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

Simeprevir for treating genotype 1 or 4 chronic hepatitis C

ERRATUM

Replacement pages following the factual accuracy check by Janssen

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Summary of submitted cost effectiveness evidence

The MS includes:

- a review of published economic evaluations of dual therapy with PR or of triple therapy with either simeprevir +PR, telaprevir + PR or boceprevir + PR.
- a de novo economic evaluation to estimate the cost effectiveness for simeprevir + PR in patients with HCV genotypes 1 and 4 and simeprevir and sofosbuvir in patients with genotype 1 who are ineligible for or intolerant to peginterferon alfa.

A systematic search of the literature was undertaken by the manufacturer to identify previous economic evaluations of anti-viral therapy in adults with chronic hepatitis C, published since 2004. Forty-three papers met the inclusion criteria, of which ten were conducted in a UK setting. No economic evaluations featuring simeprevir were identified; however, the ERG identified a 2014 cost effectiveness study of simeprevir and sofosbuvir combination therapy.

Separate economic models have been constructed for genotype 1 patients, for genotype 4 patients and for genotype 1 patients ineligible for or intolerant to peginterferon alfa, respectively. The models use a Markov approach and share a common structure. Separate base case analyses are reported for treatment-naive patients and for those who had previously been treated. The model adopts a lifetime horizon with an annual cycle length.

The modelling approach and structure adopted are based on previous models for HCV. The distribution of patients across age and gender is based on the UK HCV database and the baseline Metavir fibrosis score distribution is taken from clinical opinion. Health related quality of life has been adapted from previous appraisals for NICE. Resource use and costs have been adapted from previous appraisals for NICE.

Results are presented for lifetime costs, quality adjusted life years (QALYs) and incremental cost-effectiveness ratios (ICERs) for both treatment-naive and treatment-experienced patients. For genotype 1 patients, simeprevir + PR is slightly more effective and has lower total costs than telaprevir + PR and boceprevir + PR for both treatment-naive and treatment experienced patients. The MS reports ICERs for simeprevir + PR compared to PR of £14,206 and £9,793 per QALY in treatment-naive and treatment experienced patients respectively. For genotype 4 patients, ICERs of £11,662 and £8,896 per QALY are reported compared to PR in treatment

may not be representative of the RESTORE population. Note that the numerator (N = 12) for the RESTORE matched data is calculated from the adjusted SVR percentage (77% of 15) and is rounded to the closest integer. An important limitation in this MAIC is the absence of a common comparator to allow for detection of residual confounding, as no validation of the matching or use of relative effect measures is possible.[1] None of the eligible PR trials reported SVR12, therefore MS Table 55 compares SRV24 data from Rumi and colleagues[20] with SVR12 data from RESTORE, which the ERG considers appropriate. As stated, the MS does not undertake a statistical indirect comparison of the matched data. The ERG notes that the SVR12 for the RESTORE matched data [12 (77%)] is higher than that for the overall RESTORE population (65.4%), but slightly less than that for the treatment-naive subgroup (82.9%). The comparator SVR24 data from Rumi and colleagues,[20] on the other hand, is lower than that from the three other studies selected for consideration in the MAIC, which ranges from 50.0% to 70.6%. It is the opinion of the ERG that the data in MS Table 55 are viewed with caution. The ERG explores alternative SVR24 data in a scenario analysis (see section 4.3).

Table 3 RESTORE population characteristics and SVR after matching (MS Table 55, p. 97)

Matching parameters	Patients (N)	Effective n* (n)	Fibrosis (% S5-6 / F4)	Viral load (% HCV RNA < 600,000 IU/ml)	BMI (mean baseline)	Age (mean)	Sex (% female)	SVR N (%)
Rumi (2010)[20]	18		28%	72%	26.4	43,00	17%	8 (44%)
RESTORE matched	35	15	28%	72%	26.4	43,01	17%	12 (77%)

* effective population size after matching algorithm applied.

decompensated cirrhosis (DCC), and hepatocellular carcinoma (HCC). Although EQ-5D data were collected in the simeprevir clinical trials, the MS base case uses treatment utility decrements and increments adopted in previous economic models (citing Hartwell and colleagues, 2011[32], NICE TA200[28]). The same utility decrement is used for all treatment comparisons (irrespective of treatment experience), with treatment-specific decrements (derived from clinical trials and varying according to treatment experience) used in scenario analyses.

A systematic review was conducted to identify studies of costs and resource use (MS Section 7.5.3). Twenty one articles were identified but none related to the UK. Quantification of resource use, such as pre- and on-treatment monitoring costs, was based on previously published economic evaluations for NICE hepatitis C appraisals (citing Shepherd and colleagues 2007[33] NICE TA106[29] and Hartwell and colleagues 2011,[32] NICE TA200[28]). On-going annual HCV resource use and costs were also taken from these sources and the UK Mild HCV trial.[34] Clinician advice was sought for estimating market share of the two peginterferon alfa formulations. The cost of the Q80K polymorphism testing was assumed. Drug dosing was based on licensed dosages for each regimen, costed using the British National Formulary (BNF) (March-September 2014)[35] and applied to treatment-specific therapy durations (MS Section 7.5.5). Costs of treating adverse events were estimated by contacting pharmacies and practising hepatologists (reported in a publication by Thorlund and colleagues, 2012[36]). Where necessary, costs were inflated to 2012 prices using the Hospital & Community Health Services (HCHS) Index from the Personal Social Services Research Unit (PPSRU).[37]

Deterministic sensitivity analyses (DSA) were conducted, varying input parameters within the limits of their 95% confidence intervals (Table 100, MS Section 7.6.2, for genotype 1 patients; Table 103, MS Section 7.6.4.8 for genotype 4 patients; Table 110, Section 7.6.5.5 for simeprevir and sofosbuvir treated patients). Probabilistic sensitivity analyses (PSA) included all of the input parameters in the DSA (MS Section 7.6.3). The PSA also included distribution of Metavir fibrosis class and response to prior treatment which were not included in the DSA as they are inter-dependent (MS Table 101 for genotype 1 patients; MS Table 104 for genotype 4 patients).

The MS includes 17 scenario analyses to explore the impact of varying structural assumptions on the results of the model (MS Section 7.6.1, page 99). Some scenarios were omitted from the genotype 4 patient analyses (see MS page 178-9), and from the simeprevir and sofosbuvir analyses (see MS page 184) as these were not relevant to these patient groups.