Appraisal Consultation Document: Ledipasvir–sofosbuvir for treating chronic hepatitis C [ID742]

Comments from the Liver Section Committee of the British society of Gastroenterology (Dr [redacted], Consultant Hepatologist, Royal Devon and Exeter Hospital)

Thank you for asking the Liver Section Committee of the British society of Gastroenterology (BSG) to comment on the Appraisal Committee's preliminary recommendations for Ledipasvir–sofosbuvir combination for the treatment of Hepatitis C Virus.

The appraisal is well researched and takes into account all of the relevant evidence to date. The summaries of the clinical and cost effectiveness are reasonable interpretations of the evidence. Problems were highlighted with analysing the clinical effectiveness, as the clinical study designs were open-label, non-randomised controlled evidence, with no head-to-head studies. Historical trials of older treatments were used for comparators and there is some criticism of the selection of SVR rates for comparators from single studies and the use of an uncontrolled naive indirect comparison to estimate the relative effectiveness. However we would point out that SVR is a hard and objective end point and that the baseline characteristics of the study populations were similar except for a higher proportion of people with cirrhosis and HCV genotype 1 subtype 1a in the ledipasvir–sofosbuvir studies, previously associated with lower SVR rates. In view of the excellent SVR results and good side effect profile in the phase II studies, we think that the study designs were reasonable. Whatever the criticism of these studies, the SVR results in the ledipasvir- sofosbuvir are impressive and are a major leap forward for curing patients of Hepatitis C.

We think that the provisional recommendations are sound and a suitable basis for guidance to the NHS. However we hope that in the future there will be more evidence to make further recommendations for patients with genotype 3 and 4. Indeed whilst historically genotype 1 infected patients was a major clinical challenge in NHS practice, genotype 3 infected patients with advancing liver disease has now become the major problem facing clinicians because of the improvement in drugs that cure genotype 1 and not 3.

The BSG would also want to stress the major clinical advance that interferon free treatments offer patients. The impact on patients and clinicians (in particular the hepatitis C nurse specialists) is considerable. Current therapies containing interferon are associated with severe side effects, such as fatigue, neuropsychological effects and flu-like symptoms. Patients require close monitoring and much support from nurse specialists to complete treatment. Sofusbuvir-ledispavir has few side effects, requires short duration, has excellent cure rates and is likely to have good patient adherence for all these reasons. Curing hepatitis C will prevent death from decompensated cirrhosis and hepatocellular cancer. However being infected with HCV also causes psychological effects and can

stigmatise patients impairing their social life and ability to work and cause anxiety about transmitting the virus. The availability of clinically-effective treatment such as ledipasvir–sofosbuvir, will encourage more people to seek diagnosis and treatment.

We do not believe the appraisal discriminates against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity. The recommendations will help the vulnerable group of patients with mental illness who cannot tolerate interferon containing treatments because of neuro psychiatric side effects of interferon.