Part VI: Summary of the Risk Management Plan

Summary of risk management plan for Viekirax

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

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

This summary of the RMP for Viekirax 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 Viekirax's RMP.

I The Medicine and What it Is Used For

Viekirax is indicated in combination with other medicinal products for the treatment of chronic hepatitis C (HCV) in adults (see SmPC for the full indication). It contains ombitasvir/paritaprevir/ritonavir as the active substance and it is given by oral route of administration.

Further information about the evaluation of Viekirax' benefits can be found in Viekirax' 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/viekirax.

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

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

II.A List of Important Risks and Missing Information

Important risks of Viekirax 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 Viekirax. 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).

List of Important Risks and Missing Information	
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 Fetal development toxicity (ombitasvir/paritaprevir/ritonavir only; added to the EU RMP per CHMP request)
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	<u>Clinical trial data</u> Postmarketing cases of hepatic decompensation and hepatic failure, including liver transplantation or fatal outcomes, have been reported.
Risk factors and risk groups	Patients with moderate to severe hepatic impairment and advanced liver disease including cirrhosis.
Risk minimization measures	• SmPC Section 4.2 - Posology and method of administration: Viekirax is contraindicated in patients with moderate to severe hepatic impairment (Child-Pugh B or C). • SmPC Section 4.3 - Contraindication Patients with moderate to severe hepatic impairment (Child-Pugh B or C) are contraindicated. • Patient Information Label (PIL) Section 2 - what you need to know before you take Viekirax provides information on signs of worsening liver problems. • Monitoring of clinical signs and symptoms of hepatic decompensation included in SmPC Section 4.4. • Prescription only medicine. • Use of treatment should be initiated and supervised by specialists. • Pack size.
Important potential risk - Depression and suicide	
Evidence for linking the risk to the medicine	Post marketing data.
Risk factors and risk groups	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.

Risk minimization measures	• SmPC Section 4.4 - Special warnings and precautions for use provides information on depression and suicide. • SmPC Section 4.8 - Undesirable effects. • PIL Section 2 - What you need to know before you take Viekirax. • A recommendation for patients and caregivers to notify on mood changes and of any suicidal ideation per SmPC Section 4.4. • Prescription only medicine. • Use of treatment should be initiated and supervised by specialist. • Pack size.
Important potential risk - Hepatotoxicity among non-users of ethinyl estradiol-containing medications	
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	• SmPC Section 4.4 - special warning and precautions include information on ALT elevations associated with non-estrogen containing products. • PIL Section 2 - what you need to know before you take Viekirax provides information on signs of worsening liver problems. • SmPC Section 4.4 provides specific information on early warning signs of liver inflammation. • Prescription only medication. • Use of treatment should be initiated and supervised by specialists. • Pack size.
Important potential risk – Lack of efficacy/Risk of resistance development	
Evidence for linking the risk to the medicine	Clinical trials and post-marketing 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	• 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. • SmPC Section 4.3 special warning and precautions on genotype specific activity, combination with other antiviral agents or retreatment. • PIL Section 3 – How to take Viekirax, advise to patients on appropriate dosing and administration to achieve maximal efficacy. • Prescription only medication. • Use of treatment should be initiated and supervised by specialists. • Pack size.
Important potential risk - Fetal development toxicity (ombitasvir/paritaprevir/ritonavir only; added to the EU RMP per CHMP request)	
Evidence for linking the risk to the medicine	There are no human data regarding this potential risk. Preclinical embryo-fetal development studies have shown fetal malformations in rabbits (ombitasvir; R&D/11/406) and mice (paritaprevir/ritonavir; R&D/09/1178). Clinical trial data for pregnancy outcome.
Risk factors and risk groups	Female patients of childbearing potential who get exposed to a DAA regimen when they become pregnant or are pregnant.

Risk minimization measures	• SmPC – Section 4.4, includes information for women of childbearing potential. • SmPC – Section 4.6, includes information on contraception methods in women of childbearing potential and on potential harm to the fetus. • SmPC – Section 5.3, includes preclinical information on maternal toxicity in animal studies. • PIL Section 2, information on pregnancy and use of effective contraception methods for women of childbearing potential. • Viekirax should not be used during pregnancy and the use of highly effective contraceptive methods is recommended in women of childbearing potential in SmPC Section 4.6. • Prescription only medication. • Use of treatment should be initiated and supervised by specialists. • Pack size.

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.