Janssen's Response to the Appraisal Consultation Document

Ledipasvir/Sofosbuvir for treating chronic hepatitis C

Please find below Janssen's comments following our review of the Appraisal Consultation Document (ACD) for ledipasvir/sofosbuvir for treating chronic hepatitis C (CHC).

1. **Do you consider that all of the relevant evidence has been taken into account?**

Janssen do not agree that Gilead's (the manufacturer) choice to only conduct a naïve indirect comparison between ledipasvir/sofosbuvir and simeprevir or telaprevir is appropriate for the following reasons:

- SVR 12 rates were arbitrarily calculated using point estimates from comparator studies instead of conducting a proper meta-analysis of all relevant studies taking into account the uncertainty associated with the outcomes supporting each comparator in each treatment history group.
- A Match Adjusted Indirect Comparison (adjusting results on patient and clinical characteristics) should have been conducted in parallel to conducting naïve indirect treatment comparisons as presented by the Manufacturer. An MAIC would have helped to eliminate important differences in baseline characteristics between the trials, thus allowing comparisons on an even footing.

Whilst ledipasvir/sofosbuvir offers an important new treatment option for people with CHC, we urge the committee to reflect in its Final Appraisal Determination on the high level of uncertainty in the estimates of the cost effectiveness of ledipasvir/sofosbuvir compared with simeprevir plus pegylated interferon and ribavirin and with telaprevir plus pegylated interferon and ribavirin within their licensed populations.

2. **Do you consider that the summaries of clinical and cost effectiveness are reasonable?**

Janssen would like to clarify that telaprevir plus pegylated interferon and ribavirin is not licensed for use in genotype 4 patients and should not have been considered a comparator in the cost-effectiveness analysis in this specific sub-group of CHC patients. This was also stated by the ERG (Page 28, 3.42 of the Appraisal Consultation Document).

The oral combination of simeprevir/sofosbuvir has not been appraised by NICE for treatment of genotype 1 & 4 CHC and is not established practice in the NHS. In this context, simeprevir/sofosbuvir should not be considered as a relevant comparator to ledipasvir/sofosbuvir, as also stated by the NICE Committee.

In this context, Janssen would like to ask that all comparative analyses between ledipasvir/sofosbuvir and simeprevir/sofosbuvir in genotype 1 & 4 CHC and telaprevir plus pegylated interferon and ribavirin in genotype 4 CHC be redacted from the ACD (e.g. table 4, table 5, table 6 and table 10).

3. **Are the provisional recommendations sound and a suitable basis for guidance to the NHS?**

Clarification should be given by the Committee regarding their recommendation for treatment-experienced patients with cirrhosis for 12-week of treatment with ledipasvir/sofosbuvir.