Cost-effectiveness model for sofosbuvir in chronic hepatitis C

**Introduction**

- Hepatitis C is the result of a ribonucleic acid (RNA) virus (hepatitis C virus; HCV), which makes it a greater rate of the DNA viruses. Six major HCV genotypes (GT) and a large number of subtypes have been described in the literature, i.e. genotype 1, 2, 3, 4, 5 and 6.
- The treatment of hepatitis C infection aims at eradicating the virus and consequently preventing cirrhosis and its complications, reducing extra-hepatic manifestations, and preventing infection of other people. Depending on the HCV genotype, different treatment regimens are available.
- Sofosbuvir (SOF) is a nucleotide analogue that inhibits NS5B directed HCV RNA replication in vitro and has demonstrated high rates of sustained virological response (SVR) when given with ribavirin (RBV) to subjects with chronic GT-1,4/5/6 and GT-2 or 3 HCV infections.

**Objective**

- This study models the cost-effectiveness of SOF in treatment-naive (TN) GT4/5/6, TN GT1/2/3 unsuitable for interferon, TN GT 1/2/3 interferon eligible, GT2/3 treatment-experienced (TE) unsuitable for interferon and GT 2/3 TE interferon eligible patients in Belgium, taking into account the guidelines of the Knowledge Centre (KCE) (KCE report 78C, 2008).
- The analysis is a cost-utility analysis (CUA) for chronic hepatitis C patients GT 1, 3, 4, 5 of 6 who are IFN-eligible
- The cycle length was three months for the first two years of the analysis and yearly after. A 100 years time horizon was chosen in order to reflect the life expectancy observed in Belgium. The cycle length was three months for the first two years of the analysis and yearly after. A 100 years time horizon was chosen in order to reflect the life expectancy observed in Belgium.

**Methods**

- A cohort of 10,000 patients, with 22% of TN and 30% of TE patients initiating treatment at the cirrhotic stage or GT4/5/6 and GT-2 or 3 HCV infections.
- Patients move to the SVR health state after completing treatment if they have undetectable HCV RNA, 12 weeks (wk) after the end of treatment. They are considered to be virologically cured. Patients without a SVR face an annual probability of progressing to more advanced stages of the disease.

**Figure 1.** Markov model schematic for chronic hepatitis C (CHC)

**Table 1. Treatment strategies per indication**

<table>
<thead>
<tr>
<th>Indication</th>
<th>IFN-eligible / IFN-eligible</th>
<th>Active treatment</th>
<th>Comparator(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GT1 TN</td>
<td>IFN-eligible</td>
<td>Sofosbuvir (12 weeks)</td>
<td>TVR + PR (24 or 48 wks)</td>
</tr>
<tr>
<td>GT 1 TN</td>
<td>IFN-eligible</td>
<td>Sofosbuvir (24 weeks)</td>
<td>RIBV + PR (24 or 48 wks)</td>
</tr>
<tr>
<td>GT2 TN</td>
<td>IFN-eligible</td>
<td>Sofosbuvir (12 weeks)</td>
<td>No treatment</td>
</tr>
<tr>
<td>GT2 TE</td>
<td>IFN-eligible</td>
<td>Sofosbuvir (12 weeks)</td>
<td>No treatment</td>
</tr>
<tr>
<td>GT3 TN</td>
<td>IFN-eligible</td>
<td>Sofosbuvir (12 weeks)</td>
<td>No treatment</td>
</tr>
<tr>
<td>GT3 TE</td>
<td>IFN-eligible</td>
<td>Sofosbuvir (12 weeks)</td>
<td>No treatment</td>
</tr>
<tr>
<td>GT4/5/6 TN</td>
<td>IFN-eligible</td>
<td>Sofosbuvir (24 weeks)</td>
<td>No treatment</td>
</tr>
</tbody>
</table>

**Results**

- Although the model allows reporting of several types of economic outcomes, results are being reported as incremental costs per quality-adjusted life years (QALYs), in line with the KCE/IVDR requirements for Class 1 reimbursement applications.
- Results are presented in Table 2 per chapter of Chapter IV of the Royal Decree of 12.11.2001. Weighted ICERs are calculated based on the following assumptions for the BE CHC patient population: 59% GT 1, 19% GT 3 and 16% GT 4/5/6 patients; 55/50 use of TVR/BOC; 50/50 use of Peginterferon alfalfa-2a/Peginterferon alfalfa-2b; 30/70 distribution for IFN-eligible vs IFN-ineligible patients.
- The sub-paragrapghs §1, §2 and §3 within Chapter IV represent the subpopulations of CHC patients for which reimbursement has been granted:
  - §1: CHC patients GT 1, 3, 4, 5 of 6 who are IFN-eligible
  - §2: CHC patients GT 1, 3, 4, 5 of 6 who are IFN-ineligible (due to intolerance and/or contra-indications)
  - §3: CHC patients GT 2

**Conclusion**

PAN-genotypic cost-effectiveness has been demonstrated for sofosbuvir in comparison to the current standard of care (BOC) in Belgium. Overall, the weighted PAN-genotypic ICER is €15.75.

**References**

3. Local expert opinion, 2013.
4. Gilead Phase III trials: NEUTRINO, FISSION, POSITRON, FUSION and VALENCE studies.
14. FDA. Telaprevir (Incivek) 750 mg-Film-Coated Tablet for the Treatment of Genotype 1 Chronic Hepatitis C. FDA Advisory Committee Briefing Document, 2011.