Part VI: Summary of the risk management plan

Summary of risk management plan for Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack) (rivaroxaban)

This is a summary of the risk management plan (RMP) for Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack). The RMP details important risks of rivaroxaban, how these risks can be minimised, and how more information will be obtained about rivaroxaban's risks and uncertainties (missing information).

Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack)'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 Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack) 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 Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack)'s RMP.

I. The medicine and what it is used for

Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack) is authorised for:

Rivaroxaban Mylan 2.5 mg film-coated tablets, co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine, is indicated for the prevention of atherothrombotic events in adult patients after an acute coronary syndrome (ACS) with elevated cardiac biomarkers.

Rivaroxaban Mylan 2.5 mg film-coated tablets co-administered with acetylsalicylic acid (ASA), is indicated for the prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk of ischaemic events.

Rivaroxaban Mylan 10 mg film-coated tablets is indicated for: Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Rivaroxaban Mylan 15 mg film-coated tablets and Rivaroxaban Mylan 20 mg film-coated tablets is indicated for: Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Rivaroxaban Mylan 15 mg film-coated tablets and Rivaroxaban Mylan 20 mg film-coated tablets (Treatment initiation pack) is indicated for: Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

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

Further information about the evaluation of Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack)'s benefits can be found in Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack)'s EPAR, including in its plain-language summary, available on the EMA website, under the medicine's :https://www.ema.europa.eu/en/medicines/human/EPAR/rivaroxaban-mylan.

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

Important risks of Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack), together with measures to minimise such risks and the proposed studies for learning more about Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack)'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 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 Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack) is not yet available, it is listed under 'missing information' below.

In the case of Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack), these routine measures are supplemented with additional risk minimisation measures, mentioned under relevant risks below.

II.A List of important risks and missing information

Important risks of Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack) 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 Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack). 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.);

Part VI: Summary of safety concerns

List of important risks and missing information	
Important identified risks	• Haemorrhage
Important potential risks	• Embryo-fetal toxicity
Missing information	• Patients with severe renal impairment (CrCl < 30 mL/min) • Patients receiving concomitant systemic inhibitors of CYP 3A4 or P-gp other than azole antimycotics (e.g. ketoconazole) and HIV-protease inhibitors (e.g. ritonavir) • Remedial pro-coagulant therapy for excessive haemorrhage • Pregnant or breast-feeding women • Patients with atrial fibrillation (AF) and a prosthetic heart valve • Long-term therapy with rivaroxaban in treatment of DVT, PE, SPAF and ACS in real-life setting • Patients with significant liver diseases (severe hepatic impairment/Child Pugh C) • Patients < 18 years

II.B Summary of important risks

Important identified risk: Haemorrhage	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.3, 4.4, 4.8

Important identified risk: Haemorrhage	
	Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** Educational material for prescribers Patient alert cards

Important potential risk: Embryo-fetal toxicity	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.3, 4.6 and 5.3 Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** None

Missing information: Patients with severe renal impairment (CrCl < 30 mL/min)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2, 4.4 and 5.2 Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** None

Missing information: Patients receiving concomitant systemic inhibitors of CYP 3A4 or P-gp other than azole antimycotics (e.g. ketoconazole) and HIV-protease inhibitors (e.g. ritonavir)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.4 and 4.5 Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** None

Missing information: Remedial pro-coagulant therapy for excessive haemorrhage	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.9 Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** None

Missing information: Pregnant or breast-feeding women	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.3, 4.6 and 5.3 Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** None

Missing information: Patients with atrial fibrillation (AF) and a prosthetic heart valve	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.4 Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** None

Missing information: Long-term therapy with rivaroxaban in treatment of DVT, PE, SPAF and ACS in real-life setting	
Risk minimisation measures	**Routine risk minimisation measures:** None Prescription-only medicine Limited pack sizes

Missing information: Long-term therapy with rivaroxaban in treatment of DVT, PE, SPAF and ACS in real-life setting	
	Additional risk minimisation measures: None

Missing information: Patients with significant liver diseases (severe hepatic impairment/Child Pugh C)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2, 4.3 and 5.2 Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** None

Missing information: Patients < 18 years	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.2 Prescription-only medicine Limited pack sizes **Additional risk minimisation measures:** None

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 Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack).

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

There are no studies required for Rivaroxaban Mylan 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets and Rivaroxaban Mylan 15 mg and 20 mg film-coated tablets (treatment initiation pack).