



**Swiss Public Summary of the
Risk Management Plan (RMP)**

for

Vosevi, film-coated tablets

(Sofosbuvir/Velpatasvir/Voxilaprevir Fixed-Dose Combination)
400mg/100mg/100mg

Version 5.0 (September 2022)
Based on EU RMP version 6.1

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SUMMARY OF RISK MANAGEMENT PLAN FOR VOSEVI (SOFOSBUVIR/VELPATASVIR/VOXILAPREVIR)

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 Vosevi 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 Vosevi 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 Vosevi.

I. The Medicine and What is it Used for

Vosevi is authorized for treatment of chronic hepatitis C (CHC) in patients aged 12 years and older and weighing at least 30 kg (see SmPC for the full indication). It contains sofosbuvir (SOF), velpatasvir (VEL) and voxilaprevir (VOX) as active substances and it is given orally.

Further information about the evaluation of Vosevi's benefits can be found in Vosevi'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/vosevi>.

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

Important risks of Vosevi, together with measures to minimize such risks and the proposed studies for learning more about Vosevi'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 minimize 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 Vosevi is not yet available, it is listed under ‘missing information’ below.

II.A. List of important risks and missing information

Important risks of Vosevi 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 Vosevi. 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 Part VI.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 coinfecting patients
Important Potential Risks	None
Missing Information	Safety in pregnant women
	Safety in patients with moderate or severe hepatic impairment

II.B. Summary of Important Risks

Table Part VI 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 coinfecting patients
Evidence for linking the risk to the medicine	Cases of HBV reactivation have been reported in patients coinfecting 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.
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 coinfecting 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
Missing information	Safety in patients with moderate or severe hepatic impairment
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC Sections 4.2, 4.4 and 5.2 PL Section 3 Additional risk minimization measures: None

II.C. Post-authorization Development Plan

II.C.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 Vosevi.

II.C.2. Other Studies in Post-Authorization Development Plan

There are no studies required for Vosevi.