RISK MANAGEMENT PLAN
For
Ritonavir
Version 5.0

RMP Version to be Assessed as Part of this Application:

RMP Version Number	5.0
Data Lock Point for this RMP	01-Dec-2025
Date of Final Sign Off	13-Jan-2026
Rationale for Submitting an Updated RMP	RMP updated in line with the updated SmPC/PI and BL RMP (Norvir RMP Version: 8.2, dated: Nov 2025)
Summary of Significant Changes in this RMP	The following significant changes were made in the current RMP: • Updated Part I: Product(s) Overview section to align with the Summary of Product Characteristics (Section 4.2 Posology and method of administration) inline with Brand Lead updates and RMP (Norvir RMP Version: 8.2, dated: Nov 2025). • MAH details and Invented name was updated

Other RMP Versions Under Evaluation:

RMP Version Number	Not applicable
Submitted On	Not applicable
Procedure Number	Not applicable

Details of the Current RMP:

Version Number	4.0
Approved with Procedure	EMEA/H/C/0004549
Date of Approval (Opinion Date)	22-Aug-2022

QPPV Oversight Declaration: The content of this RMP has been reviewed and approved by the marketing authorisation applicant´s QPPV. The electronic signature is available on file.

Table of Contents

LIST OF TABLES

LIST OF ABBREVIATIONS

Abbreviation	Definition
ADR	Adverse Drug Reaction
ATC	Anatomical Therapeutic Chemical Classification System
CHMP	Committee for Medicinal Products for Human Use
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures – Human
DCP	Decentralised Procedure
DDD	Daily Defined Dose
DHPC	Direct Healthcare Professional Communication
EEA	European Economic Area
EPAR	European Public Assessment Report
EU	European Union
EURD	European Union Reference Date
HCP	Healthcare Professional
ICSR	Individual Case Safety Report
MAA	Marketing Authorization Applicant
MAH	Marketing Authorization Holder
MRP	Mutual Recognition Procedure
PAC	Patient Alert Card
PL	Package Leaflet
PPP	Pregnancy Prevention Programme
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PTC	Patient Treatment Course
PTD	Patient Treatment Days
PTM	Patient Treatment Months
PTY	Patient Treatment Years
PVA	Pharmacovigilance Agreement
QPPV	Qualified Person for Pharmacovigilance
MedDRA	Medical Dictionary for Regulatory Activities
DLP	Data Lock Point
SmPC	Summary of Product Characteristics
WHO	World Health Organization

PART I: PRODUCT(S) OVERVIEW

Table 1: Part 1.1-Product Overview

Active Substance(s) (INN or Common Name)	Ritonavir
Pharmacotherapeutic Group(s) (ATC Code)	Antivirals for systemic use, protease inhibitors (J05AE03)
Marketing Authorisation Holder	Viatris Limited
Medicinal Products to Which this RMP Refers	01
Invented Name(s) in the European Economic Area (EEA)	Ritonavir Viatris 100 mg film-coated tablets
Marketing Authorisation Procedure	Centralized (EMEA/H/C/0004549)
Brief Description of the Product	Chemical class: Protease inhibitor (PI) Ritonavir is a peptidomimetic inhibitor of human immunodeficiency virus (HIV), type 1 (HIV-1) and type 2 (HIV-2) proteases and has been approved for use in numerous countries globally. Summary of mode of action: Ritonavir is an orally active peptidomimetic inhibitor of the HIV 1 and HIV 2 aspartyl proteases. Inhibition of HIV protease renders the enzyme incapable of processing the gag-pol polyprotein precursor which leads to the production of HIV particles with immature morphology that are unable to initiate new rounds of infection. Ritonavir has selective affinity for the HIV protease and has little inhibitory activity against human aspartyl proteases. Important information about its composition: Not applicable
Hyperlink to the Product Information:	PI available in section 1.3.1 of the dossier
Indication(s) in the EEA	Current: Ritonavir is indicated as a pharmacokinetic enhancer of co-administered protease inhibitors as part of antiretroviral combination therapy in human immunodeficiency virus-1 (HIV-1) infected patients (adults and children of 2 years of age and older) Proposed: Not applicable

Dosage in the EEA	Current: Ritonavir Viatris should be prescribed by physicians who are experienced in the treatment of HIV infection. <u>Posology</u> When ritonavir is used as a pharmacokinetic enhancer with other protease inhibitors the Summary of Product Characteristics (SmPC) for the particular protease inhibitor must be consulted. The following HIV-1 protease inhibitors have been approved for use with ritonavir as a pharmacokinetic enhancer at the noted doses. *Adults* Atazanavir 300 mg once daily with ritonavir 100 mg once daily. Fosamprenavir 700 mg twice daily with ritonavir 100 mg twice daily. Lopinavir co-formulated with ritonavir (lopinavir/ritonavir) 400 mg/100 mg or 800 mg/200 mg. Tipranavir 500 mg twice daily with ritonavir 200 mg twice daily. Tipranavir with ritonavir should not be used in treatment-naïve patients. Darunavir 600 mg twice daily with ritonavir 100 mg twice daily in antiretroviral treatment (ART) experienced patients. Darunavir 800 mg once daily with ritonavir 100 mg once daily may be used in some ART experienced patients. Refer to the darunavir SmPC for further information on once daily dosing in ART experienced patients. Darunavir 800 mg once daily with ritonavir 100 mg once daily in ART-naïve patients. *Children and adolescents* Ritonavir is recommended for children 2 years of age and older. For further dosage recommendations, refer to the SmPC of other protease inhibitors approved for co-administration with ritonavir. Kindly refer SmPC section 4.2 for additional information on posology.

	Method of administration: Ritonavir Viatris film-coated tablets are administered orally and should be ingested with food. Proposed: Not applicable
Pharmaceutical Form(s) and Strengths	Current: 100 mg film-coated tablets. Proposed: Not applicable
Is the Product 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.

Part II: Module SII - Non-clinical Part of the Safety Specification

Not applicable.

Part II: Module SIII - Clinical Trial Exposure

Not applicable.

Part II: Module SIV - Populations Not Studied in Clinical Trials

Not applicable.

Part II: Module SV - Post-authorisation Experience

Not applicable.

Part II: Module SVI - Additional EU Requirements for the Safety Specification

Not applicable.

Potential for Misuse for Illegal Purposes

The product is restricted by prescription only. This is not a substance abuse drug and there is no potential for misuse of ritonavir for illegal purposes.

Part II: Module SVII - Identified and Potential Risks

SVII.1 Identification of Safety Concerns in the Initial RMP Submission

Viatris has an approved RMP (version 3.0, approved on 14-Sep-2017) for ritonavir generic medicine for centralized procedure number EMEA/H/C/0004549.

Summary of Safety Concerns	
Important Identified Risks	• PR prolongation • Immune reconstitution & inflammatory syndrome (IRIS) Manifesting as Autoimmune Disorders (such as Grave's Disease)
Important Potential Risks	• Drug-Drug Interaction (DDI) with HCV Products
Missing Information	• Limited experience with 100mg tablets in HIV-1-infected patients, including children • Geriatric population

SVII.1.1. Risks Not Considered Important for Inclusion in the List of Safety Concerns in the RMP

Not applicable.

SVII.1.2. Risks Considered Important for Inclusion in the List of Safety Concerns in the RMP

Not applicable.

SVII.2 New Safety Concerns and Reclassification with a Submission of an Updated RMP

The RMP has been updated in line with the Norvir RMP Version: 7.3, dated: September 2021 and GVP Module V – Risk management systems (Rev 2), as recommended in the Rapporteurs preliminary joint assessment report/Request for supplementary information for Ritonavir Mylan (ritonavir) EMEA/H/C/004549/R/0015, by MAH Mylan Pharmaceuticals Limited, dated 19-Apr-2022. All safety concerns have been removed from the Summary of safety concerns, with only routine pharmacovigilance activities and routine risk minimization measures in place.

SVII.3 Details of Important Identified Risks, Important Potential Risks, and Missing Information

SVII.3.1. Presentation of Important Identified Risks and Important Potential Risks

Not applicable as this RMP for ritonavir follows the same safety concerns as the safety concerns of the reference substance RMP.

SVII.3.2. Presentation of the Missing Information

Not applicable as this RMP for ritonavir follows the same safety concerns as the safety concerns of the reference substance RMP.

Part II: Module SVIII - Summary of the Safety Concerns

Table 2: SVIII- 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)

The Pharmacovigilance System Master File contains details of the system and processes that the MAH has in place to identify and characterize the risks recognised in the safety specification.

III.1 Routine Pharmacovigilance Activities

Routine pharmacovigilance activities only.

III.2 Additional Pharmacovigilance Activities

As current routine pharmacovigilance activities are sufficient, no additional pharmacovigilance activities are recommended.

III.3 Summary Table of Additional Pharmacovigilance Activities

None.

PART IV: PLANS FOR POST-AUTHORISATION EFFICACY STUDIES

Not applicable.

PART V: RISK MINIMISATION MEASURES (INCLUDING EVALUATION OF THE EFFECTIVENESS OF RISK MINIMISATION ACTIVITIES)

The safety information in the proposed product information is aligned to the reference medicinal product (Norvir, AbbVie Deutschland GmbH & Co. KG).

Risk Minimisation Plan

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 Ritonavir Viatris (ritonavir)

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

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

This summary of the RMP for Ritonavir Viatris should be read in the context of all the 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 Ritonavir Viatris's RMP.

I. The Medicine and What it is Used For

Ritonavir Viatris is authorised as a pharmacokinetic enhancer of co-administered protease inhibitors as part of antiretroviral a combination therapy in human immunodeficiency virus-1 (HIV-1) infected patients (adults and children of 2 years of age and older).

It contains ritonavir as the active substance and it is given by oral route.

Further information about the evaluation of Ritonavir Viatris's benefits can be found in Ritonavir Viatris's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Ritonavir Viatris, together with measures to minimise such 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 public (e.g. with or without prescription) can help to minimises its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse events 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 Ritonavir Viatris are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken by patients. 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 Ritonavir Viatris. 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/use in special patient populations etc.);

Table 3:Part VI.1- Summary of safety concerns

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 proposed 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 Ritonavir Viatris.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Ritonavir Viatris.

PART VII: ANNEXES

Annex 4 - Specific Adverse Drug Reaction Follow-up Forms

Not applicable.

Annex 6 - Details of Proposed Additional Risk Minimisation Activities (If Applicable)

Not applicable.