RISK MANAGEMENT PLAN
For
Prasugrel
Version 4.2

RMP Version to be Assessed as Part of this Application:

RMP Version Number	4.2
Data Lock Point for this RMP	31-Dec-2024
Date of Final Sign Off	19-May-2025
Rationale for Submitting an Updated RMP	RMP update in line with the BL RMP for Efient (prasugrel) v13.0 date of final sign off 22-Jan-2024. (version 4.0) RMP update in line with assessment report (EMA/VR/0000256926) received on 14-Apr-2025.(version 4.1) RMP update in line with assessment report (EMA/VR/0000256926) received on 19-May-2025 (version 4.2)
Summary of Significant Changes in this RMP	• Submitting the updates in new template (EMA/164014/2018 Rev.2.0.1 accompanying GVP Module V Rev.2). • RMP update in line with the BL RMP for Efient (prasugrel) v13.0 date of final sign off 22-Jan-2024 (removal of all safety concerns except for colorectal cancer and removal of additional Risk Minimisation measures (aRMM)) (version 4.0) • Changes in Part V and Annex 4 (TFU forms updated in line with BL) (version 4.1) • Rationale for submitting the RMP was updated and minor changes in TFU (Annex 4) (version 4.2).

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	3.0
Approved with Procedure	EMEA/H/C/004644
Date of Approval (Opinion Date)	16-May-2018

QPPV name: Dr Eiko Soehlke, MD MPH, EEA QPPV

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

Table of Contents

LIST OF TABLES

LIST OF ABBREVIATIONS

Abbreviation	Definition
ADR	Adverse drug reaction
ACS	Acute Coronary Syndrome
ASA	Acetylsalicylic Acid
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
CHF	Congestive Heart Failure
CV	Cardio-Vascular
EEA	European Economic Area
EU	European Union
EURD	European Union Reference Date
ICSR	Individual Case Safety Report
MAH	Marketing Authorization Holder
NSAIDs	Non-Steroidal Anti-Inflammatory Drug
PCI	Percutaneous Coronary Intervention
PL	Package Leaflet
POM	Prescription Only Medicine
PSUR	Periodic Safety Update Report
QPPV	Qualified Person for Pharmacovigilance
RMP	Risk Management Plan
SPC	Summary of Product Characteristics
STEMI	ST Segment Elevation Myocardial Infarction
TIA	Transient Ischaemic Attack
UA/NSTEMI	Unstable Angina, Non-ST Segment Elevation Myocardial Infarction
WHO	World Health Organization

PART I: PRODUCT(S) OVERVIEW

Table 1: Part 1.1-Product Overview

Active Substance(s) (INN or Common Name)	Prasugrel
Pharmacotherapeutic Group(s) (ATC Code)	Antithrombotic agents, Platelet aggregation inhibitors excluding heparin (ATC Code) – B01AC22
Marketing Authorisation Holder	Viatris Limited (IE)
Medicinal Products to Which this RMP Refers	02
Invented Name(s) in the European Economic Area (EEA)	Prasugrel Viatris 5 mg film-coated tablets; Prasugrel Viatris 10 mg film-coated tablets
Marketing Authorisation Procedure	Centralized procedure (EMEA/H/C/0004644)
Brief Description of the Product	Prasugrel belongs to pharmacotherapeutic group of Platelet aggregation inhibitors excluding heparin (ATC code: B01AC22). Prasugrel is an inhibitor of platelet activation and aggregation through the irreversible binding of its active metabolite to the P2Y12 class of ADP receptors on platelets. Each 5 mg tablet contains 5 mg prasugrel (as besilate). Each 10 mg tablet contains 10 mg prasugrel (as besilate).
Hyperlink to the Product Information:	PI available in section 1.3.1 of the dossier
Indication(s) in the EEA	Prasugrel Viatris, co-administered with acetylsalicylic acid (ASA), is indicated for the prevention of atherothrombotic events in adult patients with acute coronary syndrome (i.e. unstable angina, non-ST segment elevation myocardial infarction [UA/NSTEMI] or ST segment elevation myocardial infarction [STEMI]) undergoing primary or delayed percutaneous coronary intervention (PCI).
Dosage in the EEA	Prasugrel Viatris therapy should be initiated with a single 60 mg loading dose and then continued at 10 mg once a day (maintenance dose). A reduced maintenance dose of 5 mg should be prescribed for patients ≥ 75 years or patient weighing < 60 kg.
Pharmaceutical Form(s) and Strengths	Tablets; 5 mg and 10 mg

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.

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

SIV.1 Exclusion Criteria in Pivotal Clinical Studies Within the Development Programme

Not applicable.

SIV.2 Limitations to Detect Adverse Reactions in Clinical Trial Development Programmes

Not applicable.

SIV.3 Limitations in Respect to Populations Typically Under-represented in Clinical Trial Development Programmes

Not applicable.

Part II: Module SV - Post-authorisation Experience

Not applicable.

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

Not applicable.

Part II: Module SVII - Identified and Potential Risks

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

Viatris has RMP v3.0 approved on 16-May-2028 for prasugrel generic medicine procedure EMEA/H/C/0004644 with the following safety concerns:

Table 2: SVII- Summary of safety concerns

Summary of Safety Concerns	
Important Identified Risks	• Bleeding risks, including: ◦ Intracranial haemorrhage

Summary of Safety Concerns	
	° Gastrointestinal haemorrhage ° Intraocular haemorrhage ° Epistaxis ° PCI-related haemorrhage ° CABG-related haemorrhage ° Associated with Prasugrel use prior to coronary angiography in NSTEMI patients ° Other procedure-related haemorrhage • Hypersensitivity including angioedema • Thrombocytopenia and Thrombotic thrombocytopenic purpura
Important Potential Risks	• Drug-induced hepatic injury • Potential off-label use in patients with prior Transient Ischaemic Attack (TIA)/ stroke • Colorectal cancer
Missing Information	• Concomitant use with fibrinolytics, other tienopyridines, warfarin and chronic use of NSAIDs • Use in paediatric population • Use in pregnant/lactating women • Use in patients with compromised CV status (cardiogenic shock, class IV CHF, refractory ventricular arrhythmia) • Use in subjects with severe hepatic impairment • Use in subjects without clinical manifestation of ACS

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

In line with the approved EU RMP for Efient (prasugrel) v13.0 date of final sign off 22-Jan-2024 and GVP Module V Rev.2, safety concerns Bleeding risks (including intracranial haemorrhage, gastrointestinal haemorrhage, intraocular haemorrhage, epistaxis, PCI-related haemorrhage, CABG-related haemorrhage, associated with prasugrel use prior to coronary angiography in NSTEMI patients, other procedure-related haemorrhage), Hypersensitivity including angioedema and Thrombocytopenia and Thrombotic thrombocytopenic purpura classified as Important identified risks, Drug-induced hepatic injury and Potential off-label use in patients with prior Transient Ischaemic Attack (TIA)/ stroke classified as Important Potential risks and Concomitant use with fibrinolytics, other tienopyridines, warfarin and chronic use of NSAIDs, Use in paediatric population, Use in pregnant/lactating women, Use in patients with compromised CV status (cardiogenic shock, class IV CHF, refractory ventricular arrhythmia), Use in subjects with severe hepatic impairment and Use in subjects without clinical manifestation of ACS classified as Missing information have been removed from the list of safety concerns.

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 Prasugrel follows the same safety concerns as the safety concerns of the reference substance RMP/RMP published on CMDh/NCA website.

SVII.3.2. Presentation of the Missing Information

Not applicable as this RMP for Prasugrel follows the same safety concerns as the safety concerns of the reference substance RMP/RMP published on CMDh/NCA website.

Part II: Module SVIII - Summary of the Safety Concerns

Table 3: SVIII- Summary of safety concerns

Important Identified Risks	• None
Important Potential Risks	• Colorectal cancer
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 and routine pharmacovigilance activities beyond ADRs reporting and signal detection:

Specific adverse reaction follow-up questionnaire for the risk of:

• Colorectal cancer

The form is provided in Annex 4 - Specific Adverse Drug Reaction Follow-up Forms of the RMP.

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))

Risk Minimisation Plan

The safety information in the proposed product information is aligned to the reference medicinal product (Efient, by Substipharm).

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 Prasugrel Viatris 5 mg and 10 mg film-coated tablets (prasugrel)

This is a summary of the risk management plan (RMP) for Prasugrel Viatris5 mg and 10 mg film-coated tablets. The RMP details important risks of Prasugrel Viatris 5 mg and 10 mg film-coated tablets, how these risks can be minimised, and how more information will be obtained about Prasugrel Viatris 5 mg and 10 mg film-coated tablets 's risks and uncertainties (missing information).

Prasugrel Viatris 5 mg and 10 mg film-coated tablets 's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Prasugrel Viatris 5 mg and 10 mg film-coated tablets should be used.

This summary of the RMP for Prasugrel Viatris 5 mg and 10 mg film-coated tablets 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 Prasugrel Viatris 5 mg and 10 mg film-coated tablets 's RMP.

I. The Medicine and What it is Used For

Prasugrel Viatris 5 mg and 10 mg film-coated tablets is authorised for the prevention of atherothrombotic events in adult patients with acute coronary syndrome (i.e. unstable angina, non-ST segment elevation myocardial infarction [UA/NSTEMI] or ST segment elevation myocardial infarction [STEMI]) undergoing primary or delayed percutaneous coronary intervention (PCI). It contains prasugrel as the active substance and it is given via the oral route.

Further information about the evaluation of Prasugrel Viatris 5 mg and 10 mg film-coated tablets ’s benefits can be found in Prasugrel Viatris 5 mg and 10 mg film-coated tablets ’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 Prasugrel Viatris 5 mg and 10 mg film-coated tablets 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 patient (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 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 Prasugrel Viatris 5 mg and 10 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 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 Prasugrel Viatris 5 mg and 10 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/use in special patient populations etc.);

Table 4: Part VI.1- Summary of safety concerns

List of Important Risks and Missing Information	
Important Identified Risks	• None
Important Potential Risks	• Colorectal cancer
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 Prasugrel Viatris 5 mg and 10 mg film-coated tablets.

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

There are no studies required for Prasugrel Viatris 5 mg and 10 mg film-coated tablets.

PART VII: ANNEXES

Annex 4 - Specific Adverse Drug Reaction Follow-up Forms

Follow-up form for the risk of *Colorectal cancer*

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

You have reported an adverse reaction(s) of [Colorectal Cancer] for [Prasugrel]. This questionnaire is being sent to you for obtaining valuable additional information about the reported case to thoroughly evaluate the relation to [Prasugrel] exposure. The Questionnaire is already prefilled with all the available information collected at the time of the initial report, only additional information should be filled in. By providing as detailed information as possible, you can make a useful contribution to the safety of [Prasugrel].

Reporter

Healthcare professional Patient Other, precise:	
INFORMATION ABOUT THE REPORTER HEALTHCARE PROFESSIONAL (if applicable)	
Name:	Street:
Specialty:	Postal code:
Tel.:	City:
E-mail:	Country:

Patients:

Patient's information:
Initials: Date of birth: Age: Gender: Weight:

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

Height:

Patient's historical/ concomitant diseases (add as many lines as necessary):

- History of cancer
- Chemotherapy
- Radiotherapy
- Diabetes mellitus
- Alcohol use
- Tobacco use
- Obesity
- Surgery
- Familial history of cancer

*Please complete below with any other relevant history like an environmental risk which could contribute to the cancer development

Medical history/concurrent condition	Start date (DD/MM/YYYY)	Treatment provided	Outcome	End date (if applicable) (DD/MM/YYYY)

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

Patient's historical/ concomitant treatments (please add lines if necessary):

Treatment (drug name)	Start date (DD/MM/YYYY)	Stop date (DD/MM/YYYY)	Indication
☐			
☐			
☐			
☐			

Suspect Drug

Prasugrel	
Indication	
Start date (DD/MM/YYYY)	
Stop date (DD/MM/YYYY)	
Loading dose (in mg)	
Daily dose (in mg)	
Batch number (s)	

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

Treatment frequency	
Route of administration	
Prasugrel action taken	
Was prasugrel treatment discontinued due to any adverse event? (please describe the event)	
If prasugrel treatment was discontinued due to any adverse event, did the patient recovered from this event?	
If prasugrel treatment was discontinued due to any adverse event, was the treatment restarted later?	
Did the patient experience any adverse event after the treatment was restarted?	

Other suspect drugs:

Co-suspect medication	Start date	Stop date	Indication

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

Colorectal cancer:

Date of the cancer diagnosis (DD/MM/YYYY)	
How was the cancer discovered? (please describe if the patient presented pain, bleeding for example, which led to a cancer investigation).	
Please specify the primary site of the cancer.	
Tumor description? (please add if one tumor, metastasis and locations if applicable)	
For malignant tumor, please provide a copy of pathology report or provide the information of Stage/Grade, Staging classification and tissue source.	
Description of the corrective treatment	

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

Description of surgical treatment (if applicable)	
Did the patient improved/recovered after prasugrel treatment interruption?	
If treatment was restarted, did the cancer reappeared/ progressed?	
Patient's outcome	
Other relevant useful information	

Case description (open text)

Laboratory data

Lab tests		
Name of the test	Performed date	Results and units if applicable

Histopathology (please indicate stage/grade, staging classification and tissue source)		
Ultrasound		
CATScan		
MRI		
Others		

- Please attach copy of pathology report if available

Assessment by the reporter

Relation between adverse reaction and suspected product:
Certain Probable
Possible
Doubtful
Not related

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

Not assessable

Any other alternative etiology?

Source of information

► Date:

► Information completed by (please enter name and title):

► Reporter's signature/initials:

Please be aware that information provided to Viatris relating to you, may be used to comply with applicable laws and regulations. Viatris processes your personal or sensitive data in accordance with applicable data protection laws and the Viatris Privacy Statement, available to you either on https://www.viatris.com/en/viatris-privacy-notice or upon request.

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

Not applicable.