Cost effectiveness of paritaprevir boosted with ritonavir and ombitasvir (Viekirax®) with or without dasabuvir (Exviera®) for the treatment of genotypes 1 and 4 chronic hepatitis C infection

The NCPE has issued a recommendation regarding the cost effectiveness of paritaprevir boosted with ritonavir and ombitasvir (Viekirax®) with or without dasabuvir (Exviera®) for patients with HCV infection. The NCPE recommends reimbursement of paritaprevir boosted with ritonavir and ombitasvir (Viekirax®) with or without dasabuvir (Exviera®) for certain subpopulations of GT1 and GT4.

The HSE asked the National Centre for Pharmacoeconomics (NCPE) to carry out an assessment of the applicant's (AbbVie Ltd.) economic dossier on the cost effectiveness of paritaprevir boosted with ritonavir and ombitasvir (Viekirax®) with or without dasabuvir (Exviera®) for the treatment of hepatitis C infection. The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes clinical effectiveness and health related quality of life benefits, that the new treatment may provide and whether the cost requested by the pharmaceutical applicant is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence that may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has responsibility for commissioning or providing healthcare, public health or social care services.

National Centre for Pharmacoeconomics **February 2016**

In January 2015 AbbVie Ltd. submitted a clinical and economic dossier on the cost effectiveness of Viekirax® with or without Exviera® for the treatment of genotypes 1 and 4 chronic hepatitis C infection. Final comments were received in January 2016. Viekirax® combines two direct acting antiviral agents, paritaprevir 75mg with 12.5mg of ombitasvir boosted with 50mg of ritonavir in a co-formulated once daily tablet, with two tablets taken once daily in the morning. Dasabuvir 250mg (Exviera®) is administered twice daily together with Viekirax® for patients with genotype 1. In the recently revised EASL guidelines, Viekirax® with Exviera® is recommended for genotype 1 patients, with and without cirrhosis, while Exviera® is recommended for patients with genotype 4. Treatment duration is dependent on genotype 1 subtype (i.e. 1a or 1b) and the presence or absence of cirrhosis. Response to therapy is measured as undetectable virus 12 weeks after completion of therapy, termed the sustained viral response (SVR).

The submitted dossier included evidence on the cost-effectiveness of Viekirax® with Exviera® for genotype 1 and Exviera® for genotype 4 with or without ribavirin for the treatment of chronic hepatitis C. Of note, genotype 1 accounts for approximately 55% of chronic hepatitis C in Ireland compared to 1-3% for genotype 4. Based on the current guidelines the comparators for both genotypes are:

- Interferon containing:
    - sofosbuvir with pegylated interferon and ribavirin, and
    - simeprevir with pegylated interferon and ribavirin,
- Interferon-free:
    - sofosbuvir with ledipasvir
    - simeprevir with sofosbuvir and
    - sofosbuvir and daclatasvir

1. Clinical effectiveness

The clinical evidence submitted to support the cost-effectiveness of the AbbVie regimens included data from two placebo-controlled studies (SAPPHIRE I and II), and six open-label, randomised studies (PEARL I, II, III & IV; TURQUOISE I & II). SVR12 rates in patients with genotype 1 and 4 patients with and without cirrhosis are >90%, (patients without cirrhosis dominate the trial programme). Outcome data from real world studies worldwide indicate similar SVR rates. Due to the lack of comparator trials a comparative assessment of efficacy was not undertaken.

2. Safety

The dual and triple AbbVie combinations are generally well tolerated, with low rates of serious adverse events and treatment discontinuations. Fatigue, asthenia, headache, nausea, diarrhoea, pruritus and rash were the most common treatment-emergent adverse events when using the triple therapy regimen with RBV. Overall the regimens are associated with good tolerability and no specific safety signals of concern are apparent from Phase III trials in patients with mild cirrhosis (CTP A) and good renal function. In October 2015, the US Food and Drug Administration Agency (FDA) issued a warning stating that Viekirax® and Exviera® may increase the risk for serious liver injury, particularly in those with underlying advanced liver disease. In January 2016, the EMEA also issued a warning and recommended that the regimen should not be prescribed for patients with advanced liver disease (Child Turcotte Pugh stage B). The review group notes that this cohort of patients with advanced or decompensated liver disease were excluded from the clinical trial programmes.

3. Cost-effectiveness of AbbVie regimen

- The cost of a 56 tablet pack of Viekirax® is €13,471.00, and the cost of a 56 tablet pack of the Exviera® is €1,171.33.
- A cost-utility analysis was submitted by AbbVie Ltd. comparing a number of scenarios where the AbbVie regimens are used with or without RBV. The population represented in the economic model are patients with genotypes 1 and 4 HCV infection, both treatment naive and treatment experienced, and two patient cohorts were modelled i.e. an overall non-cirrhotic cohort (F0-F3) and a cirrhotic cohort (F4). The review team requested two further subgroups of mild (F0–F2) and F3 patients to be analysed.
- A Markov state-transition model was used to describe the progression of disease over the lifetime of a patient cohort. The model represents the natural history of chronic hepatitis C patients and allows patients to enter the model based on baseline staging of disease.
- Quality-adjusted life years (QALYs) were used to measure benefits and morbidity. Costs included drug acquisition costs, health state costs, monitoring costs and costs associated with treatment of adverse events and liver progression events i.e. decompensated cirrhosis, hepatocellular carcinoma and liver transplant. The analysis was presented from the healthcare payer's perspective.

Results

Genotype 1 treatment naïve without cirrhosis

- Viekirax® and Exviera® is cost effective versus SIM/PR in a genotype 1 overall non-cirrhotic cohort (ICER €23,248/QALY). ICERs are higher for a F0-F2 subgroup and lower for F3 alone. It is not cost-effective at a threshold of €45,000/QALY for GT1b for a mild F0-F2 cohort.
- It is dominant versus SOF/PR for GT1 overall, as well as stratified by subtype in a F0-F3 group, F3 alone and F0-F2
- The comparison versus SOF/LDV is driven by treatment duration; QALYs are very similar. A 12 week course of SOF/LDV is more expensive than the 12 week Viekirax® and Exviera® regimen; an 8 week course of SOF/LDV is cheaper than the Viekirax® and Exviera® 12 week regimen. This holds for GT1 overall, and for subtypes F0-F3, F0-F2 and F3 alone
- Viekirax® and Exviera® is less costly and less effective than SOF/SIM and SOF/DCV in a non-cirrhotic GT1 cohort

Genotype 1 treatment naïve cirrhotic

The base case analysis presented by the manufacturer assumes that 71.9% of cirrhotic patients with GT1a will receive 12 weeks of treatment, while 28.1% will receive 24 weeks. This does not represent clinical practice – the review group assumes a treatment duration of 24 weeks for all cirrhotic patients with GT1a treated with P/rO(D).

- The Viekirax® with Exviera® regimen is cost-effective when compared to SIM/PR (ICER €9,254/QALY). However, the ICER exceeds the €45,000/QALY threshold for a GT1a subgroup.
- The Viekirax® with Exviera® regimen is cost-effective when compared to SOF/PR. While SOF/PR is dominated in a GT1b cohort, it is not cost-effective in a GT1a cohort.
- Compared to SOF/LDV, the Viekirax® with Exviera® regimen demonstrates similar effect. SOF/LDV provides the cheaper option for a GT1a cohort, while the Viekirax® with Exviera® regimen appears slightly cheaper in a GT1b cohort.
- The Viekirax® with Exviera® regimen is dominated by SOF/DCV in a GT1a subgroup, but provides a saving in a GT1b cohort; while it dominates SIM/SOF.
- In a scenario where the price of the Viekirax® with Exviera® regimen is capped at 12 weeks, the Abbvie regimen provides a cost-effective treatment option for cirrhotic

GT1 patients compared to all relevant comparators.

Genotype 1 treatment experienced

The Viekirax® with Exviera® regimen is cost-effective when compared to SIM/PR for non-cirrhotic patients and when compared to SOF/LDV, QALYs are very similar with the result driven by the treatment duration of SOF/LDV (8 weeks or 12 weeks).

Genotype 4

The evaluation considered the cost-effectiveness of Viekirax® in patients with GT4 who represent 1-3% of the total population of patients with HCV infection in Ireland. Viekirax® dominates SOF/PR; no comparison with SIM/PR was presented. Viekirax® dominates SOF/LDV+RBV in a mild cohort, but is not cost-effective in a cirrhotic cohort.

An analysis assessing the cost-effectiveness of the regimens in patients with HIV co-infection was not presented.

Budget Impact Analysis

There is significant uncertainty in the future market regarding available treatments for HCV infection, making it difficult to estimate the potential market share of the AbbVie regimens over the next 5 years. There is also considerable uncertainty over the number of patients that may be treated annually in the Irish setting under the current model of care.

The applicant assumes that 650 patients will be treated for HCV infection every year. The gross budget impact is estimated to be €49,797,566 (€10,503,658 in year 1 and €9,823,477 in years 2-5).

Conclusion

The applicant, AbbVie Ltd., submitted a dossier for the dual and triple AbbVie regimens with or without ribavirin in genotypes 1 and 4 hepatitis C infection in accordance with licensed indications. The applicant presented several different scenarios across the two genotypes stratified by cirrhosis status and previous treatment experience. The AbbVie triple therapy regimen is considered cost-effective when compared to interferon-based comparators in both non-cirrhotic and cirrhotic patients. When compared to SOF/LDV in GT1 and GT4, little difference is observed in effects and difference in cost is driven by treatment duration. The

NCPE recommends reimbursement of paritaprevir boosted with ritonavir and ombitasvir (Viekirax®) with or without dasabuvir (Exviera®) for certain subpopulations of GT1 and GT4.