AWMSG Secretariat Assessment Report – Limited submission

Glecaprevir/pibrentasvir (Maviret®▼) 100 mg / 40 mg film-coated tablets

Company: AbbVie Ltd

Licensed indication under consideration: Treatment of chronic hepatitis C virus (HCV) infection in adolescents aged 12 to < 18 years.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Date of licence extension: 11 March 2019

Comparator(s)

- The comparator included in the company's submission is ledipasvir/sofosbuvir (Harvoni®).

Limited submission details

- A minor licence extension for use in adolescents aged 12 to < 18 years
- Anticipated usage in NHS Wales is considered to be of minimal budgetary impact.

Clinical effectiveness

- Glecaprevir/pibrentasvir (Maviret®) was recommended for the treatment of chronic HCV infection in adults by the All Wales Medicines Strategy Group (AWMSG) in October 2017. In December 2017 this advice was superseded by National Institute for Health and Care Excellence (NICE) guidance TA499.
- Guidance published by the Hepatology Committee of European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) in 2018 recommended that all treatment-naïve and treatment-experienced children with chronic HCV infection should be considered for treatment.
- In 2013, the National Institute for Health and Care Excellence (NICE) approved peginterferon alfa-2a (Pegasys®) and -2b (ViraferonPeg®) in combination with ribavirin (Rebetol®) for use in children and adolescents. However, the ESPGHAN and AWTTC-sought clinical expert opinion are of the view that these are no longer the treatments of choice for hepatitis C infection in adolescents. Direct-acting antiviral agents have since been licensed for use in adolescents and include ledipasvir/sofosbuvir (Harvoni®) and sofosbuvir (Sovaldi®) + ribavirin and/or peginterferon-alfa.
- Harvoni® has a statement of advice from the AWMSG for use in adolescents. AWTTC-sought clinical expert opinion however, agrees that Harvoni® may be a suitable comparator.
- The company's submission includes a single arm, open-label, phase II/III, international, multicentre study (DORA). This study evaluates the

pharmacokinetics, safety, and efficacy of glecaprevir/pibrentasvir in paediatric patients (aged 3 to < 18 years) with chronic HCV genotypes (GT) 1–6 infection.

- There are four cohorts relating to age, but it is Cohort 1 (aged 12 to < 18 years) which provided the evidence for the licence extension of the indication to adolescents using the adult co-formulated tablets (at a dose of three tablets once daily for eight weeks).
- Patients (n = 13, treatment-naïve) were first enrolled into an intensive pharmacokinetic (IPK) part of the study, followed by a non-IPK safety/efficacy part. All 13 patients included in the IPK analysis demonstrated a sustained virologic response (i.e. clearance of the virus) 12 weeks post-treatment (SVR_{12}).
- On request, data from 34 additional patients from the non-IPK analysis were submitted during the licensing procedure. In the final study population of 47 patients, most had GT 1 HCV (n=37; 78%), none in this cohort had GT 5 or 6. A total of 11 (23.4%) patients were treatment-experienced (all received a previous IFN-based regimen) and two (4.3%) were HIV/HCV co-infected. None had cirrhosis or advanced fibrosis. Three patients with GT3 HCV were treated with glecaprevir/pibrentasvir for 16 weeks.
- All 47 adolescent patients (100% [95% confidence interval: 92.4 to 100.0]) achieved SVR_{12}.
- The Committee for Medicinal Products for Human Use (CHMP) concluded that the pharmacokinetic data showed comparable exposure between adolescents and adults. No new safety concerns or serious adverse events were reported in the DORA and expanded safety study. No patients discontinued treatment due to adverse events. The CHMP concluded that the safety profile of glecaprevir/pibrentasvir in adolescents was comparable to that seen in adults.

Budget impact

- The company estimates five adolescents in Wales with chronic HCV infection are eligible for treatment with glecaprevir/pibrentasvir, based on published analysis of children aged < 18 years treated in three UK paediatric specialist liver centres during 2005–2010.
- This prevalence estimation is assumed to be stable each year, and the company suggests that all five adolescents would receive glecaprevir/pibrentasvir in Years 1-5. AWTTC-sought clinical expert opinion in Wales agrees with this estimate.
- Treatment with glecaprevir/pibrentasvir can be for a duration of 8, 12 or 16 weeks, depending on genotype, prior treatment experience and cirrhotic status.
- The company has assumed that all eligible patients are treatment-naive and non-cirrhotic; all eligible patients would be expected to receive glecaprevir/pibrentasvir for 8 weeks across all licensed genotypes (1–6).
- Treatment with Harvoni® can be for a duration of 8, 12 or 24 weeks, where the 8-week treatment duration may be considered in treatment-naive, non-cirrhotic GT1-infected patients.
- The company has assumed that the majority of eligible patients are GT1-infected, but a small proportion have GT2–6; the majority (80%) of eligible patients would be expected to receive Harvoni® for 8 weeks and the remainder for 12 weeks.
- The company estimates the annual cost of treatment with glecaprevir/pibrentasvir based on the approved Wales Patient Access Scheme (WPAS) discount is [commercial in confidence figure removed]; assuming that all five adolescents will be eligible for an 8-week course.
- Based on the price, the company estimates a net [commercial in confidence figure removed], versus treatment with Harvoni®.

Additional information

- Wales signed up to the World Health Organization (WHO) strategy 2016–2021 to eliminate hepatitis C by 2030. The All Wales Hepatitis C Treatment Roll-Out Programme was introduced in 2014.
- AWTTC is of the opinion that, if recommended, glecaprevir/pibrentasvir (Maviret®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipates that glecaprevir/pibrentasvir (Maviret®) may be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 13/6/2019 and 17/06/2019
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Glecaprevir/pibrentasvir (Maviret®) 100 mg/40 mg film-coated tablets. Reference number: 3917. September 2019.