Cost-effectiveness of boceprevir (Victrelis®) for the treatment of patients infected with genotype 1 hepatitis C virus in the Irish healthcare setting.

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Boceprevir Summary

1. An economic evaluation on the cost-effectiveness of boceprevir (Victrelis) for the treatment of adult patients infected with genotype 1 hepatitis C virus, was submitted to the National Centre for Pharmacoeconomics on the 20th August 2011. Following initial review an updated submission was received on the 7th November 2011.

2. Boceprevir is a linear peptidomimetic ketoamide serine protease inhibitor that binds reversibly to the HCV non-structural 3 (NS3) active site. Boceprevir is indicated for the treatment of chronic hepatitis C genotype infection, in combination with peginterferon and ribavirin, in adult patients with compensated liver disease who are previously untreated or who have failed previous therapy.

3. The efficacy data for the cost-effectiveness evaluation of boceprevir was derived from the phase III clinical trials. The SPRINT-2 trial was a randomised, placebo-controlled study in which previously untreated adults with HCV genotype 1 infection were assigned to one of three groups. In all three groups peginterferon alfa-2b and ribavirin were administered for 4 weeks as the lead-in period. In the control group (group 1) this was followed by placebo plus peginterferon – ribavirin for 44 weeks. Group 2 received peginterferon-ribavirin for 24 weeks and those with a detectable HCV RNA level between weeks 8 and 24 received placebo plus peginterferon-ribavirin for an additional 20 weeks. Group 3 received boceprevir plus peginterferon – ribavirin for 44 weeks.

4. In the SPRINT-2 trial 938 nonblack and 159 black patients were treated. In the non black cohort a sustained virologic response was achieved in 125 of the 311 patients (40%) in the control group, 211 of the 316 patients (67%) in group 2 and in 213 of the 311 patients (68%) in group 3. In the black cohort, a sustained virologic response was achieved in 12 of the 52 patients (23%) in group 1, in 22 of the 52 patients (42%) in group 2 and in 29 of the 55 patients (53%) in group 3. In group two, 44% of patients received peginterferon – ribavirin for 28 weeks.

5. The RESPOND trial investigated the effect of combination therapy including boceprevir plus peginterferon – ribavirin in previously treated patients with chronic HCV genotype 1 infection. Patients were randomised to one of three groups with all patients receiving a four week lead in treatment with peginterferon – ribavirin. This was followed by placebo plus peginterferon – ribavirin for 44 weeks in the control group (group 1). In group 2 patients received boceprevir plus peginterferon – ribavirin for 32 weeks and patients with detectable HCV RNA at week 8 received placebo plus peginterferon – ribavirin for an additional 12 weeks. Group 3 received boceprevir plus peginterferon – ribavirin for 44 weeks.

6. In the RESPOND study the rate of sustained virologic response was significantly higher in the two boceprevir groups i.e. 59% in group 2 and 66% in group 3 as compared with the control group at 21%. In patients with an undetectable HCV RNA at week 8, the rate of sustained virologic response was 86% after 32 weeks of triple therapy and 88% after 44 weeks of triple therapy.

7. A Markov cohort model was used to simulate the natural history of chronic hepatitis C disease. It was adapted to estimate expected costs and quality adjusted life-years (QALYs) associated with treatment strategies based on the clinical trials SPRINT-2 and RESPOND-2. The baseline liver disease state for patients at the outset of treatment was determined by the fibrosis score and the distribution of the fibrosis scores were considered similar to those in the phase 3 trials. The perspective was that of the Health Service Executive (HSE).

8. The patient characteristics of the population treated (i.e. age, gender ratio, ethnicity) were adjusted to reflect Irish epidemiological data. Once a patient develops compensated cirrhosis in the model there is a risk of developing decompensated cirrhosis and hepatocellular carcinoma. Resources identified included drug acquisition costs, monitoring costs for patients on therapy, hepatitis C health state costs and the management of adverse drug reactions. Transition probabilities and health state utility values were taken from the literature. Costs and consequences were discounted at an annual rate of 4%.

9. For treatment naïve patients the incremental cost-effectiveness ratio (ICER) for boceprevir when added to peginterferon - ribavirin was €11,411/QALY with ICERs ranging from €10,408/QALY to €16,763/QALY. The highest ICER (€16,763/QALY) was obtained for treatment naïve patients with cirrhosis. For treatment experienced patients the ICERs ranged from €2,756/QALY to €12,761/QALY.

10. Sensitivity analysis indicated that the greatest effect on the base case ICERs for treatment naïve patients was associated with changes in the time horizon, discount rate and the price of boceprevir. Reducing the sustained viral response (SVR) rate by 10% increased the ICER from €11,411/QALY to €17,742/QALY. For treatment naïve cirrhotic patients a 10% reduction in SVR rate increased the ICER to €27,926/QALY.

11. Similarly, the main influences on the base case ICER for treatment experienced patients included time horizon, discount rate and boceprevir price. Probabilistic sensitivity analysis demonstrated that the probability of boceprevir being cost-effective when added to the current standard of care in treatment naïve patients was over 96% at the €20,000/QALY threshold. In the treatment experienced population the probability of cost-effectiveness was closer to 100% at the €20,000/QALY threshold. The submitted budget impact analysis indicated an expenditure of approximately € 1.1 million in year one increasing to just under €1.6 million in year five resulting in an estimated expenditure of €6.5 million over the five year period.

12. The addition of boceprevir (Victrelis) to the current standard of care could increase drug acquisition costs by approximately €20,000 to €38,000 per patient depending on the duration of treatment. Despite this additional cost we believe that boceprevir (Victrelis) may be considered a highly cost-effective therapy when added to peginterferon – ribavirin for the treatment of patients infected with genotype 1 hepatitis C virus in the Irish healthcare setting.