Swiss Summary of the Risk Management Plan (RMP)

Maviret®
(Glecaprevir / Pibrentasvir)

100 mg/40 mg
Film-coated tablets

Version 1.0 (Dec 2016)

AbbVie AG
Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of Maviret® is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the “Arzneimittelinformation / Information sur le médicament” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Maviret® in Switzerland is the “Arzneimittelinformation/ Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. AbbVie AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Maviret®.
VI.2 Elements for a Public Summary

Glecaprevir/Pibrentasvir (Tradename)

All medicines have some risks – a risk is something unwanted that may happen when you take a medicine. A medicine is approved when there is enough evidence that, for the average patient, the benefits of taking the medicine should be greater than the risks. However, even though the benefits outweigh the risks, those possible risks remain. This public summary explains how those risks will be managed for this medicine.

If you have any questions about the information in this summary, talk to your doctor or healthcare professional.

VI.2.1 Overview of Disease Epidemiology (About Hepatitis C)

Hepatitis C virus (HCV) is a virus which infects and damages liver cells. HCV is most commonly spread through contact with the blood of someone infected with HCV. This can be through:

- Injection of illegal drugs, where needles are shared with someone with HCV;
- Receiving HCV infected blood transfusions – before 1992, blood was not screened for HCV.

Worldwide, around 3 to 4 million people become infected with HCV each year. Young adults and men are more likely to get a HCV infection. Most people who become infected with HCV have it long term – called a 'chronic' infection.

People with HCV infection over a long period are at risk of getting liver scarring (also called 'cirrhosis'), liver failure or liver cancer – these conditions may be life threatening.

VI.2.2 Summary of Treatment Benefits

About Tradename

This summary is about a combination of two medicines called:

- glecaprevir (GLE)
● pibrentasvir (PIB).

In this document, we will use the name 'Tradename'.

What is Tradename used for?

The combined medicine is used to treat long-term infection with HCV in adults.

How does Tradename work?

This medicine is a 'direct-acting anti-viral' (DAA) treatment.

What have studies shown about the benefits of Tradename?

There have been 9 studies of Tradename.

- The studies involved 2,369 patients with long-term HCV infection.
- The patients in these studies were treated for 8, 12 or 16 weeks.

Most patients in the studies had not been treated for HCV infection before. However, some patients had been treated with other HCV medicines in the past – but were not cured.

A total of 308 patients with liver scarring (cirrhosis) because of HCV were included in 4 studies.

When looked at 12 weeks after treatment had stopped:

- A total of 297/308 (96.4%) patients with liver scarring – did not show any sign of the virus in their blood;
- A total of 2010/2061 (97.5%) patients without liver scarring – did not show any sign of the virus in their blood.

VI.2.3 Unknowns Relating to Treatment Benefits (What is Not Known)

Younger and older people

There is limited or no information on the use of Tradename in:
● Patients under 18 years of age.

Patients with other illnesses

There is limited or no information on the use on Tradename in:

● Patients with more advanced (moderate to severe) liver damage;
● Patients also infected with HBV (Hepatitis B Virus);
● Patients with a liver transplant.

Pregnancy or breast-feeding

There is limited or no information on the use of Tradename in:

● Pregnant or breast-feeding women.

Studies of Tradename in young people and people who have had a liver transplant are planned – these will collect more information on how Tradename works. Until these studies are finished, we will not know how well these medicines work in these groups of people. More information on these studies can be found in section VI.2.6 'Planned Post Authorisation Development Plan (What further studies are planned?)'.

VI.2.4 Summary of Safety Concerns

Important Identified Risks (Risks we know about)

<table>
<thead>
<tr>
<th>Risk</th>
<th>What Is Known</th>
<th>Preventability (How can it be stopped)</th>
</tr>
</thead>
<tbody>
<tr>
<td>During treatment with Tradename, patients with HBV, but who do not have any symptoms of HBV, may get symptoms of HBV (called 'reactivation'). Some symptoms may be serious.</td>
<td>There may be a link between HBV coming back ('reactivation') and treatment with DAAs like Tradename.</td>
<td>Before starting treatment with Tradename, your doctor will do tests to find out if you have a past or present HBV infection. During treatment with Tradename, your doctor will carefully monitor you for early symptoms of HBV infection. If you have, or get, a HBV infection, your doctor may treat you for this.</td>
</tr>
</tbody>
</table>
## Important Potential Risks

There are some possible risks with this medicine that we know about.

<table>
<thead>
<tr>
<th>Risk</th>
<th>What Is Known (including reason why it is a possible risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased chance of having an early recurrence, or a new occurrence of a type of liver cancer called 'hepatocellular carcinoma' (HCC)</td>
<td>Hepatitis C virus (HCV) infection may become long lasting (called 'chronic HCV'). Over the course of decades, damage and scarring of the liver may develop (called 'cirrhosis'). A type of cancer called hepatocellular carcinoma (HCC), that is usually seen in patients with a damaged (cirrhotic) liver, may develop. At present, there is very little information on whether treatment with a DAA medicine for HCV may cause cancer to develop in the liver earlier than it would if the HCV infection was not treated. Also, if you have a history of HCC that has been treated, a few studies show that HCV treatment with a DAA medicine may increase the chance of the HCC recurring earlier. At the moment, there is very little information to prove this risk. Your doctor will monitor you for signs and symptoms for HCC while you are being treated with a DAA medicine like Tradename.</td>
</tr>
</tbody>
</table>
| Effects between Tradename and other medicines taken by a patient     | **Tradename effect on other medicines** Using Tradename with some other medicines can change the amount of these other medicines in the blood. This might change the effectiveness of the other medicines. Your doctor may need to change your dose of these other medicines – and they may need to keep a closer eye on these medicines.  
**Other medicines effect on Tradename** Some other medicines can change the amount of Tradename in the blood.  
- If the levels of Tradename increase – side effects from Tradename may be more severe or occur more often.  
- If the levels of Tradename decrease – then Tradename may not work as well as it should.  
Your doctor may need to change your dose of the other medicines – or ask you to stop taking these other medicines.  
**To help avoid problems with other medicines** Tell your doctor about all the medicines you are taking. This includes prescription medicines, over the counter, and herbal medicines. |
| Development of drug resistance – when the medicine stops working on the virus (the virus becomes 'resistant' to the medicine) | This virus has come back in a very small number of patients during treatment (called a 'breakthrough') or after treatment has finished (called a 'relapse'). Studies are happening now to see how long the response to treatment with Tradename lasts. |
Important Missing Information (Information that is not currently available)

<table>
<thead>
<tr>
<th>Risk</th>
<th>What is known</th>
</tr>
</thead>
</table>
| Liver damage and liver failure in patients who had moderate liver damage before taking Tradename – this can be life threatening | There may be a risk of more liver damage and liver failure in patients who already had moderate liver scarring (cirrhosis) before taking Tradename:  
  • This can be life threatening;  
  • It may mean you are not able to keep taking Tradename: this depends on how much your liver is damaged. |
| Using Tradename in patients who have had a liver transplant          | Currently, it is not known whether the safety of Tradename is the same in patients with HCV who have had a liver transplant compared to patients with HCV who have not had a liver transplant. A study in patients with HCV who have had a liver transplant is happening now. |
| Using Tradename in pregnancy                                         | There is no information on using Tradename in pregnant women.                                           |
| Using Tradename in children                                          | There is no information on the use of Tradename in children.                                           |

VI.2.5 Summary of Risk Minimisation Measures by Safety Concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks, and recommendations for minimizing them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimization measures.

The SmPC and the PL for Tradename can be found in the Tradename's European public assessment reports (EPAR) page.

This medicine has no additional risk minimization measures.
VI.2.6 Planned Post-Authorisation Development Plan (What further studies are planned?)

List of Studies in Post-Authorisation Development Plan

<table>
<thead>
<tr>
<th>Study/Activity (including study number)</th>
<th>Objectives</th>
<th>Safety Concerns/Efficacy Issue Addressed</th>
<th>Status</th>
<th>Planned date for Submission of (interim and) Final Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study M13-576</td>
<td>To assess the persistence of specific HCV amino acid substitutions associated with drug resistance in subjects who experienced virologic failure.</td>
<td>Risk of resistance development</td>
<td>Started</td>
<td>Interim: Dec 2016 Final: &lt;pending&gt;</td>
</tr>
<tr>
<td>Study M13-596</td>
<td>To assess the safety and efficacy of Tradename in approximately 90 non-cirrhotic TE and TN adult post-liver or post-renal transplant recipients with chronic HCV GT1 – 6 infection</td>
<td>Missing information: Safety in liver transplant recipients</td>
<td>Started</td>
<td>&lt;pending&gt;</td>
</tr>
<tr>
<td>Study M16-123</td>
<td>To obtain safety, efficacy, and pharmacokinetic data in pediatric patients</td>
<td>Missing information: Safety in pediatric patients</td>
<td>Planned</td>
<td>May 2019 (PIP completion date)</td>
</tr>
</tbody>
</table>

TE = treatment-experienced; TN = treatment naïve; GT = genotype; HCV = hepatitis C virus; PIP = pediatric investigation plan; PK = pharmacokinetics

Studies to assess the risk of HBV reactivation and the risk of an increased chance of having an early recurrence of HCC, or a new occurrence of HCC, may happen in the future.

Studies Which Are a Condition of the Marketing Authorisation

None of the above studies are conditions of the marketing authorization.
VI.2.7 Summary of Changes to the Risk Management Plan Over Time

This is the first edition of the Tradename Risk Management Plan.