PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

1. SUMMARY OF RISK MANAGEMENT PLAN FOR HEPSERA (ADEFOVIR DIPIVOXIL)

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

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

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

1.1. The Medicine and What is it Used for

Hepsera is authorized for treatment of chronic hepatitis B in adults with:

- Compensated liver disease with evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active liver inflammation and fibrosis. Initiation of Hepsera treatment should only be considered when the use of an alternative antiviral agent with a higher genetic barrier to resistance is not available or appropriate.

- Decompensated liver disease in combination with a second agent without cross-resistance to Hepsera.

Hepsera contains adefovir dipivoxil as the active substance and it is given orally.

Further information about the evaluation of Hepsera's benefits can be found in Hepsera's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000485/human_med_000817.jsp&mid=WC0b01ac058001d124

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

Important risks of Hepsera, together with measures to minimize such risks and the proposed studies for learning more about Hepsera'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 periodic safety update report (PSUR) assessments 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 Hepsera is not yet available, it is listed under 'missing information' below.

1.2.1. List of important risks and missing information

Important risks of Hepsera are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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 Hepsera. 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 1-1. List of Important Risks and Missing Information

Important Risks	None
Missing Information	Safety in pregnancy and lactation

1.2.2. Summary of Important Risks

Hepsera has been assigned the legal status of a medicine subject to medical prescription in the

European Union (EU), whereby Hepsera therapy should be initiated by a doctor experienced in the treatment of chronic hepatitis B (as described in section 4.2 of the SmPC).

Table 1-2. Summary of Important Risk(s) and Missing Information

Missing Information	Safety in Pregnancy and Lactation
Risk Minimization Measure(s)	Routine risk minimization measures: SmPC sections 4.6 and 5.3 PL section 2
Additional Pharmacovigilance activities	Additional pharmacovigilance activities: Antiretroviral Pregnancy Registry See Section 1.2.3 of this summary for an overview of the post-authorization development plan.

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 specific obligation of Hepsera.

1.2.3.2. Other Studies in Post-Authorization Development Plan

Table 1-3. Other Studies in Post-Authorization Development Plan

Short Study Name	Purpose of the Study
Antiretroviral Pregnancy Registry	*Objectives:* To collect information on the risk of birth defects in patients exposed to ADV during pregnancy *Safety concern(s) addressed:* Missing information: Safety in pregnancy and lactation