

## Early Access to Medicines Scientific Opinion - Public Assessment Report

### Glecaprevir/Pibrentasvir 100mg/40mg film-coated tablets

Glecaprevir/Pibrentasvir 100mg/40mg film-coated tablets is a medicine used in the Early Access to Medicines Scheme for the treatment of chronic hepatitis C (HCV) infection in adults with compensated cirrhosis and at least one of the following:

- genotypes 1, 4, 5 and 6 with compensated cirrhosis previously treated with NS5A inhibitors
- genotypes 2, 3, 5 or 6 with chronic kidney disease (stage 4 and 5)
- GT 3-infected patients previously treated with peg-interferon, ribavirin, and/or sofosbuvir

AbbVie Ltd.

EAMS 41042/0002

### Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to doctors who may wish to prescribe the unlicensed medicine under their own responsibility. More information about the scheme can be found here:

<http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccessmedicineschemeEAMS/index.htm>

The scientific opinion is based on the information supplied to the MHRA on the benefits and risks of a promising new medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to licence such a medicine. The General Medical Council's guidance on prescribing unlicensed medicines can be found here: <http://www.gmc-uk.org/mobile/news/14327>

[Name product]

### What is Glecaprevir/Pibrentasvir 100mg/40mg film-coated tablets?

Glecaprevir/Pibrentasvir 100mg/40mg film-coated tablet contains the active substances glecaprevir and pibrentasvir

### What is Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet used to treat/diagnoses/prevent?

In the context of the Early Access to Medicines Scheme, Glecaprevir/Pibrentasvir is an antiviral medicine used to treat adults with long-term hepatitis C, an infectious disease that affects the liver, caused by the hepatitis C virus.

It is for the treatment of adults with compensated cirrhosis and at least one of the following:

- patients with hepatitis C (genotypes 1, 4, 5 and 6) and have been previously treated with NS5A inhibitors
- patients with hepatitis C (genotypes 2, 3, 5 or 6) who have chronic kidney disease (stage 4 and 5)
- patients with hepatitis C (genotype 3) previously treated with peg-interferon, ribavirin, and/or sofosbuvir

### How is Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet used?

Treatment must be started and supervised by a doctor experienced in the management of patients with chronic hepatitis C.

Glecaprevir/Pibrentasvir 100mg/40mg film-coated tablet is available as tablets which contain 100mg of glecaprevir and 40mg of pibrentasvir.

For patients with hepatitis C (genotypes 1, 4, 5 and 6) who have compensated cirrhosis, with or without chronic kidney disease (stage 4 and 5), and have been previously treated with NS5A inhibitors the recommended dose is three tablets taken once a day with food for 16 weeks.

For patients with hepatitis C (genotype 3) with compensated cirrhosis, with and without chronic kidney disease, who have been previously treated with peg-interferon, ribavirin, and/or sofosbuvir and have not been previously treated with NS5A inhibitors, the recommended dose is three tablets taken once a day with food for 16 weeks.

For patients with hepatitis C (genotypes 2, 5 or 6) who have chronic kidney disease (stage 4 and 5) and have not been previously treated with NS5A inhibitors the recommended dose is three tablets taken once a day with food for 12 weeks.

### **How does Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet work?**

Glecaprevir/pibrentasvir works by stopping the hepatitis C virus from multiplying and infecting new cells. This allows the infection to be permanently eliminated from the body.

### **How has Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet been studied?**

In the context of the Early Access to Medicines Scheme, Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet was investigated in three studies; in studies M15-110 (Part 1 and 2) in which patients with or without cirrhosis who had been treated with NS5A inhibitors were included; M15-462 in which patients with chronic kidney disease stages 4 – 5 with or without cirrhosis were included and M14-868 – Part 3 in which patients with hepatitis C genotype 3 cirrhosis were included.

The main measure of effectiveness was the number of patients whose blood tests did not show any sign of hepatitis C virus 12 weeks after the end of treatment.

### **What are the benefits and risks of Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet?**

#### *Benefits*

In patients with or without cirrhosis who had previously been treated with NS5A inhibitors, 92% of them did not show any sign of hepatitis C virus 12 weeks after the end of treatment.

In patients with hepatitis C (genotypes 2, 3, 5 or 6) who have chronic kidney disease (stage 4 and 5), 98% of them did not show any sign of hepatitis C virus 12 weeks after the end of treatment.

In patients with hepatitis C genotype 3 and cirrhosis who had prior treatment experience, but were naive to an NS5A inhibitor, treated for 16 weeks 96% of them did not show any sign of hepatitis C virus 12 weeks after the end of treatment.

#### *Risks*

Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet must not be used together with the following medicines, as they may reduce the levels of Glecaprevir and pibrentasvir in the blood and thereby reduce the effectiveness of Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet;

- Rifampicin (antibiotic)
- Atazanavir (antiviral)
- Carbamazepine (anti-epileptic)
- St John's Wort (a herbal preparation used for depression and anxiety).

For further information, see the EAMS treatment protocol

**Why has Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet been given a positive Early Access to Medicine Scientific opinion?**

Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet on its own has been shown to be highly effective in clearing the hepatitis C virus from the blood of patients compensated cirrhosis. Clearance of the virus was seen in patients with genotype 3 as well as patients with chronic renal disease (genotypes 1, 2, 3, 4, 5 and 6). Clearance was also high in patients with compensated cirrhosis with (genotypes 1, 4, 5 and 6) and had failed previous treatment with NS5A inhibitors. Glecaprevir/pibrentasvir was well tolerated with a favourable safety profile.

The MHRA has considered the benefits of Glecaprevir/pibrentasvir in this serious condition and concluded that the benefits are greater than the risks.

**What are the uncertainties?**

Even though GLE /PIB has been studied in a sufficient number of patients with hepatitis C (genotypes 2, 3, 5 or 6) who have chronic kidney disease (stage 4 and 5) and patients with hepatitis C (genotype 3) with compensated cirrhosis. Only a limited number of patients with hepatitis C (genotypes 1, 4, 5 and 6) who have compensated cirrhosis and have been previously treated with NS5A inhibitors were studied, hence there is a lack of certainty regarding use of GLE/PIB in NS5A inhibitor-experienced population

**Are there on-going clinical studies?**

There is an ongoing clinical study to evaluate the use of Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet in patients with hepatitis C (genotypes 1-6) post-liver and post-renal transplant subjects

**What measures are in place to monitor and manage risks?**

A risk management plan has been developed to ensure that Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet is used as safely as possible. Based on this plan, the company that makes Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet must ensure that all healthcare professionals expected to use the medicine, as well as patients, are provided with information on the medicine including the side effects of treatment and recommendations for preventing or minimising these side effects.

Information will be collected about patients before they enter the scheme. The company will ask the healthcare professionals to report adverse events experienced by patients receiving Glecaprevir/pibrentasvir 100mg/40mg film-coated tablet through the scheme. These safety data will be reviewed and reported to the MHRA on a regular basis by the Company.

**Other information about [Glecaprevir/pibrentasvir 100mg/40mg film-coated tablets] – see EAMS Treatment Protocol**