Name	[redacted]
Organisation	Pharmacology and Therapeutics, University of Liverpool
Role	NHS Professional
Job title	[redacted]
Location	England
Conflict	No
Disclosure	We have published references with the reference data which could be used to update and validate this CE model. We will be working in parallel on a Markov model of HCV treatment, to check the assumptions and cost-effectiveness.
Comments	«Comment_Id» 770 «Comment_type» General Problems with Gileadâ€™s cost-effectiveness model of sofosbuvir/ledipasvir There appear to be six key problems with the current cost-effectiveness model of sofosbuvir/ledipasvir, as included in the recent NICE evaluation. Changes in the parameter estimates as suggested below could significantly affect the evaluation, and the suggested price of Â£35,000 per 12 week treatment course may no longer be justified. Re-infection / recurrence rates are higher in 5 year analysis of either IV drug users or HIV/HCV co-infected patients In the CE model from Gilead, the estimated risk of either recurrence or re-infection after SVR was estimated to be 0-1% (page 164 of Gilead document). However this estimate was only based on expert opinion and not on a systematic review of the literature. In a recent meta-analysis of 66 studies in 11,071 patients (presented at AASLD in November 2014), the 1 year risk was 0.23% in mono-infected patients. However this risk was 2.8% per year in IV drug users or prisoners, and 4.8% per year in people co-infected with HIV. Including these higher risks of recurrence would reduce the cost-effectiveness of sofosbuvir/ledipasvir, in a lifetime model, increasing the ICER estimate. A substantial percentage of people infected with HCV in the UK are either co-infected with HIV or are IV drug users. The Gilead CE model of sofosbuvir/ledipasvir should be re-run, including more recent estimates of re-infection rates after SVR, based on a systematic review rather than expert opinion. This re-analysis may then question the cost-effectiveness of sofosbuvir/ledipasvir in IV drug users or people with HIV/HCV co-infection.
Submission date	2015 03 05

Name	[redacted]
Organisation	Patient
Role	Patient
Job title	Hepatitis support

Location	England
Conflict	No
Disclosure	
Comments	«Comment_Id» 776 «Comment_type» General I find it incomprehensible that you propose withholding treatment with Harvoni from treatment experienced G1 and G4, on the basis that optimum treatment length (24weeks) is too expensive, cure rate 97-100%. Why can it not be allowed for the suboptimal (12 weeks)? Still a 87% cure rate. You are effectively penalising patients for having tried to cure themselves with previous treatments. You are prepared to grant the same treatment for non cirrhotics and treatment naive, but denie the most seriously ill set of patients an 87% chance of a cure, leaving them at risk of hepatic cancer and liver failure, because to give them a 100% chance of a cure would be too expensive. Your proposed guidelines seem to make no sense, those who are unable to tolorate interferon based treatments have no other option. Please consider adding this patient sub group it would not cost anymore to allow them a 12week treatment even if a 24 week treatment would have given them a better a slightly better chance.
Submission date	2015 03 06

Name	[redacted]
Organisation	Sheffield Teaching Hospitals NHS Foundation Trust
Role	NHS Professional
Job title	Consultant Physician in Infectious Diseases
Location	England
Conflict	No
Disclosure	I have received funding to attend conferences from Gilead.
Comments	«Comment_Id» 798 «Comment_type» General The recommendation of ledipasvir-sofosbuvir for the treatment of chronic hepatitis C genotype 1 and 4, for treatment naive patients (both cirrhotic and non-cirrhotic) and for non-cirrhotic treatment experienced patients is very welcome. Please could it be clarified that NICE conclude that 8 weeks of ledipasvir-sofosbuvir is recommended for all genotype 1 treatment-naÃ¯ve non-cirrhotic patients, regardless of baseline HCV viral load â€“ in spite of increased relapsed rates with the 8 week versus the 12 week treatment duration in this patient subgroup with baseline HCV RNA >6 million IU/ml. Could a 12 week treatment duration be considered to be as cost-effective in light of reduced relapse rates for genotype 1 treatment-naÃ¯ve non-cirrhotic patients with a baseline HCV RNA >6

	million IU/ml? The complete lack of recommendation for genotype 3 patients raises concerns as to what options clinicians are going to have to treat these patients, particularly patients who are intolerant of or ineligible for interferon-based treatment, for whom there are no other treatment options other than 24 weeks of sofosbuvir + ribavirin, expensive and with poor efficacy, and for patients who do not respond to pegylated-interferon + ribavirin + sofosbuvir, for whom there are no other imminent treatment options. This is especially worrying for patients who already have cirrhosis, or advanced fibrosis with imminent risk of progression to cirrhosis, who, if untreated, will have a higher risk of liver-related complications, ultimately incurring greater cost to the NHS and most importantly for the patients. Whilst it is appreciated that there is at present only preliminary data on the use of 12 weeks of ledipasvir-sofosbuvir + ribavirin for Genotype 3 infected patients, and numbers of patients being studied are small, results look promising. Will NICE re-consider recommending ledipasvir-sofosbuvir + ribavirin 12 week therapy for genotype 3 infected patients when SVR12 data is available? The only imminent alternative for these genotype 3 patients, either intolerant of or ineligible for interferon-based treatment or who do not respond to pegylated-interferon + ribavirin + sofosbuvir, will be sofosbuvir + daclatasvir +/- ribavirin. It seems unlikely that this latter regimen will be as cost-effective as 12 weeks ledipasvir-sofosbuvir + ribavirin. The lack of recommendation for treatment-experienced genotype 1 and 4 cirrhotic patients is also of concern. Whilst there will be alternative treatment options later this year for these patients in the form of ombitasvir/paritaprevir/ritonavir +/- dasabuvir + ribavirin, not all patients will be able to have these drugs on account of insurmountable drug-drug-interactions, especially for HIV-HCV coinfected patients who may not have suitable antiretroviral switch options, or with physical health contraindications to protease-inhibitor based HCV treatment. Whilst it is accepted that 24 weeks ledipasvir-sofosbuvir is not cost effective, could NICE review the growing evidence of 12 weeks ledipasvir-sofosbuvir + ribavirin to treat these patients, including consideration of experience from Gileadâ€™s Early Access Programme for decompensated cirrhotics being treated with this regimen? Many thanks for taking these points into consideration. This draft guideline
Submission date	2015 03 20