Swiss Public Summary of the Risk Management Plan (RMP)

for

Epclusa®, film coated tablets

(Sofosbuvir/Velpatasvir)

Version 7.0 (August 2022)
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SUMMARY OF RISK MANAGEMENT PLAN FOR EPCLUSA® (SOFOSBUVIR/VELPATASVIR)

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 minimize them.

The RMP summary of Epclusa 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 Epclusa in Switzerland is the „Arzneimittelinformation / Information sur le médicament“ (see www.swissmedic.ch) approved authorized by Swissmedic. Gilead Sciences Switzerland Sàrl is fully responsible for the accuracy and correctness of the content of the here published summary RMP of Epclusa.

1.1. The Medicine and What is it Used for

Epclusa is authorized for treatment of chronic hepatitis C (CHC) in patients aged 3 years and older (see SmPC for the full indication). It contains sofosbuvir (SOF) and velpatasvir (VEL) as active substances and it is given orally.

Further information about the evaluation of Epclusa’s benefits can be found in Epclusa’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/epclusa.

1.2. Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of Epclusa, together with measures to minimize such risks and the proposed studies for learning more about Epclusa’s risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

- The medicine's legal status — the way a medicine is supplied to the public (e.g. with or without prescription) can help to minimizes its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed including PSUR assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Epclusa is not yet available, it is listed under 'missing information' below.

1.2.1. List of important risks and missing information

Important risks of Epclusa are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Epclusa. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table 0-1. List of Important Risks and Missing Information

Important Identified Risks	Severe bradycardia and heart block when used with concomitant amiodarone
	HBV reactivation in HBV/HCV coinfected patients
Important Potential Risks	None
Missing Information	Safety in pregnant women

1.2.2. Summary of Important Risks

Table 0-2. Summary of Important Risk(s) and Missing Information

Important Identified Risk	**Severe bradycardia and heart block when used with concomitant amiodarone**
Evidence for linking the risk to the medicine	Cases of severe bradycardia have been observed when SOF-containing regimens are used in combination with amiodarone.
Risk factors and risk groups	Patients also taking beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease may be at increased risk for symptomatic bradycardia with coadministration of amiodarone.

Risk Minimization Measure(s)	Routine risk minimization measures: SmPC Section 4.4, 4.5, and 4.8 PL Section 2. Additional risk minimization measures: None
Important Identified Risk	**HBV reactivation in HBV/HCV coinfected patients**
Evidence for linking the risk to the medicine	Cases of HBV reactivation have been reported in patients coinfected with HBV/HCV during or after treatment with DAAs. HBV reactivation can potentially be life-threatening, as it could result in hepatitis, an increase in transaminase levels, an increase in bilirubin levels, hepatic failure and death. Rare severe cases (involving hepatic failure or death) of HBV reactivation in patients receiving SOF-containing products have been reported.
Risk factors and risk groups	Due to the small number of cases of HBV reactivation with DAAs, risk factors have not been definitively established. However, some of the cases involving HBV reactivation with SOF-containing regimens involved patients who were immunocompromised (patients coinfected with HIV or patients receiving immunosuppressants due to prior transplant). In addition, a case involving severe HBV reactivation had risk factors of NASH and Burkitt's lymphoma.
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC Section 4.4 PL Section 2 Additional risk minimization measures: None
Important Potential Risk	**None**
Missing information	**Safety in pregnant women**
Risk Minimization Measure(s)	Routine risk minimization measures SmPC Section 4.6 PL Section 2. Additional risk minimization measures: None

1.2.3. Post-authorization Development Plan

1.2.3.1. Studies which are Conditions of the Marketing Authorization

There are no studies which are conditions of the marketing authorization or a specific obligation of Epclusa.

1.2.3.2. Other Studies in Post-Authorization Development Plan

There are no studies required for Epclusa.