Part VI: Summary of the risk management plan

Summary of risk management plan for PreHevbri Suspension for Injection (Hepatitis B Vaccine (recombinant, adsorbed))

This is a summary of the risk management plan (RMP) for PreHevbri. The RMP details important risks of PreHevbri, how these risks can be minimised, and how more information will be obtained about PreHevbri's risks and uncertainties (missing information).

PreHevbri's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how PreHevbri should be used.

This summary of the RMP for PreHevbri should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European public assessment report (EPAR).

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

I. The medicine and what it is used for

PreHevbri is authorised for the active immunisation against all known subtypes of the hepatitis B virus in adults. The use of PreHevbri should be in accordance with official recommendations. It can be expected that hepatitis D will also be prevented by immunisation with PreHevbri as hepatitis D (caused by hepatitis D virus) does not occur in the absence of hepatitis B infection. (see SmPC for the full indication). It contains hepatitis B surface antigen (S, pre-S1 and pre-S2) as the active substance and it is given by intramuscular injection.

Further information about the evaluation of PreHevbri's benefits can be found in PreHevbri's EPAR, including in its plain-language summary, available on the European Medicines Agency website, under the medicine's webpage

https://www.ema.europa.eu/en/medicines/human/EPAR/prehevbri

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of PreHevbri, together with measures to minimise such risks and the proposed studies for learning more about PreHevbri's risks, are outlined below.

Measures to minimise 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 authorised 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 minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report 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 PreHevbri is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of PreHevbri are risks that need special risk management activities to further investigate or minimise 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 PreHevbri. 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	None
Important potential risks	None
Missing information	Use in patients simultaneously being administered other vaccines Use in immunocompromised patients including patients with HIV infection Use in patients with autoimmune disease Use in pregnancy or breastfeeding

II.B Summary of important risks

Missing information: Use in patients simultaneously being administered other vaccines	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.5 where advice is given that the concomitant use of PreHevbri with other vaccines is not recommended.* *SmPC section 6.2 where advice is given that due to the absence of compatibility studies, PreHevbri should not be mixed with other medicinal products.* *PL section 2 where advice is given to inform the doctor, pharmacist or nurse if you have recently received or might receive any other vaccine.* Legal status: Prescription only medicine. Additional risk minimisation measures: No additional risk minimisation measures are proposed.

Missing information: Use in immunocompromised patients including patients with HIV infection	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.4 where warning is given that immunocompromised persons may have a diminished immune response to PreHevbri. Attention should be given to ensure that a protective antibody level is maintained as defined by national recommendations and guidelines.* *SmPC section 4.4 where advice is given to not to preclude patients with HIV infection from vaccination against hepatitis B and physician should consider PreHevbri vaccination on a case by case basis, as hepatitis B infection can be serious in these patients.* *PL section 2 where warning is given that if patient have a weakened immune system, doctor may need to do a blood test to check if the vaccination has worked well enough to protect you against hepatitis.* Legal status: Prescription only medicine. Additional risk minimisation measures: No additional risk minimisation measures are proposed.

Missing information: Use in patients with autoimmune disease	
Risk minimisation measures	Routine risk minimisation measures: *PL section 2 where advice is given to inform the doctor, pharmacist or nurse if you are taking, have recently taken, or might take any other medicines.* Legal status: Prescription only medicine. Additional risk minimisation measures: No additional risk minimisation measures are proposed.

Missing information: Use in pregnancy or breastfeeding	
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.6 where advice is given that vaccination during pregnancy should only be performed if the risk-benefit ratio at individual level outweighs possible risks for the foetus.* *SmPC section 4.6 where advice is given that a decision must be made whether to discontinue breast-feeding or to abstain from PreHevbri vaccination while taking into account the benefit of breast-feeding for the child and the benefit of vaccination for the woman, as the risk to the breastfed newborn/infant cannot be excluded.* *PL section 2 where advice is given to inform the doctor, pharmacist or nurse, if patient is pregnant or think she may be pregnant, before being given PreHevbri.* *PL section 2 where advice is given to discuss with the doctor or nurse whether the risks and benefits of breast-feeding patient's child outweigh the benefit of vaccination and whether patient should stop breast-feeding as risk to the suckling child cannot be excluded.* Legal status: Prescription only medicine. Additional risk minimisation measures: No additional risk minimisation measures are proposed.
Additional pharmacovigilance activities	*PreHevbri Pregnancy Outcomes Registry* See section II.C of this summary for an overview of the post-authorisation development plan.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of PreHevbri.

II.C.2 Other studies in post-authorisation development plan

PreHevbri Pregnancy Outcomes Registry: An observational, Non-interventional (Treatment Registry) surveillance program designed to monitor and evaluate all submitted reports of PreHevbri vaccine exposure during pregnancy, as well as maternal, obstetrical, and neonatal outcomes in pregnant women who were exposed to PreHevbri during pregnancy.

Purpose of the study:

Rationale:

This Pregnancy Outcomes Registry will be initiated to record pregnancy outcomes in females exposed to PreHevbri within 28 days prior to conception or at any time during pregnancy.

Study objectives:

The objective of the Pregnancy Outcomes Registry is to monitor and evaluate all submitted reports of PreHevbri vaccine exposure during pregnancy, as well as maternal, obstetrical, and neonatal outcomes.