Response to NHS England Submission to NICE regarding the STA appraisals for new medicines to treat Hepatitis C

Submitted on behalf of Gilead Sciences Ltd.

Executive Summary

- We have serious concerns in relation to any consideration of affordability within the NICE appraisal process
- LDV/SOF is a highly cost-effective medicine for the treatment of chronic Hepatitis C, especially for patients without cirrhosis, with ICERs of £8,894 for treatment naïve non-cirrhotics and £16,566 for treatment experienced non-cirrhotics
- The treatment of patients should not be determined solely by liver fibrosis. HCV is a communicable disease, spread by blood – blood contact, that causes significant extra-hepatic manifestations in many patients, leading to reductions in quality of life prior to the progression to moderate liver damage

Even if affordability was going to be taken into account, we disagree with the assumptions and figures reported by NHS England:

- Based on previous NHS England communications, feedback from clinicians and experience from other countries, we expect that between 7,000 and 15,000 patients will be treated per year
- In the NHS England submission, a budget impact of £700m is referred to, which we understand is based on treating 32,000 patients per year despite NHS England stating that it is "*unlikely that calls for treatment access will exceed 20,000 per annum*" (pg 3). This number is also greater than the number of patients reported by NHS England as currently accessing care (28,500).
- We estimate the incremental budget impact for LDV/SOF as £85-£276 million.
- We estimate the total spend on HCV could be £259-£465million (based on list prices). This would make spend on Hepatitis C medicines ranked between 9th and 23rd in terms of medicine spend by the NHS (currently ranked 37th) – certainly not an extraordinary situation
- NHS England stated they have £592m uplift in the 2015/16 financial year. Based on the projected TAG timelines plus 90 day implementation, these medicines will require funding for 4 months in the current 2015/16 financial year (pro rata budget impact of £28-£92 million)
- NHS England currently have and expect further commercial in confidence discounts which will further reduce the budget impact

Inclusion of affordability in the NICE appraisal process

Gilead refers to its 9 June 2015 letter to NICE (Meindert Boysen) setting out our serious concerns in relation to the introduction of any consideration of affordability into NICE's appraisal process. While Gilead sets out below a substantive response to the matters raised by NHS England in advance of the deadline for comments, as noted in our correspondence of 9 June, we maintains our view that if NICE intends to consider the affordability of ledipasvir-sofosbuvir, that this approach is procedurally unfair.

The affordability of a technology is a political question for Government; it is not a matter of cost-effectiveness. In its response to consultation on the ACD in the LDV/SOF appraisal, NHS England recognised that "*affordability is not part of the consideration of the Technology Appraisal process*" - we are not aware of any change to the NICE method guide which would explain if or how affordability should be taken into account in a single technology appraisal.

The claim by NHSE that the treatment of patients with Hepatitis C will cause "damaging cuts elsewhere" is unhelpful. The purpose of NICE assessment is to provide an impartial and objective value assessment regarding a new technology based on transparent and pre-specified criteria.

NICE routinely provides positive recommendations for medicines with ICERs up to £20,000-£30,000 and with significant budget impact to the NHS. In the case of ledipasvir/sofosbuvir the ICERs are considerably lower than the threshold and the expected HCV budget is well below that observed in other disease areas. NHS England has failed to provide any evidence that the budget impact of this appraisal sits outside any threshold of typical medicines spend.

During the consultation on the ledipasvir-sofosbuvir ACD, NHS England stated a "*second access scheme for all patients with cirrhosis soon to be available*". Clinicians, patients, and NICE were led to believe this would happen by April 2015. It was also stated this would be put in place to ensure patients would not be disadvantaged and put at risk of serious and lifelong health consequences as a result of the delayed implementation of the sofosbuvir TAG. This policy was substantially delayed before finally being announced on June 10th.

The result of this policy delay and the uncertainty imposed on the funding timelines f has caused patients to have multiple appointments cancelled and rebooked, causing significant disappointment and inconvenience for both patients and clinicians as well as expense to the NHSE. It is estimated that as a result of this delay (2 months) 37 patients with cirrhosis will have progressed to decompensated cirrhosis and 57 will have developed hepatocellular carcinoma; both have severe and potentially fatal consequences. Due to these risks, in some instances patients have chosen to fund their own treatment, despite the existence of a NICE recommended medicine, as their treating physician could not guarantee when the policy might come into effect.

The suggestion by NHS England that patients can only access these treatments for the foreseeable future via an NHS England commissioning policy means there is great uncertainty for clinicians and patients regarding when they will have access to treatment. This is particularly relevant given that for the non-cirrhotic, treatment naïve patients Harvoni dominates versus current standard of care. Since LDV/SOF received European marketing authorisation an estimated 300 patients have been initiated onto a PI based regimen which

is more expensive and less effective in the non-cirrhotic group. A significant proportion of these patients may fail and then require further expensive therapy.

The restriction of the use of these new medicines will require patients who want to be treated to be subject to sub-optimal, more costly treatments with lower probability of success if they do not want to wait for treatment. There is no accountability for NHS England to provide these medicines beyond the policies in place or to introduce policies within the timeframes committed to. Aside from our concerns around the affordability estimates and scope of the NICE process, the proposed strategy is inappropriate for this patient population, given that we have already established the majority of the diagnosed patient population are lost to follow up.

Cost-effectiveness of LDV/SOF in patients without cirrhosis

In the ACD for ledipasvir-sofosbuvir LDV/SOF (23rd February 2015) the NICE committee recognised that LDV/SOF is a cost-effective use of NHS resources across patients with genotype (GT) 1 chronic Hepatitis C and in selected GT4 patients.

NICE makes decisions based on a threshold of £20,000 to £30,000 per QALY, which has historically been taken to represent the opportunity cost that the NHS accepts when thinking about whether a technology offers value for money to the NHS. As part of the PPRS discussion it was agreed that the threshold would not change, demonstrating the continued support for this threshold value.

LDV/SOF offers a cost-effective treatment option whether using the accepted threshold at £20,000 to £30,000 per QALY or even when using the artificially reduced (and extreme) ICER threshold of £13,000 per QALY, for the majority of the non-cirrhotic HCV population. For this population, which is the focus of NHS England request for an ‘only in research’ recommendation, LDV/SOF is highly cost-effective based on the incremental analysis with ICERs of £8,894 for treatment naïve (TN) non-cirrhotics (NC) and £16,566 for treatment experienced (TE) NC. This uses 48 weeks of PEG and RBV as a comparator, which tends to be used as a clinical option only where protease inhibitors (PIs) are not considered suitable.

LDV/SOF dominates versus the medicines that are standard of care for the non-cirrhotic patient population (SMV, TVR or BOC). This is because the 8 week regimen of LDV/SOF is cheaper as well as showing significantly higher efficacy (94% versus 82%, 77% or 64%). We estimate PIs are currently prescribed in at least 70% of GT1 patients treated in the UK (based on IMS data).

According to the NICE methods guide, when the budget impact is considered “high” a greater level of certainty around the ICERs is required. The probability that LDV/SOF is cost-effective at a threshold of £20,000 is 99.5% for TN NC and is 77.9% for TE NC. This latter probability rises to 99.4% at a threshold of £30,000, demonstrating there is a high level of certainty around the cost-effectiveness of LDV/SOF for GT1 and GT4 patients without cirrhosis.

As NHS England points out, as these ICERs for the majority of the non-cirrhotic population are below a threshold £13,000 per QALY, the redistribution of funding to treating Hepatitis C will result in an overall health gain.

Why patients with hepatitis C should be treated before they progress to advanced liver damage

The submission made by NHS England fundamentally misunderstands HCV disease on two counts, portraying liver fibrosis as the sole manifestation of importance and assuming that patients can somehow be targeted at precisely the right stage of their disease course to prevent escalating liver damage and mortality risk. The first assertion is completely at odds with the literature for this disease, and the latter has no evidence to suggest that it is possible.

Hepatitis C patients are a particularly vulnerable cohort, disproportionately reflecting the highest indices of deprivation. As set out in the first principle of the NHS Constitution, such patients should expect to receive additional support as a population where health and life expectancy are not keeping pace with the rest of the population. Introducing additional, exceptional budgetary tests would imply significant health risks are acceptable within this group in order to generate savings. One of the key premises of the NHS England response is that the sole goal of HCV treatment is to prevent end stage liver disease. Of particular note is the statement on page 2 that:

> "…*making new drugs available to all patients with chronic hepatitis C could represent overtreatment as up to 70% of those receiving high cost drugs would, in the absence of those drugs, have experienced little or no ill health consequences from their disease*."

Extensive evidence exists showing that HCV infection results in significant extra-hepatic co-morbidities in patients prior to the development of advanced liver fibrosis (Jacobson 2010; Samuel 2013) and that many of these can be improved by curing the HCV:

a) Autoimmune / lymphoproliferative disorders such as cryoglobinemia, autoimmune thyroid disorders, Non-Hogkins Lymphoma and lichen planus (Himoto 2012; Shengyuan 2009; Carrozzo 2014; Lodi 2010)
b) Metabolic abnormalities including steatosis, insulin resistance/diabetes, atherosclerosis (Adinolfi 2011; Lim 2014; Kawaguchi 2014; Lonardo 2014; Adinolfi 2014; Vespasiani-Gentilucci 2014)
c) Mental health effects including depression, psychiatric effects, anxiety, fatigue and cognitive impairment (Forton 2001; Schaefer 2012; Kraus 2013; Adinolfi 2015)
d) Chronic inflammation including muscle and joint pain (Zampino 2013)

Two recent publications at the EASL 2015 International Liver Congress (Vienna, Austria, April 2015) highlight the extra-hepatic burden of HCV:

- An analysis of over 3.5 million Americans showed that HCV infection is associated with a statistically significant increase in cancer diagnoses, even when liver cancers (HCC) are excluded from the overall analysis (Nyberg 2015).

- A second study found that manifestations with definitive causal associations with HCV infection (such as mixed cryoglobulinemia vasculitis, porphyria cutanea tarda, RA-like arthritis, and lichen planus) range in prevalence from 3%-23% in the US HCV population (Younossi 2015a). Manifestations without definitive causal associations (such as chronic renal disease, end-stage renal disease, type 2 diabetes mellitus, and depression) range from 0.4%-24%.

HCV infection is also associated with measurable societal burden (Di Bonaventura 2012). In addition to being associated with a patient population recognised as disadvantaged and less likely to be in work, patients with HCV have greater levels of presenteeism (present at work but not productive), absenteeism, overall work impairment and activity impairment (DiBonaventura 2011). Hepatitis C can also have an impact on a person's ability to work. In some cases there are formal restrictions e.g. healthcare professionals, dentistry, in other cases barriers are placed based on ignorance and prejudice but these are still as impactful for those involved. We are aware of UK patients unable to work in careers such as beauty therapy, hairdressing and childcare.

HCV infection has a profound effect on health-related quality of life (HRQL) in UK patients (Foster 2009), with fatigue, depression and neurocognitive deficits among the most common complaints. This reduction in HRQL is observed regardless of the stage of their liver fibrosis (early versus advanced). Data has been published showing the HRQL improvements observed in the trials of LDV/SOF (Younossi 2015a; Younossi 2015b). At baseline, patients with more advanced fibrosis had greater HRQL impairments, predominantly related to physical functioning, than those with mild liver disease. However HRQL domains related to emotional well-being and mental health were similarly low regardless of the severity of fibrosis. By the SVR12 follow-up visit most HRQL domains notably improved from baseline in both fibrosis cohorts, but work productivity and health utility improved in patients with mild fibrosis only. This suggests that maximal benefits for a patient occur when they are cured of HCV earlier in their disease course, rather than waiting until their infection has caused significant liver damage.

Issues around HCV transmission

In addition to the multiple co-morbidities of HCV, NHS England has failed to take into account that HCV is a communicable infectious disease, spread by blood – blood contact. HCV is six times more infectious than HIV and has been shown to survive, and thus remain infectious, outside of the body in microscopic blood spots for up to 6 weeks (Paintsil 2014). For this reason HCV can be spread through shared personal items such as toothbrushes and razors, tattooing equipment and equipment, in addition to needles.

The risk of onward transmission results in stigma against those infected with HCV and anxiety in those that are infected that they might pass it on to uninfected partners, family and other household members. In particular, the risk of mother to baby transmission of HCV is around 5%, and thus many HCV-infected women wishing to have a child are keen to be cured of their HCV prior to attempting to become pregnant. Denying patients treatment means that they remain at risk of transmitting. It can also give the impression that the health service does not consider HCV infection serious enough to warrant treatment, increasing the likelihood that patients will choose not to engage further with specialist care and also be less concerned about avoiding practices that might increase the risk of onward transmission.

The challenges and ethics of maintaining the entire diagnosed non-cirrhotic HCV infected population in a long term watchful waiting strategy

A watchful waiting strategy is reliant on engagement with health services at a frequency sufficient to enable identification of disease progression. However, the median time from infection to cirrhosis can vary greatly according to the combination of multiple independent factors, making it difficult to predict progression for any individual patient (Poynard 2010). This challenge is coupled with the fact that the progression of HCV induced fibrosis, as observed in UK patients (Ryder 2004), is not linear but rather increases with time.

The natural history of the disease has also been misrepresented in the NHS England response where they state "*it is estimated that 70% of patients will not develop cirrhosis*". Data from a large London clinic indicate that the percentage of patients with cirrhosis is a function of the time since infection (D'Souza 2005). In this study, 71% of patients that have been infected with HCV for >60 years had progressed to cirrhosis. Given the ongoing increases in life expectancy in England, and predominance of HCV infections in PWIDs occurring during their twenties, conservative estimates are that >50% of HCV patients could progress to cirrhosis during their lifetime (Foster 2010). Thus, treatment of the majority of patients is likely to be required, in contrast to the NHS England statement that "*making new drugs available to all patients with chronic hepatitis C could represent overtreatment as up to 70%*".

As stated by NHS England in its response, there is an "*estimated 80,000 population with confirmed chronic HCV*" in England but only approximately "*28,500 are known to the health system*". This highlights the challenges the NHS faces in preventing dis-engagement of HCV patients from care in the absence of (an effective and tolerable) treatment. A watchful waiting strategy would require the NHS to re-engage, and maintain engagement of, an approximate additional 51,500 patients and then nearly triple clinic capacity to enable them to be actively reviewed to assess their liver fibrosis progression over the next decade or two.

In England, injecting drug use is the predominant risk factor for HCV infection, comprising 90% of all cases (Public Health England 2014). This population is significantly more disadvantaged, and less engaged in the healthcare system and society as a whole, than the general population. Engagement with services is difficult for PWIDs due to multiple individual level and social level factors (Harris 2013). However, evidence is emerging from Scotland that if early treatment is offered to those that do engage (two thirds of those engaging initiated treatment (Harris 2013)) the positive experience of provision of treatment actually aids further engagement of active PWIDs with health services, resulting in reduced drug use and re-engagement with society (Ahmad 2015).

These data highlight the enormous challenges of engaging the PWID population in a long term watchful waiting strategy to monitor for liver fibrosis progression. Furthermore, such a strategy completely misses the opportunity of treating such patients to prevent both onward transmission and the detriment to their HRQL (through HCV and extra-hepatic routes). For regions with a 20–40% HCV prevalence in their PWID population, a range that incorporates the estimated median prevalence in most cities in England (Martin 2015a), treatment of PWIDs dominates treatment of ex/non-PWIDs in cost effectiveness terms (Martin 2012;

Martin 2015b). This is due to the benefits of preventing onward transmission and occurs despite the risk of reinfection, which is incorporated into the modelling.

The ethics of a treatment sequencing approach

Historically, uptake of HCV treatment has been limited due to patient and physician concerns regarding tolerability issues combined with long treatment durations (24-48 weeks) and sub-optimal efficacy outcomes (<90% cure rates). Most patients experience flu-like symptoms with IFN + RBV treatment, which also often results in neutropenia, thrombocytopenia and anaemia, plus gastrointestinal disorders and dermatologic reactions (Ferenci 2011; Hashemi 2008). In addition to the on-treatment adverse events experienced, a Hepatitis C post-treatment survey of 500 (predominantly UK) patients found that 90% of patients reported ongoing symptoms/side effects for >12 months after the treatment ended (Hepatitis C Trust, 2010). These data highlight the need to utilise IFN-free treatments, or where there are not available, IFN-sparing regimens.

The new HCV DAAs offer IFN-free (LDV/SOF) or IFN-sparing (SOF) treatments with dramatically improved tolerability and significantly increased efficacy versus IFN+RBV. Requiring patients to undergo a long duration, sub-optimal treatment course with a significant adverse event burden provides a substantial barrier to treatment, for a disease that is both communicable and ultimately life threatening.

The use of LDV/SOF first-line is a less costly strategy based on drug costs alone, as shown in the calculations below. Of note, although not incorporated below for simplicity, the inclusion of service costs would further increase the savings made for an IFN-free, shorter treatment opposite by using an interferon-free regimen with a shorter duration as the first-line treatment option.

For TN NC population, with relative drug costs of £25,987 for LDV/SOF and £10,411 for PEG+RBV versus efficacy of 94% for LDV/SOF (F0-F3) and 43.6% (F0-F2) for PEG+RBV, it is clear that not only is LDV/SOF cost effective versus PEG+RBV but it is also a cheaper way to achieve SVRs (see conservative calculation below):

- All non-cirrhotic patients receive PEG+RBV first-line followed by 12 weeks LDV/SOF for patient who fail, compared to all patients receiving LDV/SOF 8 weeks first line and 12 weeks SOF+SMV for patients who fail:
    - Average cost per patient (PEG+RBV first-line): £10,441+(1-0.436)*£38,980= **£32,426**
    - Average cost per patient (LDV/SOF first-line): £25,987+(1-0.94)*£57,380= **£29,430**

Also, the comparison with PEG+RBV for this population also shows LDV/SOF to be highly cost-effective with ICERs of £8,895 for TN NC and £15,330 for TE NC

Affordability and incremental budget impact for LDV/SOF

Multiple incorrect and grossly inflated budget impact figures have been presented to the NICE committee by NHS England, ranging from £285 million to £1.9 billion. In this NHS England submission, it is not transparent how the budget impact figures have been calculated, however it appears these figures are based on treating unrealistic numbers of patients, as well as including patients outside of scope of these NICE appraisals. NHS England's submission also relies extensively on evidence and analyses which have not been disclosed. Without access to this evidence, it is impossible to assess the weight to be attached to such material, whether it is reliable and whether it supports the position advanced by NHS England. Therefore to respond fully to the consultation, Gilead's position is that, to the extent that NHS England's submission lacks transparency, it may not properly be relied upon. To the extent that NICE intends to provide the full submission to the Appraisal Committee, it is noted that there has not been an adequate opportunity for Gilead to consider this before submitting its responses to the current consultation.

Therefore, we have provided our own budget impact estimates for LDV/SOF. The incremental budget impact for LDV/SOF, based on the NICE recommendations and realistic patient's numbers, is £85 to £276 million, as detailed below.

LDV/SOF is only recommended (as per the ACD) for GT1 and 4, which accounts for approximately 50% of the HCV population in England. As LDV/SOF and the AbbVie regimen are likely to have similar recommendations, the budget impact estimates can be considered interchangeable for the two regimens but should not be combined as they will be used to treat the same population.

Sovaldi (+RBV±PEG) has already been recommended by NICE, and therefore the budget impact should not been considered in scope.

As a direct comparison to NHS England's figures of £285-£772 million based on treating 7,000 to 32,000 patients, we also have estimated a comparable total budget impact of £259-£805 million. A table summarising the budget impact estimates is shown below.

In summary, the greatest sensitivity of the budget impact is the:

- assumptions around the number of patients to be treated per annum
- use of incremental budget impact versus total budget.
- cost of the medicines

Patient numbers	**NHS England HCV total budget**	**Gilead estimate HCV total budget**	**Gilead estimate HCV incremental budget impact**	**Gilead estimate LDV/SOF total budget**	**Gilead estimate LDV/SOF incremental budget impact**
7000	£285m	£259m	**£189m**	£125m	**£85m**
15000	NR	£465m	**£395m**	£316m	**£276m**
20000	£518m	£538m	£468m	£358m	£345m
32000	£772m	£805m	£736m	£594m	£554m

See explanation below:

In this submission and previously, NHS England has reported inconsistent and grossly inflated estimates of the budget impact for the treatment of HCV:

- In NHS England's submission to NICE dated 4th November 2014 a range of 10,000 to 15,000 patients is expected, based on the introduction of *"low side effect combination therapies available from 2015', combined with 'low control of prescribing decisions' and 'NHS policies and initiatives to screen high risk patients".*

- 10,000 to 15,000 patients was given as a range by NHS England in discussions with NICE relating to the simeprevir appraisal 19/8/2014

- In NHS England's response to the LDV/SOF ACD, a figure of £1.3 billion was cited based on treating 34,000 non-cirrhotic patients

- In the submission under review a figure of 7,000 to 32,000 patients treated resulting in a total budget impact per year of £285-£772 million

- £1.9 billion based on treating all patients but it is highlighted this is hypothetical and unrealistic

In this NHS England submission, it was stated:

"*If there is access to all patients of all stages of disease (F0-4) with chronic HCV NHS England estimated this could move patient treatment numbers to range from* ***7,000 (manageable but not currently affordable within current clinical services)*** *to* ***20,000 patients per annum which will require significant service transformation along the entire pathway*** *(from diagnosis to treatment) in order to meet expectation generated by the guidance even if this were affordable, which it is currently not.* ***NHS England believes it is unlikely that calls for treatment access will exceed 20,000 per annum".***

The budget impact analysis by NHS England assumes a range of 7,000 to 32,000 patients and total budget impact figures of £285 to £772 million. Throughout the document, NHS England use the figure of £700 million for making their point about lack of affordability despite stating that this figure relates to a number of patients that is in excess of the numbers they expect to be treated per year. For example, for the opportunity cost calculations (pg 4), and the estimate of the required budget uplift compared to the total NHS budget (paragraph 3 on pg 5 and q4 pg 9).

Based on the experience from other European countries regarding access to the new DAA medicines for the treatment of HCV:

- An increase in treatment rates between 60% to 100% compared to historic treatment rates - this would equate to 8,000-10,000 patients being treated in England

- In no country with comparable prevalence have we seen a 4-fold increase in treatment rates, which is the required increase to equate to 20,000 patients treated

To provide consistency, the Gilead budget impact estimates are based on the same minimum patient number that was used by NHS England (i.e. 7000 patients). Based on previous communications from NHS England, guidance from clinicians, and experience from other countries, the maximum number of patients treated per year with a NICE mandate is 10,000-15,000 patients; therefore the relevant range is 7,000-15,000.

The budget impact should also be assessed based on the additional or incremental budget required for the introduction of a new treatment (i.e. it should take into account current spend in this disease area). According to IMS data, during the 12 months to Feb 2015 total spend on HCV therapies in England was £144m (based on list prices) of which 60-70% was likely to be GT1 or GT4 usage. As we know the current standard of care medicines are discounted, therefore we conservatively assumed a 50% discount on current spend for the purposes of the budget impact analysis.

In addition, commercial discounts for the new medicines are not taken into account and therefore the values discussed here should be considered the absolute maximum. The NICE committee should be aware that NHS England currently have, and will have additional, commercial in confidence discounts for the new Hep C medicines. As a result, the budget impact will again be significantly reduced as a result of these discounts, and therefore the figures presented are highly conservative.

Hepatitis C is currently ranked 37th in terms of current drug spend. It is estimated that the budget could increase to £259-£465 million for the treatment of all HCV patients (not just LDV/SOF patients). To help the NICE committee understand this level of spend relative to other disease areas, this would mean Hepatitis C drug spend would increase to between 9th and 23rd. This demonstrates that total spend on Hepatitis C is by no means far in excess of 'routine' spending in different therapy areas and highlights that Hepatitis C has historically been, and currently remains, underfunded.

Table 1: Budget Impact Assumptions

	Assumptions used
Patient population	Range of patient numbers from 7,000 to 15,000 There are approximately 5000 cirrhotic patients under treater care. Under each scenario, all 5000 cirrhotic patients are treated and non-cirrhotic patients make up the difference (this is conservative as they drug costs are much lower for the non-cirrhotic patients). 20% were assumed interferon unsuitable (only relevant in GT3 and GT5/6 where all oral regimens are not the standard of care).
Genotypes	GT1 – 45%; GT2 – 5%; GT3 – 45%; GT4 – 3.5%; GT5/6 – 1.5%
Drugs	Treatments have been assigned where they currently have, or are expected to receive, a NICE recommendation: GT1 – LDV/SOF 8 weeks for TN NC and 12 weeks for the remainder of the population GT2 – PEG+RBV for TN NC and SOF+RBV 12 weeks for the remained for the population GT3 – PEG+RBV for TN NC and SOF+PEG+RBV 12 weeks for the

	remainder of the interferon eligible population. SOF+DCV for interferon unsuitable. GT4 – SMV+PEG+RBV for TN NC and LDV/SOF 12 weeks for the remainder of the population. GT5/6 – PEG+RBV for the non-cirrhotic population and SOF+PEG+RBV for the cirrhotic population. SOF+DCV for the interferon unsuitable population
Costs	All medicines are based on list prices as per the NICE methods guide
Current expenditure	It is estimated the NHS currently spends £70 million (net) on HCV medicines of which £40 million is spent on GT1 and GT4 (proportionally higher due to availability of PI regimens for GT1 only).

It should be noted that whilst NHS England stated that they have been 'surprised' by the budget required to fund HCV treatments, they have been aware of these treatments for over 2 years, and have known the price for at least 18 months (Sovaldi price published November 2013). This is sufficient time for the treatment of Hepatitis C to be included in the financial planning exercise of the NHS. As NHS England highlighted, budget planning took place for the 2015/16 financial year in December 2014. NHS England was aware of these new treatments at this time, and therefore a budget could have been planned for these treatments.

By the time NICE guidance is published and taking into account the 90 days granted NHS England to support implementation of NICE guidance, there are only approximately 4 months left in this financial year in which NHS England would need to fund these treatments under a NICE mandate. Given NHS England have a budget uplift of £592m this year, it is highly unlikely a NICE mandate for these medicines would create unaffordable demand, even under NHS England's assumptions. These medicines are affordable, with an estimated pro rata incremental budget impact of £28-£92 million for the 2015/16 financial year.

Budget planning for the next financial year takes place in December 2015, allowing NHS England sufficient time to incorporate funding for these medicines in the 2016/17 budget.

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