Evidence Review Group Report commissioned by the NIHR HTA Programme on behalf of NICE

Ombitasvir/paritaprevir/ritonavir with or without dasabuvir for treating chronic hepatitis C

ERRATUM

Replacement pages following the factual accuracy check by AbbVie

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Commentary on the robustness of submitted evidence

Strengths

- Although the ERG considered there to be some uncertainty about how systematic the company's searches for clinical effectiveness studies of 3D and 2D were, the company appears to have included all available relevant studies.
- The cost effectiveness analysis adopted a model that has been used in previous NICE appraisals[3 2 5] which has been updated in the CS with more recent evidence on costs and risk of HCC for cirrhotic patients

Weaknesses and Areas of uncertainty

- Of the clinical effectiveness studies identified in the clinical effectiveness systematic review, none directly compared 3D or 2D with the current standards of care for patients with HCV GT1 or GT4 (boceprevir + PegIFN+RBV and telaprevir + PegIFN+RBV for GT1, and PegIFN+RBV for GT4), other than by historical comparison to telaprevir studies. Instead the trials compared different 3D or 2D regimens to each other or placebo. (Although, as noted above, some academic in confidence data from two ongoing trials directly comparing 3D with telaprevir regimens was provided to the ERG during the appraisal.) Therefore, the clinical effectiveness evidence available does not directly meet the decision problem (due to the lack of comparison to relevant comparators) and the SVR12 estimates are mainly derived from what are essentially observational data (i.e. individual trial arms, rather than randomised comparisons) and subgroup analyses within trials arms. This means that no data from robust, randomised comparisons of 3D or 2D regimens against comparators listed in the scope are available to inform the economic model.
- The company excluded potentially relevant simeprevir comparators from the decision problem (including the interferon-free regimen simeprevir + sofosbuvir), due to a lack of suitable data available to inform the economic model. The ERG agrees that the company's rationale for excluding these comparators is reasonable. However, this means that no estimates of clinical effectiveness or cost effectiveness in comparison to simeprevir or interferon-free regimens are available in the CS.

- There were higher proportions of patients with mild fibrosis (e.g. fibrosis scores of F0 and F1) in the 3D studies than the historical comparator telaprevir studies, which may have biased the SVR estimates in favour of 3D.
- There were limited data available in the submission about SVR12 outcomes and other outcomes for the subgroups of patients specified to be of interest in the scope and decision problem: those with cirrhosis [one completed trial, TURQUOISE II, focused solely on people with HCV GT1 with compensated cirrhosis – although this trial randomised 380 patients, only subgroup analyses provided data relevant to the licensed indications for people with HCV GT1a (n = 121) and HCV GT1b (n = 68)], HIV co-infection (interim data, n = 63) and patients who are post-liver transplant (interim data, n = 34). In particular, no studies were identified that had been conducted in patients with HCV GT4 who had cirrhosis, who would be treated with 2D + RBV for 24 weeks, according to the licensed indication. Therefore, no data for this licensed indication are available. No efficacy data for people who are intolerant to or ineligible for interferon treatment were presented, which meant no efficacy data for this subgroup were available to inform the economic model. Instead, the company used the same efficacy data as for IFN-eligible patients for this subgroup in the model, but did not provide a justification for why this was considered appropriate.
- Overall the ERG considers that the SVR12 outcomes may be subject to bias due to the data essentially being observational data, and the 3D studies having a higher proportion of patients with mild fibrosis (e.g. fibrosis scores of F0 and F1) than the historical comparator telaprevir studies. However, the ERG acknowledges that the SVR12 rates associated with 3D and 2D are likely to be high.
- The ERG was unable to check all efficacy and transition probability data used in the CS. The layout of the electronic model did not assist critical assessment, quality assurance and error checking. The majority of referencing in the model uses cell addresses which have no logical meaning and a number of formulae in the model contain numerous nested statements and references to other worksheets.
- The model is not well validated against external data. This CS did not present any evidence of external validation of the model outputs against published evaluations of comparators (included in their systematic review of economic evidence) or against previous company submissions for NICE STAs of comparator technologies.[6 5 7]
- The economic model is dependent on the credibility of the unadjusted indirect comparisons. The ERG suggests that a more credible analysis could have been developed by ensuring consistency in the evidence base for comparators used to populate the model.

therefore reasonable not to model outcomes for these groups separately. The ERG considers one issue that may impact on the cost-effectiveness of 3D or 2D in this population is that they may require additional monitoring. Clinical expert advice to the ERG indicates that more supervision is needed of these patients, due to administration of ritonavir and the increased potential for drug interactions in these patients. However, the ERG and one of the clinical experts providing advice to the ERG consider that this is likely to have a minimal impact on the cost-effectiveness.

There are also limited data available on SVR rates for patients with cirrhosis, as the majority of the trials excluded patients with cirrhosis. Only one completed study (TURQUOISE II[17]) focussed solely on patients with cirrhosis. This RCT included 380 people with GT1 HCV and compensated cirrhosis; however, only subgroup analyses provided data that is relevant to the licensed indications for patients with HCV GT1a and GT1b. Therefore, data from a total of 189 patients are available to inform the SVR rates for the licensed indications: for the licensed indication for patients with HCV GT1a and compensated cirrhosis the n = 121, and for the licensed indication for patients with HCV GT1b and compensated cirrhosis the n = 68. Additionally, one ongoing study (of patients co-infected with HIV; TURQUOISE I) included patients with (n = 6) and without cirrhosis (n = 25) and provided subgroup analyses of SVR by cirrhosis status (see Sections 3.1.3 and 3.3.4).

No subgroup analyses are presented for people who are intolerant to or ineligible for interferon treatment, so efficacy data for this subgroup is not available to inform the economic model. Instead, the economic model uses the same efficacy data as for IFN-eligible patients, but did not provide a justification for why this was considered appropriate. The ERG considers this to be a limitation of the available efficacy data and the economic analysis presented in the CS. Furthermore, the ERG notes that there is no information in the CS about the proportion of patients included in each trial who were IFN intolerant or ineligible, so it is unclear if the 3D and 2D trials included these patients and whether they are therefore represented in the efficacy data.

The company has also reported the results of a number of other subgroup analyses of SVR outcomes within trials, including by gender, race and ethnicity, age, body mass index, fibrosis score, interleukin 28B (IL28B) genotype, diabetes history, HCV RNA level, geographic region, IP-10, and for treatment history.

The patient subgroups represented in the economic model are those by HCV sub-genotype (GT1a and GT1b), stage of fibrosis (mild, moderate and cirrhosis), treatment history (naive or experienced) and eligibility for treatment with PegIFN (see Section 4.2.2 of this report).

From the information provided on patient demographics these seem broadly similar to the other included trials in the CS

[redacted]

No details are provided regarding the stratification of randomisation by participant characteristics. Participants in MALACHITE I were randomised in to one of five treatment groups:

1. Arm A: GT1a, 3D+RBV, [redacted] (treatment in line with 3D license)
2. Arm B: GT1a, TPV+PR, [redacted]
3. Arm C: GT1b, 3D+RBV, [redacted] (treatment not in line with 3D licence)
4. Arm D: GT1b, 3D, n=83 (treatment in line with 3D licence)
5. Arm E: GT1b, TPV+PR, [redacted]

Participants in MALACHITE II were randomised to 3D+RBV (n=101) or TPV+PR (n=47).

[redacted]

Summary of SVR12 results in the MALACHITE I and II RCTs

[redacted].

Virologic relapse, virologic failure and adverse event data are not presented.

Table 27: SVR12 in the MALACHITE I (treatment naïve, non-cirrhotic)

Group	3D+RBV	3D	TPV+PR	p-value
GT1a	[redacted]		[redacted]	[redacted]
GT1b	[redacted]	[redacted]	[redacted]	3D +RBV vs TPV+PR, [redacted] 3D vs TPV+PR, [redacted]

Data from the Company clarification response A9.2

Table 28: SVR12 in MALACHITE II (treatment experienced, non-cirrhotic)

3D+RBV	TPV+PR	p-value
[redacted]	[redacted]	[redacted]

Data from the Company clarification response A9.2

[redacted]

3.4 Summary

In their systematic review, the company identified seven Phase III RCTs (six in HCV GT1 patients and one in HCV GT4 patients) that provided outcome data from individual study arms that were relevant to the licensed indications for 3D and 2D. Additionally, the company identified two Phase II trials in HCV GT1 patients, one of which provided information relevant to the licensed indications (M14-103[27]), while the other (AVIATOR[26]) – a dose finding study – did not. Interim results for ongoing trials were additionally presented. All GT1 trials compared different 3D regimens to either each other (four trials) or to placebo (two trials), and to a historical telaprevir comparator. The GT4 trial compared different 2D regimens in different GT4 patient populations.

In the licence for 3D and 2D, the recommended treatment duration and co-administration of ribavirin depends on cirrhosis status and, for GT1 patients, on HCV genotype subgroup (i.e. GT1a or GT1b). We summarise here the results for the trial arms or subgroups within trial arms where the treatment regimens were in line with the licensed indications, as not all data presented by the company were relevant to the licence. For GT1a patients, SVR12 rates ranged from 95.0% to 97% and for GT1b patients, ranged from 98.5% (patients with compensated cirrhosis) to 100%, with all the GT1 studies demonstrating superiority of 3D to a historical telaprevir comparator on the SVR12 outcome. A meta-analysis of SVR12 from trial arms in line with the licensed indications for all participants for 3D in HCV GT1 showed an average SVR12 of 96.5% (95% CI 94.6 to 97.7). All GT4 patients (n = 91) in the one GT4 trial achieved SVR. On treatment relapse and failure rates were low for both GT1 and GT4 patients (0-1% and none, respectively). Treatment with 3D or 2D appeared to have a minimal impact on patients' HRQoL. Common adverse events were fatigue, headache, nausea and insomnia. Up to 7.9% of patients with GT1 HCV experienced a serious adverse event, but few serious or severe adverse events were observed in patients with GT4 HCV.

4.2 Critical appraisal of the company's submitted economic evaluation

Company's review of published economic evaluations

The CS presents a systematic review of published economic evaluations including ombitasvir/paritaprevir/ritonavir and dasabuvir (with or without ribavirin) and selected comparators listed in the NICE scope (full details of search strategies are presented in Appendix 10 of the CS). The objectives for the review (Table 67 on pages 224 to 225 of the CS) list the included comparators as telaprevir+PegIFN+RBV, boceprevir+PegIFN+RBV and or PegIFN+RBV dual therapy and make no reference to sofosbuvir or simeprevir. The review was carried out as an update to the review report by Hartwell and colleagues[1] with a start date of 1st January 2009 and end date of 2nd April 2014. This was approximately eight months prior to the submission of the CS and the ERG feels that update searches should have been conducted prior to submission (see discussion in section 3.1.1 of this report). The company presented a PRISMA flow diagram (Figure 22, page 227 of CS). The searches identified 1,386 references (1,108 after de-duplication) of which 1,094 were excluded on the basis of title and abstract and 5 were excluded on the basis of full-text assessment. The 9 included studies are summarised in Table 68 (pages 228 to 238) of the CS.

No economic evaluations including 3D or 2D (with or without ribavirin) were identified in the review. The majority of the included studies reported comparisons of either telaprevir+PegIFN+RBV or boceprevir+PegIFN+RBV (or both) against PegIFN+RBV dual therapy, although two reported evaluations of shortened duration of therapy with PegIFN+RBV. Quality assessment of included studies is reported in Table 69 (pages 239 to 242) of the CS. However, no interpretation or conclusions of this quality assessment were provided in the CS, nor is there any narrative review of the results of included studies.

Critical appraisal of company's submitted economic evaluation

The ERG has considered the methods applied in the economic evaluation in the context of the critical appraisal questions listed in Table 30 below, drawn from common checklists for economic evaluation methods (e.g. Drummond and colleagues[38]).

- Sofosbuvir+simeprevir for GT4 IFN-ineligible patients.

For GT1 IFN-eligible patients, included comparators are sofosbuvir+PegIFN+RBV, telaprevir+PegIFN+RBV, boceprevir+PegIFN+RBV and PegIFN+RBV and are modelled in line with their respective marketing authorisations. The CS states (in section 2.7 page 45) that boceprevir+PegIFN+RBV and PegIFN+RBV are not widely used for HCV GT1 in current UK clinical practice. The implication (though not explicitly stated in the CS) of the statement (that boceprevir+PegIFN+RBV and PegIFN+RBV are not widely used for HCV GT1 in current UK clinical practice) is that telaprevir+PegIFN+RBV would be the current standard of care for the majority of protease inhibitor-tolerant GT1 HCV patients receiving anti-viral treatment in the UK. The ERG clinical advisors agree that PegIFN+RBV dual therapy would not be used in GT1 patients unless there was a reason not to include a protease inhibitor in the treatment regimen. However the ERG clinical advisors suggest that boceprevir would be used as frequently as telaprevir in GT1 patients. The CS includes both peginterferon alfa-2a (Pegasys, Roche Products Ltd) and peginterferon alfa-2b (ViraferonPeg, Merck, Sharp and Dohme Ltd) weighted by market share.

For GT1 IFN-ineligible patients, given the exclusion of sofosbuvir+RBV and sofosbuvir+simeprevir, the only included modelled comparator is best supportive care.

For GT4 non-cirrhotic IFN-eligible patients the included comparators are sofosbuvir +PegIFN+RBV and PegIFN+RBV which are modelled in line with their respective marketing authorisations. For G4 IFN-ineligible patients, given the exclusion of sofosbuvir+RBV and sofosbuvir+simeprevir, the only included comparator is best supportive care.

4.2.4 Clinical Effectiveness

The key clinical event affected by anti-viral treatment in the economic model is the proportion of patients achieving SVR. This was obtained for each patient group by genotype from the corresponding 3D and 2D studies (summarised in Table 72, page 252 to 256 of the CS) and from individual trials of included comparators. Details of the SVR calculation and data sources are presented in Section 7.3.1 of the CS. Other outcomes obtained from the key trials are treatment duration (reported in Table 113 for 3D and 2D and in Table 114 for included comparators, pages 362 to 364 of the CS) and adverse events (reported in Table 75, page 256 of the CS for 3D and 2D and throughout section 7.3.1 of the CS for the included comparators). Ranges for the parameters used in deterministic sensitivity analyses are given in Table 125 (page 392) of the CS and for the probabilistic sensitivity analyses in Table 129 (pages 400 to 402) of the CS.

colleagues.[47] The model developed for the CS contains two updates compared with models reported in previous appraisals.[3 2] These are:

- that patients undergoing an SVR from the compensated cirrhosis state remain at higher risk of HCC than those who underwent SVR from the mild or moderate CHC states the general population who have not experienced CHC. This transition probability was sourced to a study published by Cardoso and colleagues.[46] As with previous models the CS assumes that those who undergo SVR from the mild or moderate CHC states face the same risk of HCC as the general population who have not experienced CHC;
- that patients who undergo SVR are at risk of re-infection with CHC (at a constant probability of 0.01), based on expert opinion.

The ERG have identified a recent large study (Bruno and colleagues[50]) of the incidence of HCC in cirrhotic patients, with and without SVR. This study included only patients with cirrhosis, whereas Cardoso and colleagues included both patients staged at F3 and F4. In addition the duration of follow up and sample size was larger in the study reported by Bruno and colleagues. The ERG suggest this may be a better source for populating the model with these transition probabilities and test the impact of using these data, on the cost effectiveness results, in additional analyses.

Adverse events

The health effects of adverse events associated with each of the regimens are included in the economic model as incidences. The adverse events included in the model are: anaemia, neutropenia, thrombocytopenia, rash and depression. The adverse event incidences are drawn from the same sources as the SVRs (see Table 38). The CS is not explicit regarding the grade of included adverse events included in the model except for neutropenia and thrombocytopenia.

Table 39 Baseline health state utilities and sources

Health-state	Utility	Source
Mild HCV	0.77	Wright et al 2006[4]
Moderate HCV	0.66	Wright et al 2006[4]
Compensated cirrhosis	0.55	Wright et al 2006[4]
Recovered (no HCV, history of mild fibrosis)	0.82	Calculated – add 0.05 to utility for mild HCV
Recovered (no HCV, history of moderate fibrosis)	0.71	Calculated – add 0.05 to utility for moderate HCV
Recovered (no HCV, history of compensated cirrhosis)	0.60	Calculated – add 0.05 to utility for CC
Decompensated cirrhosis	0.45	Wright et al 2006[4]
Hepatocellular carcinoma	0.45	Wright et al 2006[4]
Liver transplant	0.45	Wright et al 2006[4]
Post-liver transplant	0.67	Wright et al 2006[4]

Method and values for estimating post-SVR utility derived from Wright et al 2006[4]

On-treatment utility decrements are applied to the state-specific utilities while patients are in treatment-eligible health states, for the duration of treatment – as a result these treatment-specific utility decrements are only applied during the first year (first cycle) of the model. On-treatment disutilities for comparator technologies were extracted from previous company submissions to NICE (where available), [6 5 7] with different utility decrements applied for treatment-naïve or treatment-experienced patients. These are summarised in Table 109 of the CS (page 354).

On-treatment disutilities for 3D and 2D are reported in Table 110 (page 354-355) of the CS. Separate values by fibrosis stage, genotype sub-group, previous treatment experience and duration of treatment are reported in Table 110, and in Table 111 (page 356) of the CS. The CS does not discuss the reasoning behind estimating different disutilities for each fibrosis stage or genotype sub-group, although further details were provided in response to a request for clarification. The CS does not appear to consider the clinical meaningfulness or statistical plausibility of the differences identified. Furthermore the CS does not discuss the plausibility of including positive values (i.e. an assumption which appears to apply for a number of the groups that patients are better on-treatment than off it) – for example GT1b patients with mild and moderate fibrosis have positive utility decrements while on-treatment as do GT4 patients with mild and moderate fibrosis. The ERG is concerned that the utility decrements

Table 42 Drug acquisition costs

	Genotype	Fibrosis stage	Tx naïve/ experienced	Treatment duration (weeks)	Ombitasvir/ paritaprevir/ ritonavir	Dasabuvir	Ribavirin (1000mg/day)	Total cost
3D+RBV	GT1a	Non-cirrhotic	either	12	32,199.99	2,799.99	888.72	35,888.70
3D+RBV	GT1a	Cirrhotic	either	24	64,399.98	5,599.98	1,777.44	71,777.40
3D	GT1b	Non-cirrhotic	either	12	32,199.99	2,799.99		34,999.98
3D+RBV	GT1b	Cirrhotic	either	12	32,199.99	2,799.99	888.72	35,888.70
2D+RBV	GT4	Non-cirrhotic	either	12	32,199.99		888.72	33,088.71
2D+RBV	GT4	Cirrhotic	either	24	64,399.98		1,777.44	66,177.42
					Sofosbuvir	PegIFN	RBV	Total cost
Sofosbuvir+ PegIFN+RBV	GT1, GT4	Non-cirrhotic	either	12	34,983	1,493	888.72	37,365
					Boceprevir	PegIFN	RBV	Total cost
Boceprevir+ PegIFN+RBV	Any	Any	either	48	30,800	5,971	3,555	40,326
Response-guided treatment	Any	Non-cirrhotic	Naïve	28	16,800	3,483	2,074	22,357
Response-guided treatment	Any	Non-cirrhotic	Experienced	48	22,400	5,971	3,555	31,926
					Telaprevir	PegIFN	RBV	Total cost
Telaprevir+ PegIFN+RBV	Any	Any	either	48	22,398	5,971	3,555	31,924
Telaprevir+ PegIFN+RBV	Any	Non-cirrhotic	Naïve	24	22,398	2,986	1,777	27,161
Telaprevir+ PegIFN+RBV	Any	Non-cirrhotic	Prior relapser	24	22,398	2,986	1,777	27,161
						PegIFN	RBV	Total cost
PegIFN+RBV	GT1,GT4	Any	either	48		5,971	3,696	9,667
PegIFN+RBV	GT1,GT4	Any	either	48		9,570	3,209	12,779

4.2.9 Assessment of Uncertainty

One-way sensitivity analyses

The CS reports the results of nine deterministic sensitivity analyses (DSA). These include:

- four DSA for GT1 treatment-naive IFN-eligible patients: one for each comparator (Sofosbuvir+PegIFN+RBV, telaprevir+PegIFN+RBV, boceprevir+PegIFN+RBV, PegIFN+RBV) compared with ombitasvir/paritaprevir/ritonavir
- two DSA for GT1 treatment-experienced IFN-eligible patients: one for each comparator (telaprevir +PegIFN+RBV, PegIFN+RBV) compared with ombitasvir/paritaprevir/ritonavir
- two DSA for GT4 treatment-naive IFN-eligible patients: one for each comparator (Sofosbuvir+PegIFN+RBV, PegIFN+RBV) compared with ombitasvir/paritaprevir/ritonavir
- one DSA for GT4 treatment-experienced IFN-eligible patients: for best supportive compared with ombitasvir/paritaprevir/ritonavir

The parameters of 49 one-way sensitivity analyses, which are common to all comparisons, are presented in Table 128 (page 394 to 395) of the CS. While the majority of the DSA are truly one-way analyses (varying one parameter value, while holding all others constant), some involve varying at least two inputs simultaneously (for example treatment-related attributes such as SVR or rate of AE are varied for both intervention and comparator in a single DSA). Methodological assumptions (such as alternative choice of discount rate) and variation in baseline assumptions (such as mean cohort age and distribution across stage of fibrosis) have not been included in the DSA, but are included in scenario analyses reported in the CS.

The ranges applied in the DSA are clearly stated in Table 128 and are based on a mixture of statistically derived measures of variation (such as standard errors or 95% confidence intervals) and arbitrarily defined ranges (±20%for utilities or ±50% for costs). No justification is provided for adopting particular limits when using arbitrary ranges in the DSA. Table 128 reports that SVRs and AE rates are varied using ±1.96 SD of base values. It is not clear from the CS whether this variation is based on standard deviation (as implied by the SD notation) or a standard error (which would be more appropriate if considering variation according to a 95% confidence interval. It is also unclear from the CS where the SD has been calculated from as tables reporting the SVRs used in the model report number of responders and total number of patients. Given these data are available it might have been more appropriate to

draw the DSA limits for SVRs from beta distributions, parameterised using the numbers of responders and non-responders in the included trials. Results of the DSAs are presented as tornado diagrams (section 7.7.7, Figures 29 to 37, pages 413 to 422 of the CS).

Health state utilities (in particular for the recovered health state with history of mild or moderate fibrosis) appear to be influential on the cost effectiveness estimates across all DSA. Overall variation in certain of the utility values was more influential on cost effectiveness results than was variation in SVR.

Variation in SVR seemed to more influential in the DSA comparisons of 3D with telaprevir+PegIFN+RBV and in the comparison of 2D with sofosbuvir+PegIFN+RBV.

The CS does not provide a narrative overview or discussion alongside each DSA or for each genotype-treatment history comparison, but offers a summary and conclusion in Section 7.7.10 stating that the incremental cost/QALY results [are] most sensitive to utility values for progressive disease states and their associated recovered states.

Scenario Analysis

The MS reports the results of twenty one scenario analyses examining the impact on the ICER (relative to a common baseline, such as PegIFN+RBV for GT1 treatment-naive IFN-eligible patients). The scenario analyses are presented as tabulations (up to four tables for each scenario, resulting in a total of 39 tables) with no accompanying narrative or discussion of the results. As a result it very difficult to interpret what the scenario analyses show. Since a number of the scenario analysis involve varying individual or groups of input parameters between pre-defined ranges the ERG feel that some of these analyses would be better presented graphically, as with the tornado diagrams for the DSA. It might also be easier to interpret the scenario analyses if the CS indicated some form of priority for the analyses – for example, which of the three scenario analyses using different efficacy estimates for PegIFN+RBV (14-16) might represent the most reasonable alternative to the base case

7 DISCUSSION

7.1 Summary of clinical effectiveness issues

The company's clinical effectiveness systematic review identified six phase 3 trials and one phase 2 trial that provided results from individual trial arms or subgroups that met the licensed indications for 3D in treating people with HCV sub-genotypes GT1a and GT1b. The company additionally identified a Phase 2 trial of GT1 patients, which did not meet the licensed indications, because the dose of dasabuvir used in the trial was lower than in the licence. Five trials compared different 3D regimens to each other and to a planned historical telaprevir comparator. Only two trials, which compared 3D regimens with placebo, provided evidence that was directly relevant to the decision problem and NICE's scope in terms of having a relevant, randomised comparator (i.e. placebo may approximate best supportive care). However, these studies did not measure SVR outcomes in the placebo arm, so SVR data from these trials were also from individual trial arms. Only one trial was identified of 2D regimens in patients with HCV GT4. This compared different 2D regimens, with two of the three arms presented in the CS providing data relevant to the licensed indication. No data were presented for the 2D + RBV 24 weeks regimen for people with HCV GT4 with cirrhosis.

One of the main issues with the clinical effectiveness data presented in the CS is the lack of comparison to relevant comparators listed in the scope, including the current standards of care for GT1 patients (boceprevir + PegIFN+RBV and telaprevir + PegIFN+RBV, other than by historical comparison to telaprevir regimens) and GT4 patients (PegIFN + RBV), as well as sofosbuvir and simeprevir regimens preliminarily approved for HCV GT1 and GT4 patients by NICE. This means that no robust, randomised comparisons for SVR12 outcomes from 3D or 2D regimens against the comparators listed in the decision problem are available to inform the economic model. Although the ERG acknowledges that the SVR rates associated with 3D and 2D are likely to be high, the ERG considers the evidence presented in the results section of the clinical effectiveness review may be subject to bias due to the data being derived from what are essentially observational data (individual trial arms and subgroups).

7.2 Summary of cost effectiveness issues

The MS includes evidence on the cost-effectiveness of 3D (with or without RBV) and 2D (with RBV) compared with current standard care in patients infected with either GT1 or GT4 CHC.