EU Risk Management Plan for Tenofovir disoproxil

No 62/25

RMP version to be assessed as part of this application:

RMP Version number:	V 5.1	
Data lock point for this RMP:	16 February 2026	
Date of final sign off:	23 February 2026	
Rationale for submitting an updated RMP:	Update based on reference product VIREAD (RMP V27.0, DLP: 8 May 2025, final sign off: 28 October 2025). Merging of procedures EMEA/H/C/004120; PL/H/0639/001/DC and IS/H/0252/001/DC into one joint risk management plan.	
Summary of significant changes in this RMP:	Part I: Product(s) Overview	Details for procedures PL/H/0639/001/DC and IS/H/0252/001/DC were added.
	Part II: Module SVIII Summary of the Safety Concerns	Important Identified risks: *Renal Toxicity; Bone events due to proximal renal tubulopathy / loss of bone mineral density* and Missing Information: *Safety in pregnancy and lactation; Safety in patients with renal impairment* were removed.
	Part III: Pharmacovigilance Plan	All Specific adverse reaction follow-up questionnaires were removed.
	Part VI: Summary of the RMP	Summary of risk management plan for procedures PL/H/0639/001/DC and IS/H/0252/001/DC was added.
	Part VII: Annexes	**Annex 4 –** All Specific adverse reaction follow-up questionnaires were removed.
Other RMP versions under evaluation:	RMP version number:	Not applicable.
	Submitted on:	Not applicable.
	Procedure number:	Not applicable.
Details of the currently approved RMP:	RMP version number:	V5.0 V5.0 V8.0
	Approved with procedure:	EMEA/H/C/004120 PL/H/0639/001/DC IS/H/0252/001/DC
	Date of approval (opinion date):	15 September 2022 19 April 2024 25 November 2022
QPPV name:	Miloslava NYKODEMOVA, MD	

ZENTIVA

QPPV (or delegate) signature:	The content of this RMP has been reviewed and approved by the marketing authorisation holder's QPPV. The electronic signature is available on file.

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List of Abbreviations

ALT	Alanine aminotransferase
APR	Antiretroviral Pregnancy Registry
ATC	Anatomical Therapeutic Chemical classification
CPT	Child-Pugh-Turcotte
DNA	Deoxyribonucleic acid
EEA	European Economic Area
EMA	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
eCTD	Electronic Common Technical Document
GVP	Good pharmacovigilance practices
HBe	Hepatitis B envelope
HBeAg	Hepatitis B envelope antigen
HBV	Hepatitis B virus
Hbs	Hepatitis B surface
HCP	Healthcare professionals
HIV	Human immunodeficiency virus
INN	International Non-proprietary Name
MAH	Marketing Authorisation Holder
NRTI	Nucleotide reverse transcriptase inhibitor
PBMCs	Peripheral blood mononuclear cells
PL	Package leaflets
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
QPPV	Qualified Person for Pharmacovigilance
SmPC	Summary of Product Characteristics

Part I: Product(s) Overview

Table Part I.1 – Product Overview

Active substance(s) (INN or common name)	Tenofovir disoproxil
Pharmacotherapeutic group(s) (ATC Code)	Antiviral for systemic use; nucleoside and nucleotide reverse transcriptase inhibitors ATC code: J05AF07
Marketing Authorisation Holder	Zentiva, k.s.
Medicinal products to which this RMP refers	3
Invented name(s) in the European Economic Area (EEA)	Tenofovir disoproxil Zentiva 245 mg film-coated tablets Tenofovir Zentiva, 245 mg, tabletki powlekane Virofob 245 mg filmuhúðaðar töflur
Marketing authorisation procedure	Centralised EMEA/H/C/004120/0000 Decentralised PL/H/0639/001/DC IS/H/0252/001/DC
Brief description of the product	<u>Chemical class</u>: Tenofovir disoproxil is absorbed and converted to the active substance tenofovir, which is a nucleoside monophosphate (nucleotide) analogue.
	<u>Summary of mode of action:</u> Tenofovir is converted to the active metabolite, tenofovir diphosphate, an obligate chain terminator, by constitutively expressed cellular enzymes. Tenofovir diphosphate has an intracellular half-life of 10 hours in activated and 50 hours in resting peripheral blood mononuclear cells (PBMCs). Tenofovir diphosphate inhibits HIV 1 reverse transcriptase and the HBV polymerase by direct binding competition with the natural deoxyribonucleotide substrate and, after incorporation into DNA, by DNA chain termination. Tenofovir diphosphate is a weak inhibitor of cellular polymerases α, β, and γ.
	<u>Important information about its composition:</u> None.
Hyperlink to the Product Information	Please refer to section 1.3.1 in eCTD.
Indication(s) in the EEA	<u>Current</u>:

	HIV 1 infection "Product name" is indicated in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected adults. "Product name" is also indicated for the treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents, aged 12 to < 18 years. The choice of "Product name" to treat antiretroviral experienced patients with HIV-1 infection should be based on individual viral resistance testing and/or treatment history of patients. **Hepatitis B infection** "Product name" is indicated for the 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 inflammation and/or fibrosis. - evidence of lamivudine-resistant hepatitis B virus. - decompensated liver disease. "Product name" is indicated for the treatment of chronic hepatitis B in adolescents 12 to < 18 years of age with: - compensated liver disease and evidence of immune active disease, i.e. active viral replication, persistently elevated serum ALT levels and histological evidence of active inflammation and/or fibrosis. *For details please refer to section 1.3.1 in eCTD*
	Proposed: Not applicable.
Dosage in the EEA	Current: Therapy should be initiated by a physician experienced in the management of HIV infection and/or treatment of chronic hepatitis B. Posology *HIV-1 and chronic hepatitis B* *Adults and adolescents aged 12 to < 18 years and weighing ≥ 35 kg* The recommended dose of "Product name" for the treatment of HIV or for the treatment of chronic hepatitis B is 245 mg (one tablet) once daily taken orally with food. The decision to treat paediatric patients (adolescents) should be

	based on careful consideration of individual patient needs and with reference to current paediatric treatment guidelines including the value of baseline histological information. The benefits of long-term virologic suppression with continued therapy must be weighed against the risk of prolonged treatment, including the emergence of resistant hepatitis B virus and the uncertainties as regards the long term impact of bone and renal toxicity. Serum ALT should be persistently elevated for at least 6 months prior to treatment of paediatric patients with compensated liver disease due to HBeAg positive chronic hepatitis B; and for at least 12 months in patients with HBeAg negative disease. <u>Duration of therapy in adult and adolescent patients with chronic hepatitis B</u> The optimal duration of treatment is unknown. Treatment discontinuation may be considered as follows: - In HBeAg positive patients without cirrhosis, treatment should be administered for at least 12 months after HBe seroconversion (HBeAg loss and HBV DNA loss with anti-HBe detection on two consecutive serum samples at least 3-6 months apart) is confirmed or until HBs seroconversion or there is loss of efficacy. Serum ALT and HBV DNA levels should be followed regularly after treatment discontinuation to detect any late virological relapse. - In HBeAg negative patients without cirrhosis, treatment should be administered at least until HBs seroconversion or there is evidence of loss of efficacy. Treatment discontinuation may also be considered after stable virological suppression is achieved (i.e. for at least 3 years) provided serum ALT and HBV DNA levels are followed regularly after treatment discontinuation to detect any late virological relapse. With prolonged treatment for more than 2 years, regular reassessment is recommended to confirm that continuing the selected therapy remains appropriate for the patient. In adult patients with decompensated liver disease or cirrhosis, treatment cessation is not recommended. *For more details on Posology please refer to section 1.3.1 in eCTD.*
	<u>Proposed</u>: Not applicable.
Pharmaceutical form(s) and strengths	<u>Current</u>: EMEA/H/C/004120/0000 Each film coated tablet contains **tenofovir disoproxil phosphate** (equivalent to 245 mg of tenofovir disoproxil).

	PL/H/0639/001/DC Each film coated tablet contains **tenofovir disoproxil fumarate** (equivalent to 245 mg of tenofovir disoproxil). IS/H/0252/001/DC Each film coated tablet contains **tenofovir disoproxil succinate** (equivalent to 245 mg of tenofovir disoproxil).
	Proposed: Not applicable.
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety Specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

Not applicable for generic medicinal products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SII - Non-clinical part of the safety specification

Not applicable for generic medicinal products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SIII - Clinical trial exposure

Not applicable for generic medicinal products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SIV - Populations not studied in clinical trials

Not applicable for generic medicinal products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SV - Post-authorisation experience

Not applicable for generic medicinal products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SVI - Additional EU requirements for the safety specification

Potential for misuse for illegal purposes

Not applicable for generic medicinal products as per Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2) effective since 31 March 2017.

Part II: Module SVII - Identified and potential risks

SVII.1 Identification of safety concerns in the initial RMP submission

Not applicable.

SVII.2 New safety concerns and reclassification with a submission of an updated RMP

The list of safety concerns was harmonised with the reference product VIREAD.
Link: https://www.ema.europa.eu/en/medicines/human/EPAR/viread (last update: 18/11/2025)

SVII.3 Details of important identified risks, important potential risks, and missing information

Not applicable.

Part II: Module SVIII - Summary of the safety concerns

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities (such as adverse reactions reporting and signal detection) are considered sufficient for the product.

Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:

Specific adverse reaction follow-up questionnaires:

Not applicable.

Other forms of routine pharmacovigilance activities:

Not applicable.

III.2 Additional pharmacovigilance activities

Not applicable.

III.3 Summary Table of Additional Pharmacovigilance Activities

Not applicable.

Part IV: Plans for Post-authorisation Efficacy Studies

Not applicable.

Part V: Risk Minimisation Measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

The safety information in the approved product information is aligned to the reference medicinal product.

V.1. Routine Risk Minimisation Measures

Not applicable.

V.2. Additional Risk Minimisation Measures

Not applicable.

V.3. Summary of Risk Minimisation Measures

Not applicable.

Part VI: Summary of the Risk Management Plan

Summary of risk management plan for Tenofovir disoproxil Zentiva (tenofovir disoproxil)

This is a summary of the risk management plan (RMP) for Tenofovir disoproxil Zentiva 245 mg film-coated tablets. The RMP details important risks of Tenofovir disoproxil Zentiva 245 mg film-coated tablets and how more information will be obtained about Tenofovir disoproxil Zentiva 245 mg film-coated tablets risks and uncertainties (missing information).
Tenofovir disoproxil Zentiva 245 mg film-coated tablets summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tenofovir disoproxil Zentiva 245 mg film-coated tablets should be used.

This summary of the RMP for Tenofovir disoproxil Zentiva 245 mg film-coated tablets 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 Tenofovir disoproxil Zentiva 245 mg film-coated tablets RMP.

I. The medicine and what it is used for

Tenofovir disoproxil Zentiva 245 mg film-coated tablets is authorised for HIV 1 infection and hepatitis B infection in adults and adolescents aged 12 to < 18 years (see SmPC for the full indication). It contains tenofovir disoproxil as the active substance and it is given orally.

Further information about the evaluation of Tenofovir disoproxil Zentiva 245 mg film-coated tablets benefits can be found in Tenofovir disoproxil Zentiva 245 mg film-coated tablets 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/tenofovir-disoproxil-zentiva.

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

Important risks of Tenofovir disoproxil Zentiva 245 mg film-coated tablets, together with measures to minimise such risks and the proposed studies for learning more about Tenofovir disoproxil Zentiva 245 mg film-coated tablets 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 so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

II.A List of important risks and missing information

Important risks of Tenofovir disoproxil Zentiva 245 mg film-coated tablets 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 Tenofovir disoproxil Zentiva 245 mg film-coated tablets. 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	None

II.B Summary of important risks

The safety information in the approved Product Information is aligned to the reference medicinal product.

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 Tenofovir disoproxil Zentiva 245 mg film-coated tablets.

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

There are no studies required for Tenofovir disoproxil Zentiva 245 mg film-coated tablets.

Part VI: Summary of the Risk Management Plan

Summary of risk management plan for Tenofovir Zentiva; Virofob (tenofovir disoproxil)

This is a summary of the risk management plan (RMP) for Tenofovir Zentiva; Virofob. The RMP details important risks of Tenofovir Zentiva; Virofob and how more information will be obtained about Tenofovir Zentiva; Virofob risks and uncertainties (missing information).
Tenofovir Zentiva; Virofob summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tenofovir Zentiva; Virofob should be used.

Important new concerns or changes to the current ones will be included in updates of Tenofovir Zentiva; Virofob RMP.

I. The medicine and what it is used for

Tenofovir Zentiva; Virofob is authorised for HIV 1 infection and hepatitis B infection in adults and adolescents aged 12 to < 18 years (see SmPC for the full indication). It contains tenofovir disoproxil as the active substance and it is given orally.

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

Important risks of Tenofovir Zentiva; Virofob, together with measures to minimise such risks and the proposed studies for learning more about Tenofovir Zentiva; Virofob 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 so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

II.A List of important risks and missing information

Important risks of Tenofovir Zentiva; Virofob 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 Tenofovir Zentiva; Virofob. 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	None

II.B Summary of important risks

The safety information in the approved Product Information is aligned to the reference medicinal product.

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 Tenofovir Zentiva; Virofob.

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

There are no studies required for Tenofovir Zentiva; Virofob.

Annex 4 - Specific adverse drug reaction follow-up forms

Not applicable.

Annex 6 - Details of proposed additional risk minimisation activities (if applicable)

Not applicable.