# PART I: SUMMARY OF THE RISK MANAGEMENT PLAN

## SUMMARY OF RISK MANAGEMENT PLAN FOR VEMLIDY (TENOFOVIR ALAFENAMIDE)

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

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

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

### I. The Medicine and What is it Used for

Vemlidy is authorized for treating chronic hepatitis B (CHB), an infectious disease that affects the liver, in patients aged 12 years and older weighing at least 35 kg. It contains tenofovir alafenamide (TAF) as the active substance and it is given orally.

Further information about the evaluation of Vemlidy's benefits can be found in Vemlidy'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/vemlidy

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

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

## II.A. List of important risks and missing information

Important risks are those 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 Vemlidy. 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** | None |
| **Important Potential Risks** | None |
| **Missing Information** | Long-term safety information in adults and children 6 years of age and older weighing at least 25 kg |
| | Development of resistance in long-term use |
| | Safety in pregnancy and lactation |

## II.B. Summary of Important Risks

Vemlidy has been assigned the legal status of a medicine subject to medical prescription in the European Union (EU), whereby Vemlidy therapy should be initiated by a doctor experienced in the management of chronic hepatitis B (as described in section 4.2 of the SmPC).

**Table Part VI.2. Summary of Important Risk(s) and Missing Information**

| Missing information | Long-term safety information in adults and children 6 years of age and older weighing at least 25 kg |
|---|---|
| Risk Minimization Measure(s) | No risk minimization measures |
| Additional Pharmacovigilance activities | Additional pharmacovigilance activities:<br>Clinical studies in adults with CHB (studies GS-US-320-0108, GS-US-320-0110)<br>Clinical study in children and adolescents with CHB (study GS-US-320-1092)<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Missing information** | **Development of resistance in long-term use** |
| Risk Minimization Measure(s) | No risk minimization measures |
| Additional Pharmacovigilance activities | Additional pharmacovigilance activities:<br>Clinical studies in adults with CHB (GS-US-320-0108, GS-US-320-0110)<br>See Section II.C of this summary for an overview of the post-authorization development plan. |
| **Missing information** | **Safety in pregnancy and lactation** |
| Risk Minimization Measure(s) | Routine risk communication:<br>SmPC sections 4.6 and 5.3<br>PL section 2 |
| Additional Pharmacovigilance activities | Additional pharmacovigilance activities:<br>Antiretroviral Pregnancy Registry<br>See Section II.C of this summary for an overview of the post-authorization development plan. |

## 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 specific obligation of Vemlidy.

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

**Table Part VI.3. Other Studies in Post-Authorization Development Plan**

| Short Study Name | Purpose of the Study |
|---|---|
| **GS-US-320-0108**<br>Phase 3, randomized, double-blind study to evaluate the safety and efficacy of TAF versus tenofovir disoproxil fumarate (TDF) in hepatitis B e antigen (HBeAg)-negative participants with CHB | *Objectives:*<br>To evaluate the safety and efficacy of TAF vs TDF in HBeAg-negative adult participants with CHB<br>*Safety concern(s) addressed:*<br>Missing information: Long-term safety information in adults; Development of drug resistance in long-term use |
| **GS-US-320-0110**<br>Phase 3, randomized, double-blind study to evaluate the safety and efficacy of TAF versus TDF in HBeAg-positive participants with CHB | *Objectives:*<br>To evaluate the safety and efficacy of TAF vs TDF in HBeAg-positive adult participants with CHB<br>*Safety concern(s) addressed:*<br>Missing information: Long-term safety information in adults; Development of drug resistance in long-term use |
| **GS-US-320-1092**<br>A randomized, double-blind evaluation of the pharmacokinetics (PK), safety, and antiviral efficacy of TAF in children and adolescent participants with CHB | *Objectives:*<br>To evaluate the safety and efficacy of TAF in adolescents with CHB and to evaluate the PK, safety and efficacy of TAF in children with CHB<br>*Safety concern(s) addressed:*<br>Missing information: Long-term safety information in children 6 years of age and older weighing at least 25 kg |
| **Antiretroviral Pregnancy Registry** | *Objectives:*<br>To collect information on the risk of birth defects in patients exposed to TAF during pregnancy<br>*Safety concern(s) addressed:*<br>Missing information: Safety in pregnancy and lactation |