

## **Part VI: Summary of the Risk Management Plan**

### **Summary of risk management plan for Exviera**

This is a summary of the RMP for Exviera (Dasabuvir). The RMP details important risks of Exviera, how these risks can be minimized, and how more information will be obtained about Exviera's risks and uncertainties (missing information).

Exviera's SmPC and its package leaflet (PIL) give essential information to HCPs and patients on how Exviera should be used.

This summary of the RMP for Exviera should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which are part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Exviera's RMP.

#### **I The Medicine and What it Is Used For**

Exviera is indicated for use in combination with other medicinal products for the treatment of chronic HCV infection in adults (see SmPC for the full indication). It contains dasabuvir as the active substance and it is given by oral route of administration.

Further information about the evaluation of Exviera's benefits can be found in Exviera's EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage: <https://www.ema.europa.eu/en/medicines/human/EPAR/exviera>.

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

Important risks of Exviera, together with measures to minimize such risks and the proposed studies for learning more about Exviera'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 PIL and SmPC addressed to patients and HCPs;
- 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 patient (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 periodic safety update report (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 Exviera is not yet available, it is listed under "missing information" below.

## II.A List of Important Risks and Missing Information

Important risks of Exviera 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 Exviera. 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).

<b>List of Important Risks and Missing Information</b>	
Important identified risks	Hepatic decompensation and hepatic failure in patients with cirrhosis.
Important potential risks	Depression and suicide Hepatotoxicity among non-users of ethinyl estradiol-containing medications Lack of efficacy/Risk of resistance development
Missing information	None.

## II.B Summary of Important Risks

**Important identified Risk - Hepatic decompensation and hepatic failure in patients with cirrhosis.**

Evidence for linking the risk to the medicine	<p><u>Clinical trial data</u></p> <p>Postmarketing cases of hepatic decompensation and hepatic failure, including liver transplantation or fatal outcomes, have been reported.</p>
Risk factors and risk groups	<p>Patients with moderate to severe hepatic impairment and advanced liver disease including cirrhosis.</p>
Risk minimization measures	<ul style="list-style-type: none"> <li>• SmPC section 4.2 - Posology and method of administration: Exviera should not be used in patients with moderate to severe hepatic impairment (Child-Pugh B or C). Exviera is administered with Viekirax which is contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C).</li> <li>• Patient Information Label (PIL) Section 2 - what you need to know before you take Exviera provides information on signs of worsening liver problems.</li> <li>• Monitoring of clinical signs and symptoms of hepatic decompensation included in SmPC section 4.4</li> <li>• Prescription only medicine.</li> <li>• Use of treatment should be initiated and supervised by specialists.</li> <li>• Pack size.</li> </ul>
<p><b>Important potential risk - Depression and suicide</b></p>	
Evidence for linking the risk to the medicine	<p>Postmarketing data.</p>
Risk factors and risk groups	<p>Risk groups may include HCV patients with prior medical histories of psychiatric conditions, including depression/major depression, bipolar disorder, anxiety, unspecified psychiatric conditions, or substance abuse.</p>

Risk minimization measures	<ul style="list-style-type: none"> <li>• SmPC section 4.4 - Special warnings and precautions for use provides information on depression and suicide.</li> <li>• SmPC section 4.8 - Undesirable effects.</li> <li>• PIL Section 2 - What you need to know before you take Exviera.</li> <li>• A recommendation for patients and caregivers to notify on mood changes and of any suicidal ideation per SmPC section 4.4.</li> <li>• Prescription only medicine.</li> <li>• Use of treatment should be initiated and supervised by specialist.</li> <li>• Pack size.</li> </ul>
<b>Important potential risk - Hepatotoxicity among non-users of ethinyl estradiol-containing medications</b>	
Evidence for linking the risk to the medicine	Clinical trial dataset.
Risk factors and risk groups	Patients taking Viekirax and Exviera with or without ribavirin.
Risk minimization measures	<ul style="list-style-type: none"> <li>• SmPC section 4.4 - special warning and precautions include information on ALT elevations associated with non-estrogen containing products in patients taking Viekirax and Exviera with or without ribavirin.</li> <li>• PIL Section 2 - what you need to know before you take Exviera provides information on signs of worsening liver problems.</li> <li>• SmPC section 4.4 provides specific information on early warning signs of liver inflammation.</li> <li>• Monitor cirrhotic patients for clinical signs and symptoms and hepatic laboratory tests per SmPC section 4.4.</li> <li>• Prescription only medication.</li> <li>• Use of treatment should be initiated and supervised by specialists.</li> <li>• Pack size.</li> </ul>
<b>Important potential risk – Lack of efficacy/Risk of resistance development</b>	
Evidence for linking the risk to the medicine	Clinical trials and postmarketing reports.

Risk factors and risk groups	Off-label use, poor compliance, and medication errors (e.g., inappropriate schedule of drug administration) may result in suboptimal drug exposures that may lead to treatment failure. For antiviral agents, this may lead to subsequent viral resistance development.
Risk minimization measures	<ul style="list-style-type: none"> <li>• SmPC section 4.2 – Posology and method of administration, includes information on dosage and duration of treatment for patients for genotype 1a, 1b and 4 pending cirrhotic status.</li> <li>• SmPC section 4.3 special warning and precautions on genotype specific activity, combination with other antiviral agents or retreatment.</li> <li>• PIL Section 3 – How to take Exviera, advise to patients on appropriate dosing and administration to achieve maximal efficacy.</li> <li>• Prescription only medication.</li> <li>• Use of treatment should be initiated and supervised by specialists.</li> <li>• Pack size.</li> </ul>

## **II.C Post-Authorization Development Plan**

### **II.C.1 Studies Which are Conditions of the Marketing Authorization**

There are no planned or ongoing studies that are conditions of the marketing authorization.

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

There are no other ongoing studies that are part of a post-authorization development plan.