Part VI: Summary of the risk management plan

Summary of risk management plan for Rivaroxaban Orion (rivaroxaban)

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

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

Important new concerns or changes to the current ones will be included in updates of Rivaroxaban Orion's RMP.

I. The medicine and what it is used for

Rivaroxaban Orion is authorized 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

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

Rivaroxaban Orion 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 Orion 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 Orion 15mg and 20mg in children and adolescents below 18 years and with a body weight of 30 kg or more is additionally indicated to treat blood clots and prevent re-occurrence of blood clots in the veins or in the blood vessels of the lungs, following initial treatment of at least 5 days with injectable medicines used to treat blood clots (see SmPCs for the full indications).

It contains rivaroxaban as the active substance and it is given by mouth.

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

Important risks of Rivaroxaban Orion, together with measures to minimise such risks and the proposed studies for learning more about Rivaroxaban Orion'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 Rivaroxaban Orion, 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 Rivaroxaban Orion 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 rivaroxaban. 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);

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 and 4.8. PL sections 2 and 4.

Important identified risk: Haemorrhage	
	Prescription only medicine. Additional risk minimisation measures: Educational pack

Important potential risk: embryo-fetal toxicity	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.3, 4.6 and 5.3. PL section 2. Prescription only medicine. 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 and 4.4. PL sections 2 and 4. Prescription only medicine. 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 sections 4.4 and 4.5. PL section 2. Prescription only medicine. Additional risk minimisation measures: None

Missing information: Remedial pro-coagulant therapy for excessive haemorrhage	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.3 and 4.6.

Missing information: Remedial pro-coagulant therapy for excessive haemorrhage	
	PL section 2. Prescription only medicine. Additional risk minimisation measures: None

Missing information: Pregnant or breast-feeding women	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.3 and 4.6. PL section 2. Prescription only medicine. 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 and 4.8. PL sections 2 and 4. Prescription only medicine. 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. 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:

Missing information: Patients with significant liver diseases (severe hepatic impairment/Child Pugh C)	
	SmPC sections 4.2, 4.3 and 5.2. PL section 2. Prescription only medicine. Additional risk minimisation measures: None

Missing information: Patients < 18 years	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.2. PL section 2. Prescription only medicine. Additional risk minimisation measures: None

II.C Post-authorisation development plan

There are no studies required for Rivaroxaban Orion.