EU Risk Management Plan for emtricitabine/tenofovir disoproxil

No 53/26

RMP version to be assessed as part of this application:

RMP Version number:	V 7.0	
Data lock point for this RMP:	19 June 2026	
Date of final sign off:	26 June 2026	
Rationale for submitting an updated RMP:	Update based on reference medicinal product Truvada (RMP V20.0, DLP: 8 May 2025, final sign off: 28 October 2025).	
Summary of significant changes in this RMP:	Part II: Module SVIII Summary of the Safety Concerns	Missing Information *Safety in pregnancy and lactation (TD)* was removed.
	Part III: Pharmacovigilance Plan	Specific Adverse Reaction Follow-up Questionnaires were updated to be in line with the reference product. Only questionnaire for *Lack of efficacy in pre-exposure prophylaxis* is in place.
	Part VI: Summary of the RMP	This section was updated based on the above mentioned changes.
	Part VII: Annexes	**Annex 4:** Specific Adverse Reaction Follow-up Questionnaire for *Lack of efficacy in pre-exposure prophylaxis* was added. Follow-up form for renal toxicity, Follow-up form for renal tubulopathy, Follow-up form for bone events, Pregnancy report form (to report pregnancy before outcome is known) and Pregnancy outcome report (to be used when pregnancy outcome is known) were removed. **Annex 8:** This section was updated based on the above mentioned changes.
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:	V6.0
	Approved with procedure:	EMEA/H/C/004137/WS2486/0025
	Date of approval (opinion date):	9 November 2023
QPPV name:	Miloslava NYKODEMOVA, MD	
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.	

ZENTIVA

Table of contents

ZENTIVA

List of Abbreviations

ATC	Anatomical Therapeutic Chemical classification
ADR	Adverse Drug Reaction
DNA	Deoxyribonucleic acid
EMA	European Medicines Agency
EU	European Union
EEA	European Economic Area
eCTD	Electronic Common Technical Document
ETZ	Emtricitabine/Tenofovir disoproxil Zentiva
HIV (HIV-1)	Human immunodeficiency virus (type 1)
INN	International Non-proprietary Name
MAA	Marketing Authorisation Applicant
MAH	Marketing Authorisation Holder
NRTI	Nucleoside reverse transcriptase inhibitor
PL	Package Leaflet
PrEP	Pre-exposure prophylaxis
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
QPPV	Qualified Person for Pharmacovigilance
SmPC	Summary of Product Characteristics
TD	Tenofovir disoproxil

Part I: Product(s) Overview

Table Part I.1 – Product Overview

Active substance(s) (INN or common name)	emtricitabine/tenofovir disoproxil
Pharmacotherapeutic group(s) (ATC Code)	Antivirals for systemic use, antivirals for treatment of HIV infections, combinations (ATC code: J05AR03)
Marketing Authorisation Holder/Applicant	For EMEA/H/C/004137: Zentiva, k.s. (for PT/H/1616/001 MAH in RMS: ZENTIVA PORTUGAL, LDA) (for HU/H/1003/001MAH in RMS: Zentiva, k.s.)
Medicinal products to which this RMP refers	3
Invented name(s) in the European Economic Area (EEA)	Emtricitabine/Tenofovir disoproxil Zentiva 200 mg/245 mg film-coated tablets (related to the procedure EMEA/H/C/004137) Emtricitabina + Tenofovir Zentiva 200 mg + 245 mg comprimidos revestidos por película (related to the procedure PT/H/1616/001) Dunotrisin 200 mg/245 mg filmtabletta (related to the procedure HU/H/1003/001)
Marketing authorisation procedure	Centralised EMEA/H/C/004137 Decentralised PT/H/1616/001 HU/H/1003/001 (previously IS/H/0250/001)
Brief description of the product	<u>Chemical class:</u> Emtricitabine is a nucleoside analogue of cytidine. Tenofovir disoproxil is converted in vivo to tenofovir, a nucleoside monophosphate (nucleotide) analogue of adenosine monophosphate. Both emtricitabine and tenofovir have activity that is specific to human immunodeficiency virus (HIV-1 and HIV-2) and hepatitis B virus.
	<u>Summary of mode of action:</u> Emtricitabine and tenofovir disoproxil are phosphorylated by cellular enzymes to form emtricitabine triphosphate and tenofovir diphosphate, respectively. In vitro studies have shown that both emtricitabine and tenofovir can be fully phosphorylated when combined together in cells. Emtricitabine triphosphate and tenofovir diphosphate competitively inhibit HIV-1 reverse transcriptase, resulting in DNA chain termination. Both emtricitabine triphosphate and tenofovir diphosphate are weak inhibitors of mammalian DNA polymerases and there was no evidence of toxicity to mitochondria in vitro and in vivo.
	<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>: *Treatment of HIV-1 infection*

	"Product name" is indicated in antiretroviral combination therapy 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. *Pre-exposure prophylaxis (PrEP):* "Product name" is indicated in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents at high risk.
	Proposed: Not applicable.
Dosage in the EEA	Current: "Product name" should be initiated by a physician experienced in the management of HIV infection. Posology *Treatment of HIV in adults and adolescents aged 12 years and older, weighing at least 35 kg* One tablet, once daily. *Prevention of HIV in adults and adolescents aged 12 years and older, weighing at least 35 kg* One tablet, once daily. Separate preparations of emtricitabine and tenofovir disoproxil are available for treatment of HIV-1 infection if it becomes necessary to discontinue or modify the dose of one of the components of "product name". If a dose of "product name" is missed within 12 hours of the time it is usually taken, "product name" should be taken as soon as possible and the normal dosing schedule should be resumed. If a dose of "product name" is missed by more than 12 hours and it is almost time for the next dose, the missed dose should not be taken and the usual dosing schedule should be resumed. If vomiting occurs within 1 hour of taking "product name", another tablet should be taken. If vomiting occurs more than 1 hour after taking "product name" a second dose should not be taken. For further details please refer to section 1.3.1 in eCTD.
	Proposed: Not applicable.
Pharmaceutical form(s) and strengths	Current: Film-coated tablets containing 200 mg of emtricitabine and 245 mg of tenofovir disoproxil.
	Proposed (if applicable): 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 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 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 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 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 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 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 Truvada.
Link: Truvada, INN-emtricitabine / tenofovir disoproxil (europa.eu) (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	• HIV-1 acquisition, including infection resulting from non-adherence (PrEP indication) (ETZ) • Development of resistance in patients with unrecognized or acute HIV-1 infection (PrEP indication) (ETZ)
Important potential risks	• None
Missing information	• None

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

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:

Specific adverse reaction follow-up questionnaire for "Lack of efficacy in pre-exposure prophylaxis "

The questionnaire is designed to collect information on causes of seroconversion and HIV-1 resistance mutations in patients who seroconvert when using emtricitabine/tenofovir disoproxil for PrEP.

The form is provided in Annex 4 of the RMP.

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

V.1. Routine Risk Minimisation Measures

Table Part V.1: Description of routine risk minimisation measures by safety concern

Safety concern	Routine risk minimisation activities
HIV-1 acquisition, including infection resulting from non-adherence (PrEP indication)	Routine risk communication: SmPC sections 4.4 PL sections 2 and 3 Routine risk minimization activities recommending specific clinical measures to address the risk: SmPC Section 4.4: Warning that HIV-1 uninfected individuals should be counselled at frequent intervals to strictly adhere to the recommended Emtricitabine/Tenofovir disoproxil daily dosing schedule. Other routine risk minimisation measures beyond the Product Information: Prescription only medicine.
Development of resistance in patients with unrecognized or acute HIV-1 infection (PrEP indication)	Routine risk communication: SmPC sections 4.3 and 4.4 PL section 2 Routine risk minimization activities recommending specific clinical measures to address the risk: SmPC Section 4.4: Warning that individuals should be re-confirmed to be HIV-negative at frequent intervals (e.g., at least every 3 months) using a combined antigen/antibody test while taking Emtricitabine/Tenofovir disoproxil for PrEP. Other routine risk minimisation measures beyond the Product Information: Prescription only medicine.

V.2. Additional Risk Minimisation Measures

PrEP educational materials

Educational materials for physicians and individuals at risk on the risk of HIV-1 acquisition, including infection resulting from non-adherence and the risk of development of resistance in individuals at risk with unrecognized or acute HIV-1 infection (PrEP indication) *Educational materials to be circulated to physicians who may be involved in treating adult and adolescent patients with the product in order to inform them on the risk of HIV-1 acquisition and the risk of development of resistance in individuals at risk with unrecognised or acute HIV-1 infection. Educational materials also to be handled to individuals at risk.*

Objectives:
Physicians and individuals at risk to understand the risk of acquisition of HIV-1 or development of resistance while the administration of the product.

Rationale for the additional risk minimisation activity:
The MAH of the reference medicinal product is conducting a risk minimization activity in a form of Educational Programme for physicians and individuals at risk. Similar activity to be conducted for Emtricitabine/ Tenofovir disoproxil.

Target audience and planned distribution path:
The educational materials to be delivered to prescribers. The patient part of materials is supposed to be handled over to individuals at risk. The process should be very similar to the one used for the reference medicinal product. The national specialities will be adapted at national level with the national competent authorities as well as implementation plan.

Plans to evaluate the effectiveness of the interventions and criteria for success:
The MAH will evaluate the effectiveness of risk minimisation measures on ongoing basis within continuous risk-benefit evaluation. The implementation of Educational materials according to the plan in all countries where the products are marketed will be tracked.

The key messages of additional risk minimisation measures are provided in the RMP Annex 6.
Removal of additional risk minimisation activities
Rationale for the removal: Removal of HIV paediatric renal educational brochure for the risk of renal toxicity, in line with the reference medicinal product update (Truvada, EMEA/H/C/WS2320).

V.3. Summary of Risk Minimisation Measures

Table Part V.3: Summary table of pharmacovigilance activities and risk minimisation activities by safety concern

Safety concern	Risk minimisation measures	Pharmacovigilance activities
HIV-1 acquisition, including infection resulting from non-adherence (PrEP indication)	Routine risk minimisation measures: SmPC section 4.4 PL section 2 and 3 Prescription only medicine. Routine risk minimization activities recommending specific clinical measures to address the risk: SmPC Section 4.4: Warning that HIV-1 uninfected individuals should be counselled at frequent intervals to strictly adhere to the recommended Emtricitabine/Tenofovir disoproxil daily dosing schedule. Additional risk minimisation measures: Education program for prescribers to help them educate individuals at high risk of acquiring HIV-1 infection.	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Targeted follow-up questionnaire for lack of efficacy, seroconversion and/or resistance mutation(s). Additional pharmacovigilance activities: None

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Development of resistance in patients with unrecognized or acute HIV-1 infection (PrEP indication)	Routine risk minimisation measures: SmPC section 4.3 and 4.4 PL section 2 Prescription only medicine. Routine risk minimization activities recommending specific clinical measures to address the risk: SmPC Section 4.4: Warning that individuals should be re-confirmed to be HIV-negative at frequent intervals (e.g., at least every 3 months) using a combined antigen/antibody test while taking Emtricitabine/Tenofovir disoproxil for PrEP. Additional risk minimisation measures: Education program for prescribers to help them educate individuals at high risk of acquiring HIV-1 infection.	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Targeted follow-up questionnaire for lack of efficacy, seroconversion and/or resistance mutation(s). Additional pharmacovigilance activities: None

Part VI: Summary of the Risk Management Plan

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

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

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

This summary of the RMP for Emtricitabine/Tenofovir disoproxil Zentiva 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 Emtricitabine/Tenofovir disoproxil Zentiva's RMP.

I. The medicine and what it is used for

Emtricitabine/Tenofovir disoproxil Zentiva is authorised for antiretroviral combination therapy for the treatment of HIV-1 infected adults and adolescents. It is also authorised for pre-exposure prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents at high risk (see SmPC for the full indication). It contains emtricitabine and tenofovir as the active substances and it is given by oral route.

Further information about the evaluation of Emtricitabine/Tenofovir disoproxil Zentiva's benefits can be found in Emtricitabine/Tenofovir disoproxil Zentiva'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/emtricitabine-tenofovir-disoproxil-zentiva.

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

Important risks of Emtricitabine/Tenofovir disoproxil Zentiva, together with measures to minimise such risks and the proposed studies for learning more about Emtricitabine/Tenofovir disoproxil Zentiva'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 the case of Emtricitabine/Tenofovir disoproxil Zentiva, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

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 Emtricitabine/Tenofovir disoproxil Zentiva 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 Emtricitabine/Tenofovir disoproxil Zentiva. 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).

Summary of safety concerns	
Important identified risks	• HIV-1 acquisition, including infection resulting from non-adherence (PrEP indication) (ETZ) • Development of resistance in patients with unrecognized or acute HIV-1 infection (PrEP indication) (ETZ)
Important potential risks	• None
Missing information	• None

II.B Summary of important risks

Summary of important risks that have corresponding additional risk minimisation activities are:

HIV-1 acquisition, including infection resulting from non-adherence (PrEP indication)	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 PL section 2 and 3 Prescription only medicine. Routine risk minimization activities recommending specific clinical measures to address the risk: SmPC Section 4.4: Warning that HIV-1 uninfected individuals should be counselled at frequent intervals to strictly adhere to the recommended Emtricitabine/Tenofovir disoproxil Zentiva daily dosing schedule. Additional risk minimisation measures: Education program for prescribers to help them educate individuals at high risk of acquiring HIV-1 infection.
Development of resistance in patients with unrecognized or acute HIV-1 infection (PrEP indication)	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3 and 4.4 PL section 2

	Prescription only medicine. <u>Routine risk minimization activities recommending specific clinical measures to address the risk:</u> SmPC Section 4.4: Warning that individuals should be re-confirmed to be HIV-negative at frequent intervals (e.g., at least every 3 months) using a combined antigen/antibody test while taking Emtricitabine/Tenofovir disoproxil Zentiva for PrEP. <u>Additional risk minimisation measures:</u> Education program for prescribers to help them educate individuals at high risk of acquiring HIV-1 infection.

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 Emtricitabine/Tenofovir disoproxil Zentiva.

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

There are no studies required for Emtricitabine/Tenofovir disoproxil Zentiva.

Part VI: Summary of the Risk Management Plan

Summary of risk management plan for Emtricitabina + Tenofovir Zentiva and Dunotrisin (emtricitabine/tenofovir disoproxil)

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

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

Important new concerns or changes to the current ones will be included in updates of Emtricitabina + Tenofovir Zentiva and Dunotrisin's RMP.

I. The medicine and what it is used for

Emtricitabina + Tenofovir Zentiva and Dunotrisin are authorised for antiretroviral combination therapy for the treatment of HIV-1 infected adults and adolescents. It is also authorised for pre-exposure prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 infection in adults and adolescents at high risk (see SmPC for the full indication). It contains emtricitabine and tenofovir as the active substances and it is given by oral route.

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

Important risks of Emtricitabina + Tenofovir Zentiva and Dunotrisin, together with measures to minimise such risks and the proposed studies for learning more about Emtricitabina + Tenofovir Zentiva and Dunotrisin'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 the case of Emtricitabina + Tenofovir Zentiva and Dunotrisin, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

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 Emtricitabina + Tenofovir Zentiva and Dunotrisin 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 Emtricitabina + Tenofovir Zentiva and Dunotrisin. 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).

Summary of safety concerns	
Important identified risks	• HIV-1 acquisition, including infection resulting from non-adherence (PrEP indication) (ETZ) • Development of resistance in patients with unrecognized or acute HIV-1 infection (PrEP indication) (ETZ)
Important potential risks	• None
Missing information	• None

II.B Summary of important risks

Summary of important risks that have corresponding additional risk minimisation activities are:

HIV-1 acquisition, including infection resulting from non-adherence (PrEP indication)	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 PL section 2 and 3 Prescription only medicine. Routine risk minimization activities recommending specific clinical measures to address the risk: SmPC Section 4.4: Warning that HIV-1 uninfected individuals should be counselled at frequent intervals to strictly adhere to the recommended Emtricitabina + Tenofovir Zentiva or Dunotrisin daily dosing schedule. Additional risk minimisation measures: Education program for prescribers to help them educate individuals at high risk of acquiring HIV-1 infection.
Development of resistance in patients with unrecognized or acute HIV-1 infection (PrEP indication)	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3 and 4.4 PL section 2 Prescription only medicine. Routine risk minimization activities recommending specific clinical measures to address the risk: SmPC Section 4.4: Warning that individuals should be re-confirmed to be HIV-negative at frequent intervals (e.g., at least every 3 months) using a combined antigen/antibody test while taking Emtricitabina + Tenofovir Zentiva or Dunotrisin for PrEP.

	<u>Additional risk minimisation measures:</u> Education program for prescribers to help them educate individuals at high risk of acquiring HIV-1 infection.

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 Emtricitabina + Tenofovir Zentiva or Dunotrisin.

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

There are no studies required for Emtricitabina + Tenofovir Zentiva or Dunotrisin.

Annex 4 - Specific adverse drug reaction follow-up forms

Follow-up forms

Lack of efficacy in pre-exposure prophylaxis questionnaire

EMTRICITABINE+TENOFOVIR

Specific adverse reaction/event Follow-up Form

Lack of Efficacy, Seroconversion and/or Resistance Mutation(s) Targeted Questionnaire

Global database ID:

Country of occurrence:

Patient information

Date of the follow up (DD/MM/YYYY):
Patient initials (first, last):
Gender: Male ☐ Female ☐
Age:

1/ Please provide the start date of Zentiva Emtricitabine + Tenofovir (PrEP) (DAY/MONTH/YEAR):
2/ Please provide Zentiva Emtricitabine + Tenofovir (PrEP) lot number, if available: ☐ N/A Are any of the Zentiva Emtricitabine + Tenofovir (PrEP) tablets available for analysis? ☐ YES (if yes, we may contact you) ☐ NO 3/ Was the individual tested for HIV prior to starting Zentiva Emtricitabine + Tenofovir (PrEP)? ☐ NO ☐ YES DATE (DAY/MONTH/YEAR) / / Type of HIV test used:

ZENTIVA

Result:

Antigen	Antibody
☐ Positive	☐ Positive
☐ Negative	☐ Negative
☐ Result not available	☐ Result not available

4/ Was the individual´s HBV status confirmed before starting Zentiva Emtricitabine + Tenofovir (PrEP)?

☐ YES Result:

☐ NO

5/ What was the individual´ sex at birth?

☐ Male

☐ Female

6/ What is the individual´s gender identity?

☐ Male

☐ Female

7/ What is the individual´s sexual behavior pattern?

☐ Man who has sex with men

☐ Transgender woman who has sex with men

☐ Man who has sex with women

☐ Woman who has sex with men

☐ Woman who has sex with women

☐ Other, please specify: _____

8/ What was the reason for prescribing PrEP (check all that apply)?

☐ Inconsistent or no condom use

☐ Unsafe intravenous drug use

☐ Partner is infected with HIV

☐ Exchange of sex for commodities (such as money, food or shelter)

☐ Partner/ multiple partners known to be from a high prevalence area or social network

☐ Sex under the use of recreational drugs (chemsex)

☐ Other (Please specify):

9/ Was the individual prescribed Zentiva Emtricitabine + Tenofovir (PrEP) once-daily?

☐ Yes

☐ No

If not, what was the reason?

10/ Was the individual counselled about safe sex practises?

☐ Yes
☐ No

11/ Was the individual practicing safe sex before the reported HIV seroconversion, including using condoms consistently and correctly?

☐ Yes
☐ No

12/ How frequently was the individual´s HIV status tested?

☐ Every month
☐ Every 3 months
☐ Less frequently than every 3 months
☐ Other, please specify:

Please provide the HIV test results in the table below:

13/ Please complete the following table and/or attach printouts if unable to fit on chart:

Date (Day/Month/Year):	HIV status test result	Genotype/Phenotype testing result
Prior to initiating Zentiva Emtricitabine + Tenofovir (PrEP)		
While taking Zentiva Emtricitabine + Tenofovir (PrEP, prior to reported HIV seroconversion)		
At time of reported HIV seroconversion and subsequently		

14/ For patients with resistance mutation(s), was the mutation(s):

☐ Acquired during Zentiva Emtricitabine + Tenofovir (PrEP)
Please specify clinical reasoning:

☐ Transmitted
Please specify clinical reasoning:

☐ Unknown

15/ Was the individual tested for other sexually transmitted infections (e.g. gonorrhoea, chlamydia, HPV)?

☐ No

☐ Yes

Which STIs was the individual tested for? Please specify:

How frequently was the individual tested?

☐ Every month

☐ Every 3 month

☐ Less frequently than every 3 months

☐ Other, please specify:

16/ Was the individual adherent to Zentiva Emtricitabine + Tenofovir (PrEP) as prescribed?

☐ Yes

☐ No

If no, please estimate the individual´s degree of non-adherence with treatment:

The individual missed on average……. doses per week and missed an average of…….doses per month.

What was the reason the individual missed doses/didn´t adhere to the prescribing dosing schedule?

☐ The individual wasn´t willing to take Zentiva Emtricitabine + Tenofovir (PrEP) daily.

What was the reason?

☐ The individual decided to stop taking Zentiva Emtricitabine + Tenofovir (PrEP).

When (Day/Month/Year)?

What was the reason?

☐ The individual forgot to take Zentiva Emtricitabine + Tenofovir (PrEP)

☐ The individual was experiencing side effects to Zentiva Emtricitabine + Tenofovir (PrEP). What was the side effect?

☐ The individual didn´t get a refill on time

☐ The individual lost the medication

☐ The individual didn´t want others to know he/she was taking Zentiva Emtricitabine + Tenofovir (PrEP)

☐ The individual experienced/ was aware of negative reactions or opinions with regards to Zentiva Emtricitabine + Tenofovir (PrEP) use (e.g. verbal abuse/ comments)

☐ Other, please specify:

17/ Was Zentiva Emtricitabine + Tenofovir (PrEP) stopped after HIV seroconversion was confirmed?

☐ Yes ☐ Please provide stop date (Day/Month/Year):

☐ No ☐ Please list any other anti-retroviral therapies that were initiated after seroconversion:

_____

18/ Please specify the individual´s concomitant medications (including any herbal therapy):

(☐ None ☐ Unknown)

Thank you for taking time to provide this information.
Your patient's welfare is important to us.

ZENTIVA

Annex 6 - Details of proposed additional risk minimisation activities

Approved key messages of the additional risk minimisation measures

The Marketing Authorisation Holder (MAH) shall ensure that all physicians who are expected to prescribe/use Emtricitabine/Tenofovir disoproxil in adults and adolescents for PrEP are provided with a physician educational pack containing the Summary of Product Characteristics and an appropriate educational brochure, as detailed below:

- PrEP educational brochure for prescribers entitled 'Important Safety Information for Prescribers About Emtricitabine/Tenofovir disoproxil for a Pre-exposure Prophylaxis (PrEP) Indication'
- PrEP Checklist for prescribers
- PrEP educational brochure for the individual at risk entitled 'Important Information About Emtricitabine/Tenofovir disoproxil to Reduce the Risk of getting Human Immunodeficiency Virus (HIV) Infection'
- PrEP reminder card

PrEP educational brochure for prescribers:

- Reminder of the key safety information regarding the use of Emtricitabine/Tenofovir disoproxil for PrEP in adults and adolescents
- Reminder of factors to help identify individuals at high risk of acquiring HIV-1
- Reminder on the risk of development of HIV-1 drug resistance in undiagnosed HIV-1–Infected individuals
- Provides safety information on adherence, HIV testing, renal, bone and HBV status

PrEP Checklist for prescribers:

- Reminders for evaluations/counselling at the initial visit and follow-up

PrEP educational brochure for the individual at risk (to be provided by healthcare provider [HCP]):

- Reminders on what the individual should know before and while taking Emtricitabine/Tenofovir disoproxil to reduce the risk of getting HIV infection
- Reminder on the importance of strict adherence to the recommended dosing regimen
- Provides information on how to take Emtricitabine/Tenofovir disoproxil
- Provides information on the possible side effects
- Provides information on how to store Emtricitabine/Tenofovir disoproxil

PrEP reminder card for the individual at risk (to be provided by HCP):

- Reminders to adhere to the dosing schedule.
- Reminder to attend scheduled clinic visits.