect of the HCV pathway but are not reassured by the complete absence of any detail in the NHSE response with regards plans for increased screening and diagnosis. If the treatment population is going to be restricted due to an access scheme then the latter point must be addressed.

- The NHSE response outlines the need to allow for a more extensive time period so as to assess emerging evidence. The time frame of 18 months – 5 years has been detailed with regards developing a multiple technology appraisal etc. There is a lack of clarity on what will actually be delivered by NSHE in this time frame other than collection if 'real world data' which we presume will ultimately be the responsibility of the treatment centres and not NHSE.

- There are concerns that the current NHSE access programme has been reliant on a small number of individuals and as a result communication of information and translation of developments has been, at times, less than optimal. There are also concerns that the lack of transparency as to 'who is in control' of an access scheme has proved challenging when questions arise. This is not an issue we have had in previous treatment pathways for HCV

and have always had a 'point of contact'. NHSE would need to ensure greater transparency with regards contact personnel in future potential schemes.

- We are concerned that the approach from NHSE to a high cost therapy has changed abruptly. The evidence base in terms of numbers for the new anti-virals is arguably more robust than the studies used to look at earlier agents such as Telaprevir and Boceprevir. The percentage of cirrhotic patients has been outlined as low in the NHSE response but in fact the number of cirrhotic patients and special populations such as those co-infected with HIV has increased. Also it is our understanding that reinfections or onwards transmissions (including or excluding either) have not been previously included in a NICE appraisal such as this and therefore should not be used by NHSE as a cost effectiveness uncertainty.

- We are concerned that cost effectiveness is heavily focused on within the NHSE response. We would dispute that if NHSE had concerns are issues with the currently used NICE cost effectiveness model then this should have been addressed last year so that amendments could have potentially been made to the calculations in advance of this response. NHSE need to be clearer on what they want to achieve with regards data on affordability V cost effectiveness. There remains a lack of definition on what overall value they attach to a patient achieving a SVR especially those with less advanced fibrosis

- If one or more agents in development comes out more appealing in terms of 'direct drug cost' and has acceptable SVR rates will NHSE retract its wish for an OIR specification?

- The NHSE response outlines that anti-viral treatment could be commissioned on an evaluative basis for fixed 2 year period with robust data collection and analysis led by regional networks – does the NHSE feel that they can commit to this time frame to have a full strategy in place? We are concerned as a result of the time lags we have seen in the current development of strategies. A commitment to a time frame would need to be transparent.

- *Watchful waiting* as described in the NHSE response is not seen as routine practice in many HCV treatment centres. As a result of the tolerability of PR being so low it is important that patients who are as clinically fit as possible get initiated on this regimen. The longer the patient is left the greater their risk of developing complications on treatment or becoming ineligible for exposure to interferon. Watchful waiting was more aligned with the practice of waiting for the currently licensed anti-virals to become available so that better tolerated and more efficacious treatments could be offered.

- Capacity issues outlined in the NHSE response existed with interferon treatment and are likely to be greater if this continues to be the sole treatment available for non-cirrhotics. Interferon requires regular monitoring due to its side effects and tolerability issues. The newer agents require less intensive support once a pre readiness screen has been completed to ensure adherence.

- Concerns with regards development of NS5A resistance outlined in the NHSE response lacks some validity based on the fact that a restricted commissioned access scheme will not remove the risk of developing resistant variants. The risk is present in either a restricted or unrestricted access scheme.

- Whilst we appreciate that NHSE has finite resources and that we are in a state of economic recovery we would argue that the newly licensed anti-viral have been known about for over

2 years. We are concerned that there is a lack of recognition that these new agents were aware of by NHSE and that this further supports the lack of acknowledgement as to the burden of viral hepatitis. Certainly Horizon Scanning, the sole purpose of which is to assist with 'budget planning' highlighted the majority of the new agents coming on board back in 2013.

- There is confusion with regards treatment number predictions in the NHSE response and the range 7,000-20,000 (F0-F4) is not realistic. There is a discontent between their argument with regards capacity and potential treatment numbers. There needs to be recognition that a clinician or treatment centre will only treat a number of patients that s/he can to do so safely.

As a pharmacy led group we have been at the forefront of the delivery of the first phase of the NHSE commissioned scheme and have been involved in the discussions with regards the cirrhotic and potential F3 policy. At times the disconnect between NHSE, CRGs and those at the ground level has been frustrating. There has been a lack of uniformity in the translation of information to treatment centres and as a result this had led to a lot of reacting to new policy changes as opposed to being proactive. If NHSE are successful in delaying open access to the new antiviral and move forward with a further commissioned access scheme we would seek policies which are delivered in a much more streamlined fashion and which have the clarity that is needed.

The decompensated cirrhotic access scheme required significant workforce input from a pharmacy standpoint. We undertook the later without any additional funding or support and in conjunction with our current clinical roles. If a similar access scheme was to be supported by NHSE then there would need to be some form of additional funding acknowledgement at a local and national commissioning level for specialist pharmacy input. We believe that it is clear from phase 1 of the NHSE access scheme that pharmacists are essential in the delivery of the newer anti –virals.

We thank you again for inviting us to comment on the NHSE response and we welcome all future involvement with NICE.

Yours Sincerely,

On behalf of the Gastroenterology and Hepatology UKCPA Group