NICE National Institute for Health and Care Excellence

NICE guidance

Sofosbuvir–velpatasvir for treating chronic hepatitis C

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Sofosbuvir–velpatasvir is recommended as an option for treating chronic hepatitis C in adults, as specified in table 1, only if the company provides the drug with the discount agreed in the simple discount agreement.

Table 1 Sofosbuvir–velpatasvir for treating chronic hepatitis C in adults

HCV genotype	Liver disease stage	Treatment	Recommendation according to treatment history
1	With or without compensated cirrhosis	Sofosbuvir–velpatasvir	Recommended for treated or untreated
2	Without cirrhosis	Sofosbuvir–velpatasvir	Untreated: Recommended only for people who cannot tolerate interferon or it is not suitable for them Treated: Recommended
2	Compensated cirrhosis	Sofosbuvir–velpatasvir	Recommended for treated or untreated
3	Without cirrhosis	Sofosbuvir–velpatasvir	Recommended for treated or untreated
3	Compensated cirrhosis	Sofosbuvir–velpatasvir (with or without ribavirin)	Recommended for treated or untreated
4	With or without compensated cirrhosis	Sofosbuvir–velpatasvir	Recommended for treated or untreated
5	With or without compensated cirrhosis	Sofosbuvir–velpatasvir	Recommended for treated or untreated
6	With or without compensated cirrhosis	Sofosbuvir–velpatasvir	Recommended for treated or untreated

HCV genotype	Liver disease stage	Treatment	Recommendation according to treatment history
1 to 6	Decompensated cirrhosis	Sofosbuvir–velpatasvir (with ribavirin)	Recommended for treated or untreated

Treated: the person's hepatitis C has not adequately responded to interferon-based treatment.

1.2 It is recommended that the decision to treat and prescribing decisions are made by multidisciplinary teams in the operational delivery networks put in place by NHS England, to prioritise treatment for people with the highest unmet clinical need.

1.3 This guidance is not intended to affect the position of patients whose treatment with sofosbuvir–velpatasvir was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

2 The technology

Description of the technology

2.1 Sofosbuvir–velpatasvir (Epclusa, Gilead) is a fixed-dose combination drug. Sofosbuvir inhibits hepatitis C virus (HCV) non-structural viral protein NS5B ribonucleic acid (RNA)-dependent RNA polymerase. Velpatasvir inhibits HCV non-structural protein NS5A.

Marketing authorisation

2.2 Sofosbuvir–velpatasvir has a marketing authorisation in the UK for treating chronic hepatitis C virus (HCV) infection in adults. This includes genotypes 1–6 HCV in people with or without compensated or decompensated cirrhosis.

Adverse reactions

2.3 The summary of product characteristics states that headache, fatigue and nausea are the most common adverse reactions (incidence of 10% or more). For full details of adverse reactions and contraindications, see the summary of product characteristics.

Recommended dose and schedule

2.4 Sofosbuvir–velpatasvir is taken orally. The recommended dose is 1 tablet once daily, for 12 weeks. Each tablet contains 400 mg sofosbuvir and 100 mg velpatasvir. The marketing authorisation states that decompensated cirrhosis should be treated with sofosbuvir–velpatasvir in combination with ribavirin, for 12 weeks. Ribavirin plus sofosbuvir–velpatasvir may also be considered for people with genotype 3 HCV who have compensated cirrhosis.

Price

2.5 Sofosbuvir–velpatasvir costs £12,993.33 per 28-day pack. The total cost of a 12-week treatment course is £38,980. Ribavirin costs £246.65 per 56-tablet pack. The total cost of a 12-week treatment course of sofosbuvir–velpatasvir with ribavirin is £40,089.93.

2.6 The company has a simple discount agreement which provides a discount to the list price of sofosbuvir–velpatasvir at the point of purchase or invoice. The level of the discount is commercial in confidence.

3 Evidence

The appraisal committee considered evidence submitted by Gilead and a review of this submission by the evidence review group. See the committee papers for full details of the evidence.

4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of sofosbuvir–velpatasvir, having considered evidence on the nature of chronic hepatitis C and the value placed on the benefits of sofosbuvir–velpatasvir by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

Clinical need and practice

4.1 The committee heard from the clinical and patient experts that having treatment options that are free from peginterferon alfa, with or without ribavirin, is important to people with chronic hepatitis C because of the associated adverse reactions, which can lead to irreversible complications. The patient experts explained that some people refuse treatment with peginterferon alfa, which increases their risk of future complications associated with chronic hepatitis C infection. The committee noted that the use of peginterferon alfa is gradually reducing in clinical practice because of the introduction of newer direct-acting antivirals, particularly for genotypes 1 and 4 hepatitis C virus (HCV). However, it was aware that peginterferon alfa, with or without ribavirin, is still a major component of the treatment regimen for other HCV genotypes. It agreed that there is an unmet need for interferon- and ribavirin-free regimens, particularly for genotype 3 HCV (which accounts for approximately 44% of the population of people with hepatitis C). The clinical experts considered that sofosbuvir–velpatasvir is a breakthrough treatment because of its simple dosing regimen, minimal adverse effects and interactions with other drugs, and effectiveness in decompensated cirrhosis (which may reduce the need for liver transplant). Therefore the committee recognised the importance of having an additional effective and tolerable treatment for people with chronic hepatitis C and concluded that sofosbuvir–velpatasvir could be a valuable option, especially for genotype 3 HCV.

Comparators for sofosbuvir–velpatasvir

4.2 The committee noted that the company did not include boceprevir and telaprevir (both taken with peginterferon alfa and ribavirin) as comparators because they are no longer used in clinical practice, although the NICE scope included them. The committee was also aware that the company had modelled some comparators in scenario analyses only (excluding them from its base case) because it considered they are not used in clinical practice. For example, daclatasvir with peginterferon alfa plus ribavirin, and simeprevir with peginterferon alfa plus ribavirin, in people with genotype 4 HCV. The committee heard from the clinical experts that boceprevir and telaprevir are not currently used in clinical practice in the UK, because the toxicity associated with peginterferon alfa plus ribavirin is worsened by adding boceprevir or telaprevir. It heard that peginterferon alfa plus ribavirin and daclatasvir or simeprevir are not used to treat genotype 4 HCV because there are several interferon-free regimens available for this population. The committee concluded that it was appropriate to exclude these comparators from the analyses.

4.3 The committee was aware that the use of peginterferon alfa plus ribavirin is reducing for some HCV genotypes (see section 4.1), and questioned the clinical experts about its relevance. It heard that peginterferon alfa plus ribavirin is the first choice treatment for people with mild, untreated genotype 2 HCV, and understood that its use for other HCV genotypes has not completely stopped. The committee concluded that peginterferon alfa plus ribavirin is a relevant comparator across all HCV genotypes.

4.4 The committee was aware that for people with decompensated cirrhosis, the company compared sofosbuvir–velpatasvir plus ribavirin with ledipasvir–sofosbuvir plus ribavirin. The committee understood that ledipasvir–sofosbuvir plus ribavirin has a marketing authorisation in the UK for decompensated cirrhosis, but that it is not recommended by NICE for this subgroup. It heard from the clinical experts that the clinical commissioning policy for chronic hepatitis C permits the use of ledipasvir–sofosbuvir plus ribavirin in this population, and concluded that it is a relevant comparator.

Clinical effectiveness

Sustained virological response

4.5 The committee considered the key clinical evidence for sofosbuvir–velpatasvir, which came from 4 randomised controlled phase III clinical trials (ASTRAL-1, -2, -3 and -4). The trials included people who had not had treatment for their hepatitis C, and people whose hepatitis C had not adequately responded to interferon-based treatment. ASTRAL-1, -2 and -3 included people with compensated cirrhosis; ASTRAL-4 included people with decompensated cirrhosis. The committee was aware that the evidence review group (ERG) considered that the trials were generally well conducted, although there was a higher risk of bias in ASTRAL-2 and -3 because they were open-label studies. The committee noted that the trial results showed high sustained virological response at 12 weeks irrespective of HCV genotype, cirrhosis stage or treatment history; the sustained virological response ranged from 89% (for people with previously treated genotype 3 HCV and compensated cirrhosis) to 100% (in several subgroups). The committee concluded that the trials showed that sofosbuvir–velpatasvir is effective for treating chronic hepatitis C across all subgroups in all genotypes.

Effect of drug-resistant HCV mutations on treatment outcome

4.6 The committee noted consultation comments that the sustained virological response for sofosbuvir–velpatasvir in ASTRAL-3 was lower in people with drug-resistant HCV mutations. The committee noted the comments from the clinical experts that routine testing for drug-resistant HCV mutations is not part of current clinical practice in the UK. It was aware that the European Association for the Study of the Liver's guideline on treating hepatitis C (2016) does not recommend systematic testing for HCV resistance before treatment. The clinical experts explained that resistance testing is difficult to do and there is no agreement on how to interpret the results. The committee noted that, of the 25 people with drug-resistant mutations who had sofosbuvir–velpatasvir in ASTRAL-3, only 4 did not have a sustained virological response. The committee concluded that there is insufficient evidence to consider the group of people with

drug-resistant mutations separately to the overall population, and that it would not reflect current clinical practice.

Adverse effects

4.7 The committee was aware that the most commonly reported adverse events are headache, fatigue and nausea. It noted that the results showed that sofosbuvir–velpatasvir has a relatively favourable tolerability profile, especially when compared with the peginterferon alfa plus ribavirin regimen. The committee concluded that the adverse events associated with sofosbuvir–velpatasvir are generally tolerable.

Cost effectiveness

Model structure

4.8 The committee noted that the structure of the model and its assumptions about the natural history of the disease are similar to models submitted for other NICE technology appraisals for chronic hepatitis C. It was aware that the company had grouped people with mild and moderate fibrosis into a single health state (non-cirrhotic), and agreed that this was consistent with how people are diagnosed in current practice. The committee concluded that the structure of the model is acceptable for decision-making.

Reinfection and future transmission of hepatitis C virus

4.9 The committee was aware that the company's base-case model did not allow for reinfection after a sustained virological response, and that the ERG explored including an annual reinfection probability of 2.4% from a meta-analysis by Aspinall et al. (2013). The committee heard from the ERG that the model was sensitive to assumptions about reinfection. The clinical experts stated that 2.4% is an overestimate of the risk of reinfection, because most people having treatment for chronic hepatitis C are not current drug users and therefore their

risk of reinfection is low. The clinical experts considered that the estimate of 2.4% was based on outdated studies that are not generalisable to the UK population. The committee noted that the company did not include risk of future virus transmission in the model. It was aware that excluding reinfection may overestimate the health benefits of more effective treatments, and that excluding transmission may underestimate the benefits, but agreed that these opposing effects might not be equal. The committee agreed that it would have preferred to see a model including both reinfection and transmission, but appreciated that this would have needed a different (and potentially more complex) model structure. The committee, noting the comments from clinical experts, agreed that the ERG's reinfection estimate of 2.4% was too high. It concluded that, without a model that incorporated both reinfection and transmission, cost-effectiveness results excluding reinfection and transmission (as in the company's base case) were acceptable for its decision-making.

Estimates of sustained virological response in the model

4.10 The committee noted that the sustained virological response rates for the comparators in the company's model were selected from individual arms of selected randomised controlled trials; the company used 1 source for each treatment in each subgroup. The committee was aware that the company could not perform network meta-analyses for all subgroups in the model and that, for the 2 subgroups in which network meta-analyses were feasible, the results were associated with several limitations. The committee agreed that it was appropriate for the company not to use the results of its network meta-analysis to inform efficacy inputs in the model. The committee heard from the ERG that the company's choice of study for each comparator was often arbitrary; although the ERG considered that the company's justification for each choice was valid, it suggested that equally valid justification could have been provided for alternative sources. The committee was aware that the company's approach of selecting results from a single arm of a study means that the results were open to the risks of bias associated with observational studies. It noted that the company could have calculated a mean sustained virological response for each treatment in each subgroup using all available sources. The committee heard from the company that for 85 of the 118 sustained virological response rates used in the model, only 1 source was available. However the committee agreed with the ERG that,

because each result was selected from a single arm of a study, the company should have included other study types such as uncontrolled and non-randomised studies. The committee concluded that the company's method of estimating efficacy in the model introduced some uncertainty in the results.

4.11 The committee noted that, according to the company's deterministic sensitivity analyses, the cost-effectiveness results were sensitive to the sustained virological response for peginterferon alfa plus ribavirin in people without cirrhosis; estimates for other comparators had less of an effect. The committee questioned the clinical experts on the appropriateness of the company's estimates of sustained virological response for peginterferon alfa plus ribavirin in people without cirrhosis, using the estimate of 71% in untreated genotype 3 HCV as an example. It heard from the company that 71% was a conservative estimate in this population, because the results of its meta-analyses (done in response to clarification questions from NICE) ranged from 59% to 67%. The committee questioned whether people with certain baseline characteristics such as mild disease, younger age and low viral load would have higher sustained virological response rates with peginterferon alfa plus ribavirin. It heard from the clinical experts that it is possible to identify people who are more likely to respond to peginterferon alfa plus ribavirin, but that this is not routine practice in the UK. The clinical experts suggested that the sustained virological response for peginterferon alfa plus ribavirin might be much lower than 71% for some populations, and agreed that the company's estimates were generalisable to current practice when considering everyone with untreated genotype 3 HCV. Having concluded that the company's estimates of sustained virological response introduced some uncertainty in the results, but hearing that the rates for peginterferon alfa plus ribavirin were appropriate, the committee concluded that results based on the company's estimates of sustained virological response were acceptable for its decision-making.

Genotype-specific transition probabilities for developing compensated cirrhosis

4.12 The committee was aware that the company had assumed that progression from the non-cirrhotic to the compensated cirrhosis health state is faster in genotype 3 HCV than in other genotypes. The clinical experts agreed with this

assumption. The committee understood that this approach is consistent with previous NICE technology appraisals in hepatitis C, but noted that this is the first appraisal in which evidence supporting the calculation of HCV genotype-specific transition probabilities has been submitted. The committee heard from the clinical experts that the study selected by the company to inform these transition probabilities (Kanwal et al. 2014) is generalisable to current practice in the UK. However, the committee was concerned that the company had used unadjusted results from Kanwal et al. rather than the prespecified analyses which adjusted for patients' baseline characteristics. The company could not provide a rationale for using the unadjusted data, and the committee concluded that its decision-making should be based on analyses using the adjusted results from Kanwal et al., which the ERG had included in exploratory analyses for some subgroups.

Transition probabilities for disease progression in people with cirrhosis

4.13 The committee noted that the company had used transition probabilities for compensated or decompensated cirrhosis to hepatocellular carcinoma from Cardoso et al. (2010), and had not considered estimates from Fattovich et al. (1997) for these transitions. The committee heard from the company that this is consistent with previous NICE technology appraisals in chronic hepatitis C, and that the Cardoso data are more recent and therefore more appropriate. The committee recalled its conclusion from previous technology appraisals for hepatitis C that these transition probabilities lay somewhere between the estimates from Cardoso and Fattovich. It heard from the clinical experts that data from Fattovich et al. are generalisable to current practice, and was aware that the ERG had done exploratory analyses using transition probabilities from Fattovich et al. in some subgroups. The committee concluded that both sources should be taken into account in its decision-making.

Utility values

4.14 The committee was aware that the company used utility data from the literature in line with previous NICE technology appraisals for chronic hepatitis C (health state baseline values from Wright et al. 2006 and a utility increment after

sustained virological response of 0.04 from Vera-Llonch et al. 2013). The committee noted the ERG's concerns that trial data are preferable to published utility values. It heard from the company that SF-36 data from the clinical trials of sofosbuvir–velpatasvir had not been formally mapped to produce SF-6D utility values for use in the economic model at the time of the submission. The committee emphasised that when available, it prefers utility values collected from the clinical trials of the intervention under evaluation to those estimated from other sources, but it was prepared to accept the estimates from Wright et al. and Vera-Llonch et al. in the economic analyses.

4.15 The committee was aware that the company had applied on-treatment utility increments (increased quality of life) and decrements (decreased quality of life), to represent the varying effect of different treatments. The committee understood that the company applied decrements for regimens containing peginterferon alfa or ribavirin to reflect the poor tolerability of these treatments. It understood that the company applied utility increments for direct-acting antivirals to reflect the benefits of rapidly suppressing the hepatitis C virus and the improved tolerability profile. The committee was concerned that including treatment-specific changes in utility could lead to double counting, because the company also included utility increments for achieving sustained virological response and utility decrements for each adverse event, but it noted that the effect of removing them was negligible. The committee concluded that it was acceptable to include treatment-specific utility increments and decrements, but noted that there were uncertainties in the company's approach.

Pricing arrangements

4.16 The committee noted that the company has a confidential simple discount agreement for sofosbuvir–velpatasvir, with the discount applied at the point of purchase or invoice. It also noted that confidential reduced contract prices for the comparators, agreed between each company and the Commercial Medicines Unit, were included in the analyses done by the ERG, when known and if important to the committee's decision-making. The committee understood that the contract prices were the prices that the NHS pays for these treatments. The committee noted that NICE's guide to the methods of technology appraisal prefers using nationally available price reductions in the reference-case analysis

to reflect the price relevant to the NHS. The committee concluded that the contract prices were the most relevant prices to the NHS and therefore the appropriate prices on which to base its decision.

Most plausible incremental cost-effectiveness ratios

4.17 The committee was aware that incremental cost-effectiveness ratios (ICERs) incorporating its preferred assumptions about transition probabilities (see sections 4.12 and 4.13) were available for only 2 subgroups: people with untreated genotype 2 HCV without cirrhosis, and people with untreated genotype 3 HCV without cirrhosis. The committee understood that, because of the large number of subgroup analyses in the appraisal, the ERG could not do all of its exploratory analyses in all subgroups. The committee was aware that the ERG chose to focus on the comparison with peginterferon alfa plus ribavirin in untreated genotypes 2 and 3 HCV in people without cirrhosis because these were the comparisons that produced the highest ICERs for sofosbuvir–velpatasvir, in both the company's base case and the ERG's alternative base case. The committee noted that, in these 2 subgroups, using the adjusted data from Kanwal et al. increased the company's base-case ICERs for sofosbuvir–velpatasvir by approximately £700–£2,700 per quality-adjusted life year (QALY) gained compared with peginterferon alfa plus ribavirin. Using transition probabilities from Fattovich et al. instead of Cardoso et al. increased the ICERs for sofosbuvir–velpatasvir by approximately £2,500 to £4,500 (see table 2). Recalling its conclusion that the transition probabilities for disease progression lay somewhere between the Cardoso and Fattovich estimates, the committee concluded that the most plausible ICERs for sofosbuvir–velpatasvir compared with peginterferon alfa plus ribavirin lay between:

- £35,091 and £39,783 per QALY gained for people with untreated genotype 2 HCV and without cirrhosis
- £15,923 and £18,362 per QALY gained for people with untreated genotype 3 HCV and without cirrhosis.

Table 2 Incremental cost-effectiveness ratios for sofosbuvir–velpatasvir compared with peginterferon alfa plus ribavirin

Subgroup	Analysis	Source of transition probabilities for disease progression: Cardoso (2010)	Source of transition probabilities for disease progression: Fattovich (1997)
Untreated genotype 2 HCV without cirrhosis and eligible for interferon	Company base case (unadjusted data from Kanwal et al.)	£32,595	£37,125
Untreated genotype 2 HCV without cirrhosis and eligible for interferon	ERG exploratory analysis of company base case (adjusted data from Kanwal et al.)	£35,091	£39,783
Untreated genotype 3 HCV without cirrhosis and eligible for interferon	Company base case (unadjusted data from Kanwal et al.)	£15,199	£17,540
Untreated genotype 3 HCV without cirrhosis and eligible for interferon	ERG exploratory analysis of company base case (adjusted data from Kanwal et al.)	£15,923	£18,362

Source of transition probability does not include the transition probabilities from the non-cirrhotic to compensated cirrhosis health state (taken from Kanwal et al. 2014).

4.18 The committee discussed the most plausible ICERs for sofosbuvir–velpatasvir compared with relevant comparators in all other subgroups, in which the company's base-case ICERs were considerably lower than the ICERs for

sofosbuvir–velpatasvir compared with peginterferon alfa plus ribavirin in genotypes 2 and 3 HCV. The committee considered the likely effect of including its preferred assumptions on the company's base-case ICER. It agreed that the ICERs would likely increase by a similar magnitude as in the 2 subgroups explored by the ERG and concluded that they would remain below £20,000 per QALY gained regardless of HCV genotype, treatment history and cirrhosis stage. Exact ICERs for all comparisons cannot be reported because the contract prices for the comparators in this appraisal are confidential and cannot be disclosed.

Recommendations

Genotypes 1 and 3–6 HCV

4.19 The committee agreed that, after accounting for its preferred assumptions about transition probabilities, the ICERs for sofosbuvir–velpatasvir for HCV genotypes 1 and 3–6 were lower than £20,000 per QALY gained compared with all relevant comparators, regardless of genotype, treatment history and cirrhosis stage. The committee concluded that sofosbuvir–velpatasvir was cost effective and could be recommended for treating HCV genotypes 1 and 3–6 in people with:

- untreated disease with or without compensated cirrhosis
- treated disease with or without compensated cirrhosis.

4.20 The committee noted that the marketing authorisation for sofosbuvir–velpatasvir states that ribavirin may be added to sofosbuvir–velpatasvir for people with genotype 3 HCV with compensated cirrhosis (see section 2). However it was not presented with analyses of sofosbuvir–velpatasvir plus ribavirin for this population. It noted that ribavirin has a much lower acquisition cost than sofosbuvir–velpatasvir, and agreed that adding ribavirin to the treatment regimen would likely have minimal effect on the ICERs, which were lower in people with compensated cirrhosis than for people without cirrhosis. The committee agreed that, in practice, adding ribavirin to sofosbuvir–velpatasvir would be a clinical decision based on discussion between the patient and their clinician. The committee concluded that sofosbuvir–velpatasvir plus ribavirin could be recommended as a cost-effective use of NHS resources for treating genotype 3

HCV in people with compensated cirrhosis.

Genotype 2 HCV

4.21 The committee discussed the group of people with genotype 2 HCV. It agreed that, given that the ICERs for sofosbuvir–velpatasvir were below £20,000 per QALY gained after accounting for its preferred assumptions about transition probabilities, sofosbuvir–velpatasvir was cost effective compared with all comparators for treated and untreated disease with compensated cirrhosis and for treated disease without cirrhosis. The committee concluded that sofosbuvir–velpatasvir could be recommended for treating genotype 2 HCV in people with:

- untreated disease with compensated cirrhosis
- treated disease with or without compensated cirrhosis.

4.22 The committee discussed the group of people with untreated genotype 2 HCV who do not have cirrhosis. For people who can have interferon treatment, the committee noted that peginterferon alfa plus ribavirin is the only active treatment option because sofosbuvir plus ribavirin (see NICE's guideline on sofosbuvir plus ribavirin) is only recommended for people with untreated disease if they cannot tolerate interferon or it is not suitable for them. The committee noted that the ICER for sofosbuvir–velpatasvir compared with peginterferon alfa plus ribavirin was above £30,000 per QALY gained when accounting for its preferred assumptions about transition probabilities. Therefore it concluded that sofosbuvir–velpatasvir could not be recommended as a cost-effective use of NHS resources for untreated genotype 2 HCV in people without cirrhosis who can have interferon. For people who cannot tolerate interferon or it is not suitable for them, the committee noted that the ICERs for sofosbuvir–velpatasvir were below £20,000 per QALY gained after accounting for its preferred assumptions about transition probabilities. It agreed that sofosbuvir–velpatasvir was cost effective compared with sofosbuvir plus ribavirin. Therefore, the committee concluded that sofosbuvir–velpatasvir could be recommended as a cost-effective use of NHS resources for untreated genotype 2 HCV for people without cirrhosis, only if they cannot tolerate interferon or it is not suitable for them.

Decompensated cirrhosis

4.23 The committee agreed that, after accounting for its preferred assumptions about transition probabilities, the ICERs for sofosbuvir–velpatasvir plus ribavirin compared with ledipasvir–sofosbuvir plus ribavirin for decompensated cirrhosis were lower than £20,000 per QALY gained. The committee concluded that sofosbuvir–velpatasvir plus ribavirin could be recommended as a cost-effective use of NHS resources for treating decompensated cirrhosis.

Other considerations

4.24 The committee was aware of NHS England's ongoing planning to put in place the capacity needed to make new oral treatments for hepatitis C available. The committee heard that the capacity to treat hepatitis C in all eligible people in the NHS according to NICE's recommendations is still developing. Given that there is not yet a steady state of implementation of the hepatitis C guidance, it was considered necessary to continue to include recommendations relating to treatment and prescribing decisions included in previous NICE guidance for the oral hepatitis C treatments in the guidance.

Innovation

4.25 The committee considered whether sofosbuvir–velpatasvir could be considered innovative, and whether the company's economic analysis had captured all changes in health-related quality of life. The committee agreed with the company that there is an unmet need for interferon- and ribavirin-free regimens in people with chronic hepatitis C, particularly for genotype 2 or 3 HCV, but concluded that these health gains are likely to have been included in the QALY calculations. The committee agreed that there were other benefits for people with chronic hepatitis C (for example, possible regression of fibrosis) and wider benefits to society (for example, reduced transmission of HCV, improved earning capacity) that were not captured in the QALY calculation and that, if taken into account, were likely to decrease the ICERs. However, the committee noted that it had taken these potential benefits into account when considering the cost

effectiveness of sofosbuvir–velpatasvir and concluded that its recommendations for each population remained unchanged.

Equality issues

4.26 The committee noted the potential equality issues raised by the company and a professional organisation that there are proportionately more people from Asian and minority ethnic groups, and more people who inject drugs, who have genotype 3 or genotype 4 HCV than other HCV genotypes. Having decided that sofosbuvir–velpatasvir should be recommended for HCV genotypes 3 and 4, the committee agreed that its recommendations for these groups do not have a different effect on people protected by the equality legislation than on the wider population. The committee noted that its recommendations on sofosbuvir–velpatasvir were irrespective of whether or not the person uses injectable drugs. The committee then discussed the group for whom it could not recommend sofosbuvir–velpatasvir as a cost-effective use of NHS resources: untreated genotype 2 HCV in people without cirrhosis, who can have interferon. The committee was aware, from the evidence discussed during a previous technology appraisal for hepatitis C, that the proportion of people from Asian and minority ethnic groups was not disproportionately higher for genotype 2 HCV than for other genotypes. It also noted that the ICER for sofosbuvir–velpatasvir compared with peginterferon alfa in untreated genotype 2 HCV without cirrhosis ranged from £35,100 to £39,800 per QALY gained. Based on the evidence presented, the committee agreed that its recommendations were fair and concluded that no further consideration of potential equality issues was needed to meet NICE's obligation to promote equality of access to treatment.

5 Implementation

5.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

5.2 The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.

5.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has chronic hepatitis C and the doctor responsible for their care thinks that sofosbuvir–velpatasvir is the right treatment, it should be available for use, in line with NICE's recommendations.

5.4 The company has arranged a simple discount agreement which provides a discount to the list price of sofosbuvir–velpatasvir at the point of purchase or invoice. The level of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the simple discount agreement should be directed to the company's customer service on +44 (0)203 681 4681 or at UKcustomer.services@gilead.com.

6 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

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