RISK MANAGEMENT PLAN

For

Acetylsalicylic acid/ Clopidogrel

Version 2.1

RMP version to be assessed as part of this application:

RMP version number	2.1
Data lock point for this RMP	21-Jun-2023
Date of final sign off	04-Aug-2023
Rationale for submitting an updated RMP	RMP updated in line with the updated PI (Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI) and Duoplavin (reference medicinal product)`s RMP .
Summary of significant changes in this RMP	RMP updated in line with the updated PI (Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI). Addition of important identified risk "Major bleeding (including ICH)" and a specific adverse reaction follow-up questionnaire inline with Duoplavin (reference medicinal product)`s RMP .

Other RMP versions under evaluation:	
RMP Version number:	2.0
Submitted on:	26-Jun-2023
Procedure number:	EMEA/H/C/004996

Details of the current RMP:	
Version number	1.2
Approved with procedure	EMEA/H/C/004996
Date of approval (opinion date)	09-Jan-2020

Approver	Dr. Dhaval Panchal, Head of Global Safety Surveillance, Risk Management & Clinical Safety *The signatory is authorised by the Global Head PSRM and EEA-QPPV to sign this RMP*
Signature	
E-mail address of contact person	[redacted]

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ADP	Adenosine Diphosphate
ATC	Anatomical Therapeutic Chemical Classification System
ASA	Acetylsalicylic acid
CMDh	Coordination Group for Mutual recognition and Decentralised Procedures – Human
EEA	European Economic Area
EU	European Union
HCP	Healthcare Professional
ICH	Intracranial haemorrhage
MAA	Marketing Authorization Applicant
MAH	Marketing Authorization Holder
PL	Package leaflet
QPPV	Qualified Person for Pharmacovigilance
MedDRA	Medical Dictionary for Regulatory Activities
DLP	Data Lock Point
SPC	Summary of Product Characteristics
WHO	World Health Organization

PART I: PRODUCT(S) OVERVIEW

Table 1 Part I.1 – Product overview.

Active substances (INN or common name)	Acetylsalicylic acid/ Clopidogrel
Pharmacotherapeutic group (ATC Code)	Antithrombotic agents, platelet aggregation inhibitors excl. Heparin, ATC Code: B01AC30.
Marketing Authorisation Applicant	Mylan
Medicinal products to which this RMP refers	01
Invented names in the European Economic Area (EEA)	Clopidogrel/Acetylsalicylic acid Mylan 75 mg/75 mg film-coated tablets Clopidogrel/Acetylsalicylic acid Mylan 75 mg/100 mg film-coated tablets
Marketing Authorisation procedure	EMEA/H/C/004996 Countries: EEA
Brief description of the product:	Acetylsalicylic acid inhibits platelet aggregation by irreversible inhibition of prostaglandin cyclo-oxygenase and thus inhibits the generation of thromboxane A2, an inducer of platelet aggregation and vasoconstriction. This effect lasts for the life of the platelet. Clopidogrel is a prodrug, one of whose metabolites is an inhibitor of platelet aggregation. Clopidogrel must be metabolised by CYP450 enzymes to produce the active metabolite that inhibits platelet aggregation. The active metabolite of clopidogrel selectively inhibits the binding of adenosine diphosphate (ADP) to its platelet P2Y12 receptor and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation. Due to the irreversible binding, platelets exposed are affected for the remainder of their lifespan

	(approximately 7-10 days) and recovery of normal platelet function occurs at a rate consistent with platelet turnover. Platelet aggregation induced by agonists other than ADP is also inhibited by blocking the amplification of platelet activation by released ADP.
Hyperlink to the Product Information:	PI available in module 1.3.1 of the dossier
Indications in the EEA	Current: Clopidogrel/Acetylsalicylic acid Mylan is indicated for the secondary prevention of atherothrombotic events in adult patients already taking both clopidogrel and acetylsalicylic acid (ASA). Clopidogrel/Acetylsalicylic acid Mylan is a fixed-dose combination medicinal product for continuation of therapy in: - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction) including patients undergoing a stent placement following percutaneous coronary intervention - ST segment elevation acute myocardial infarction in medically treated patients eligible for thrombolytic therapy
	Proposed: Clopidogrel/Acetylsalicylic acid Mylan is indicated for the secondary prevention of atherothrombotic events in adult patients already taking both clopidogrel and acetylsalicylic acid (ASA). Clopidogrel/Acetylsalicylic acid Mylan is a fixed-dose combination medicinal product for continuation of therapy in: - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction) including patients undergoing a stent placement following percutaneous coronary intervention (PCI)

	- ST segment elevation acute myocardial infarction (STEMI) in patients undergoing PCI (including patients undergoing a stent placement) or medically treated patients eligible for thrombolytic/fibrinolytic therapy
Dosage in the EEA	Current: Clopidogrel/Acetylsalicylic acid Mylan 75 mg/75 mg film-coated tablets Clopidogrel/Acetylsalicylic acid Mylan 75 mg/75 mg film-coated tablets should be given as a single daily 75 mg/75 mg dose. Clopidogrel/Acetylsalicylic acid Mylan 75 mg/100 mg film-coated tablets Clopidogrel/Acetylsalicylic acid Mylan 75 mg/100 mg film-coated tablets should be given as a single daily 75 mg/100 mg dose Clopidogrel/Acetylsalicylic acid Mylan fixed-dose combination is used following initiation of therapy with clopidogrel and ASA given separately, and replaces the individual clopidogrel and ASA products. - In patients with non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction): The optimal duration of treatment has not been formally established. Clinical trial data support use up to 12 months, and the maximum benefit was seen at 3 months (see section 5.1). If the use of Clopidogrel/Acetylsalicylic acid Mylan is discontinued, patients may benefit with continuation of one antiplatelet medicinal product. - In patients with ST segment elevation acute myocardial infarction: Therapy should be started as early as possible after symptoms start and continued for at least four weeks. The benefit of the combination of clopidogrel with ASA

	beyond four weeks has not been studied in this setting (see section 5.1). If the use of Clopidogrel/Acetylsalicylic acid Mylan is discontinued, patients may benefit with continuation of one antiplatelet medicinal product. If a dose is missed: - Within less than 12 hours after regular scheduled time: patients should take the dose immediately and then take the next dose at the regular scheduled time. - For more than 12 hours: patients should take the next dose at the regular scheduled time and should not double the dose.
	Proposed: Posology *Adults and elderly* Clopidogrel/Acetylsalicylic acid Mylan 75 mg/75 mg film-coated tablets Clopidogrel/Acetylsalicylic acid Mylan should be given as a single daily 75 mg/75 mg dose. Clopidogrel/Acetylsalicylic acid Mylan 75 mg/100 mg film-coated tablets Clopidogrel/Acetylsalicylic acid Mylan should be given as a single daily 75 mg/100 mg dose Clopidogrel/Acetylsalicylic acid Mylan fixed-dose combination is used following initiation of therapy with clopidogrel and ASA given separately and replaces the individual clopidogrel and ASA products. *In patients with non-ST segment elevation acute coronary syndrome* (unstable angina or non-Q-wave myocardial infarction):

	The optimal duration of treatment has not been formally established. Clinical trial data support use up to 12 months, and the maximum benefit was seen at 3 months (see section 5.1). If the use of Clopidogrel/Acetylsalicylic acid Mylan is discontinued, patients may benefit with continuation of one antiplatelet medicinal product. *In patients with ST segment elevation acute myocardial infarction*: - For medically treated patients, Clopidogrel/Acetylsalicylic acid Mylan therapy should be started as early as possible after symptoms start and continued for at least four weeks. The benefit of the combination of clopidogrel with ASA beyond four weeks has not been studied in this setting (see section 5.1). If the use of Clopidogrel/Acetylsalicylic acid Mylan is discontinued, patients may benefit with continuation of one antiplatelet medicinal product. - When PCI is intended, Clopidogrel/Acetylsalicylic acid Mylan treatment should be started as early as possible after symptoms start and continued up to 12 months (see section 5.1). If a dose is missed: - Within less than 12 hours after regular scheduled time: patients should take the dose immediately and then take the next dose at the regular scheduled time. - For more than 12 hours: patients should take the next dose at the regular scheduled time and should not double the dose.
Pharmaceutical form and strengths Current	Clopidogrel/Acetylsalicylic acid Mylan 75 mg/75 mg film-coated tablets

	Yellow, oval shaped, biconvex, film-coated tablets, debossed with "CA2" on one side of the tablet and "M" on the other side. Clopidogrel/Acetylsalicylic acid Mylan 75 mg/100 mg film-coated tablets Pink, oval shaped, biconvex, film-coated tablets, debossed with "CA3" on one side of the tablet and "M "on the other side.
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

Part II: Module SVII - Identified and potential risks

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

This is a MAA for a fixed combination product in which the safety concerns available in the RMP from the public domain have been adopted by the MAH (Algirin 500 mg, procedure number SK/H/0170/001/DC (acetylsalicylic acid) and Plovtt 7mg, procedure number CZ/H/0719/001/DC (clopidogrel), CMDh website).

Table 2 SVII: Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Haemorrhage (including gastrointestinal haemorrhage, increased menstrual bleeding during menorrhagia) • Intracranial haemorrhage • Hypersensitivity reactions

Summary of safety concerns	
	• Liver impairment • Gastric or duodenal ulcer • Drug interactions • Sever skin reaction, including Steven-Johnsons syndrome, toxic epidermal necrolysis • Deterioration of renal function • Use in 3rd trimester of pregnancy • Lactation • Major Bleeding • Thrombotic thrombocytopenic purpura • Acquired haemophilia A • Cross reactivity among thienopyridines • Diminished antiplatelet response of clopidogrel in patients with genetically reduced CYP2C19 function • Reduction in pharmacological activity of clopidogrel in presence of CYP2C19 inhibitors
Important potential risks	• Reye's syndrome • Use in 1st and 2nd trimester of pregnancy
Missing information	• Use during breastfeeding • Use during pregnancy • Use in paediatric population • Use in patients with hepatic impairment • Use in patients with renal impairment • Use in patients during the first 7 days after acute ischaemic stroke

SVII.1.1. Risks not considered important for inclusion in the list of safety concerns in the RMP

The applicant acknowledges the existence of safety concerns for acetylsalicylic acid and clopidogrel, as stated in the list of summaries of safety concerns published on CMDh website (Algirin 500 mg, procedure number SK/H/0170/001/DC and Plovtt 7mg, procedure number CZ/H/0719/001/DC, CMDh website). However, the applicant revisited the list of safety concerns in accordance with the revised terminology of important identified and important potential risks and missing information as presented in revision 2 of the European Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 2), effective since March 2017 (EMA/838713/2011 Rev 2) and it was identified that the following safety concerns:

- Haemorrhage (including gastrointestinal haemorrhage, increased menstrual bleeding during menorrhagia)
- Intracranial haemorrhage
- Hypersensitivity reactions
- Liver impairment
- Gastric or duodenal ulcer
- Drug interactions
- Sever skin reaction, including Steven-Johnsons syndrome, toxic epidermal necrolysis
- Deterioration of renal function
- Use in 3rd trimester of pregnancy
- Lactation
- Major Bleeding
- Thrombotic thrombocytopenic purpura
- Acquired haemophilia A
- Cross reactivity among thienopyridines
- Diminished antiplatelet response of clopidogrel in patients with genetically reduced CYP2C19 function
- Reduction in pharmacological activity of clopidogrel in presence of CYP2C19 inhibitors
- Reye's syndrome

- Use in 1st and 2nd trimester of pregnancy
- Use during breastfeeding
- Use during pregnancy
- Use in paediatric population
- Use in patients with hepatic impairment
- Use in patients with renal impairment
- Use in patients during the first 7 days after acute ischaemic stroke

should not be included to the list of safety concerns for this RMP as they require no further characterisation, are followed up via routine pharmacovigilance (signal detection and adverse reaction reporting), and for which the risk minimisation messages in the product information are adhered by prescribers and they became part of standard clinical practice.

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 MAH has updated the RMP in line with the updated PI (Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI). The MAH also acknowledges the existence of safety concerns for the reference product Duoplavin available on the EMA website (publication date 16-Feb-2023).

The following risk was included as important identified risk in line with the reference product RMP:

- Major bleeding (including ICH)

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 Acetylsalicylic acid/Clopidogrel follows the same safety concerns as the safety concerns of the reference substance RMP.

SVII.3.2. Presentation of the missing information

Not applicable.

Part II: Module SVIII - Summary of the safety concerns

Table 3 SVIII: Summary of safety concerns

Summary of safety concerns	
Important identified risks	Major bleeding (Including ICH)
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/or characterize the risks recognised in the safety specification.

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities beyond ADRs reporting and signal detection:

Specific adverse reaction follow-up questionnaires for Major bleeding (including ICH):

The forms are provided in Annex 4 - Specific adverse event 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)

The safety information in the proposed product information is aligned to the reference medicinal product (DuoPlavin, by Sanofi Winthrop Industrie).

Risk Minimisation Plan

V.1. Routine Risk Minimisation Measures

Not applicable.

V.2. Additional Risk Minimisation Measures

Routine risk minimisation activities are sufficient to manage the safety concerns of the medicinal product.

V.3 Summary of Risk Minimisation Measures

Not applicable.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablets **(**Acetylsalicylic acid/Clopidogrel**).**

This is a summary of the risk management plan (RMP) for Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablets. The RMP details important risks of acetylsalicylic acid/ clopidogrel, how these risks can be minimised, and how more information will be obtained about acetylsalicylic acid/ clopidogrel's risks and uncertainties (missing information).

Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablet'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 Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg 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 Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablets 's RMP.

I. The medicine and what it is used for

Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablets is authorised for the secondary prevention of atherothrombotic events in adult patients already taking both clopidogrel and acetylsalicylic acid. It contains acetylsalicylic acid/ clopidogrel as the active substances and it is given by oral route of administration.

Further information about the evaluation of Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablet's benefits can be found in Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablet'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 Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg 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 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, including 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 Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablets is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg 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 Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg 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: Summary of safety concerns

List of important risks and missing information	
Important identified risks	Major bleeding (including ICH)
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 Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablets.

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

There are no studies required for Clopidogrel/Acetylsalicylic acid Mylan 75mg/75mg film-coated tablets and Clopidogrel/Acetylsalicylic acid Mylan 75mg/100mg film-coated tablets.

Annex 4 - Specific adverse event follow-up forms

- Major bleeding (including ICH)

TARGETED FOLLOW UP FORM

Viatris Case No.:

Reported Events:

Patient's Details:

Date: _____

Information Provided By:

(Enter Name and Title) _____ Signature/Initials: _____

Patient Name or Initials: _____ Patient Birth Date or Age: _____

Gender:	**Race:** O Caucasian O Asian	O **lb**	**Height:** O **in**
F O M O	O Black O Other	**Weight:**_____ O **kg**	_____ O **cm**

[redacted]

Reported Drug: Acetylsalicylic acid/Clopidogrel

Lot/Control Number (if available): **Indication:**

_____ _____

Dose: _____ **Frequency**:_____ **Formulation**:_____

Start Date:_____**Dose when event occurred:** _____**Route**:_____

Drug D/C? O No O Yes **Date D/C:**_____**If Discontinued, did the event resolve?** O Yes O No

Drug Restarted? O No O Yes **Date Restarted**: _____**If restarted, did the event reoccur?** O Yes O No

Cerebral Haemorrhage

Primary Diagnosis for the reported event(s):

Hospitalization for this event? ☐ Yes ☐ No

General Questions:

1. What was the anatomic site of bleeding: _____
2. What was the cause of bleeding: _____
3. Grade of bleeding: _____

Was there a procedure performed? O Yes O No (please specify):

Presenting Signs/Symptoms

☐ Headache ☐ Impaired Consciousness ☐ Visual impairment

☐ Hypertension ☐ Nausea ☐ Dizziness/Vertigo

☐ Altered Mental status ☐ Vomiting ☐ Seizure

☐ Focal Neurologic signs:_____

☐ Other symptoms/signs:_____

Concurrent/Recent Events (CNS)

☐ Head trauma ☐ Ischemic stroke ☐ Gastritis

☐ Renal failures ☐ TIA ☐ Corticosteroids

☐ Hepatic failure ☐ Sepsis ☐ Eclampsia

☐ Neurosurgery(type): ☐ Hypertensive crisis ☐ Meningitis

_____ ☐ Other **Relevant Past Medical History (CNS)**

☐ Ischemic stroke ☐ Intracranial neoplasm ☐ Chronic liver disease

☐ Haemorrhagic stroke ☐ CNS AV malformation ☐ Renal impairment

☐ TIA ☐ Hypertension ☐ Alcoholism

☐ Head Trauma ☐ Cirrhosis ☐ Sepsis

☐ Other ☐ Bleeding disorder ☐ Smoking

Concomitant Meds/Substances (include prescription, OTC and herbal)

☐ NSAID:_____ ☐ Antiplatelet agents:_____

☐ Warfarin ☐ Heparin

☐ Others:_____

Relevant Laboratory Tests

	Normal range for your institution	Baseline value for patient Date:	Abnormal value Date:	Improvement value Date:
Hemoglobin				
Hematocrit				
WBC				
Platelets				
INR/Prothrombin time				
aPTT				
d-Dimer				
Creatinine				
Other:_____				

Imaging Results (Ultrasound, MRI, CT)

[redacted]

Treatment

Was special treatment required? ☐ Yes ☐ No

☐ Blood Transfusion: #units: Date:

☐ Platelet transfusion(s): #units: Date:

☐ FFP/Plasma concentrate transfusion(s): # Date:

☐ Inotropic support:

☐ Surgery/surgical procedure: (please specify)

☐ Other:

Was this event related to a Viatris drug? If yes, please provide name of drug:

	☐ Yes	☐ Likely	☐ Unlikely	☐ No	☐ Unknown
Were any events related to the Viatris Drug? If yes, please name the drug and list event(s) and relatedness:					

Event outcome:

☐ Recovered/resolved

☐ Resolved with sequelae

☐ Unknown

☐ Not recovered/resolved

☐ Fatal

☐ Other

If 'Other', please specify:

_____

General Bleeding

Primary Diagnosis for the reported event(s):

Hospitalization for this event? ○ Yes ○ No

General Questions

1. What was the anatomic site of bleeding:_____
2. What was the cause of bleeding:_____
3. Grade of bleeding:_____

Medical History / Risk Factors:

☐ Haematological Disorder ☐ Liver disease ☐ Esophageal varices
☐ Prior Bleeding Episodes ☐ Alcohol use/abuse ☐ Gastric ulcer
☐ Other_____

Medications at the time of event: please include prescription, OTC and herbal preparations

☐ Heparin ☐ Aspirin
☐ Clopidogrel ☐ NSAIDs
☐ Glycoprotein IIb/IIIa Inhibitor ☐ Oral anticoagulant
☐ Anti-thrombin therapy ☐ Fibrinolytic/ Thrombolytic therapy
☐ Acetaminophen or paracetamol ☐ Other, please specify: _____

Laboratory Tests/Investigations (please fill in the appropriate lab values with units, dates and lab values for your institution where applicable)

Lab Data	Normal Range	Baseline Value	Most Abnormal	Improvement Value
		Date:	Date:	Date:
INR/Prothrombin Time (PT)				
Platelet Count				
APTT				
Serum Creatinine				
Hemoglobin				
Hematocrit				
Other:___				

Relevant Diagnostic Testing

☐ Ultrasound

Other testing performed:

Treatment

☐ Blood Transfusion: #units: Date:

☐ Platelet transfusion(s): #units: Date:

☐ FFP/Plasma concentrate transfusion(s): #units Date:

☐ Inotropic support:

☐ Surgery/surgical procedure: (please specify)

☐ Other:

Was this event related to a Viatris drug? If yes, please provide name of drug:

	☐ Yes	☐ Likely	☐ Unlikely	☐ No	☐ Unknown
Were any events related to the Viatris Drug? If yes, please name the drug and list event(s) and relatedness:					

Event outcome:

☐ Recovered/resolved

☐ Not recovered/resolved

☐ Resolved with sequelae

☐ Fatal

☐ Unknown

☐ Other

If 'Other', please specify:

Procedural Bleeding:

Primary Diagnosis for the reported event(s):

Hospitalization for this event? ○ Yes ○ No

General Questions

1. What was the anatomic site of bleeding:_____
2. What was the cause of bleeding:_____
3. Grade of bleeding:_____

Was there a procedure performed? ○ No ○ Yes (please specify):

Information on Procedure/Surgery

☐ Elective surgery/Procedure ☐ Describe surgery procedure_____

☐ Urgent surgery/Procedure ☐ Estimated blood loss (ml)_____

☐ Describe reason for surgery/procedure:

Medical History:

☐ Prior surgical/procedural bleed ☐ Prior Haemorrhage

☐ Bleeding disorder:_____ ☐ Chronic liver disease

☐ Family history of bleeding ☐ Chronic renal disease

☐ Chemotherapy ☐ Other:_____

Concomitant Meds/Substances (include prescription, OTC and herbal)

☐ NSAIDs:_____ ☐ Antiplatelet agents:_____

☐ Warfarin:_____ ☐ Thrombolytic agents:_____

☐ Aspirin (dose): _____ ☐ Heparin (dose):_____

☐ Antithrombin agents:_____ ☐ Other: _____

Laboratory Tests	Normal range for your institution	Baseline value for patient	Abnormal value	Improvement value
		Date:	Date:	Date:
Hemoglobin				
WBC				
Platelets				
INR/Prothrombin time				
aPTT				
Other:_____				
Other:_____				

Other Relevant Study	Results
Ultrasound	
Renal CT/MRI	
Other:	

Was this event related to a Viatris drug? If yes, please provide name of drug:

	☐ Yes	☐ Likely	☐ Unlikely	☐ No	☐ Unknown
Were any events related to the Viatris Drug? If yes, please name the drug and list event(s) and relatedness:					

Treatment

☐ Intravenous fluids

☐ Platelet transfusion (units):_____

☐ RBC transfusion (units):_____

☐ Fresh frozen pl(units):_____

☐ Other (specify):_____

Event outcome:

☐ Recovered/resolved

☐ Not recovered/resolved

☐ Resolved with sequelae

☐ Fatal

☐ Unknown

☐ Other

If 'Other', please specify:

_____

Reporter's Details:

I certify that this Questionnaire is accurate and truthful to the best of my knowledge and does not contain any false, fictitious, or fraudulent statements.

Name: Sign

Occupation: Date:

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 www.viatris.com/en/privacy-statement or upon request.

Additional Information:

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

Not applicable