Part VI: Summary of the risk management plan

Summary of risk management plan for Xiltess / Blomensy / *Rivaroxaban Biogaran 2.5 mg, 10 mg, 15 mg, 20 mg film-coated tablets*

This is a summary of the risk management plan (RMP) for rivaroxaban. 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's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how rivaroxaban should be used.

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

Part VI.1. The medicine and what it is used for

Xiltess/ Blomensy */ Rivaroxaban Biogaran 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.

Xiltess/ Blomensy*/ Rivaroxaban Biogaran 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.

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

Part VI.2. The medicine and what it is used for

Xiltess/ Blomensy */ Rivaroxaban Biogaran 10 mg film – coated tablets are indicated for the* prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.

Xiltess/ Blomensy */ Rivaroxaban Biogaran 10 mg film – coated tablets are indicated for the* 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 administration.

Part VI.3. The medicine and what it is used for

Xiltess / Blomensy */ Rivaroxaban Biogaran 15 mg film – coated tablets are indicated for the* 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.

Xiltess / Blomensy */ Rivaroxaban Biogaran 15 mg film – coated tablets are indicated for the* 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 administration.

Paediatric population:

Xiltess / Blomensy */ Rivaroxaban Biogaran 15 mg film-coated tablets are indicated for the* treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in children and adolescents aged less than 18 years and weighing from 30 kg to 50 kg after at least 5 days of initial parenteral anticoagulation treatment.

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

Part VI.4. The medicine and what it is used for

Xiltess / Blomensy */ Rivaroxaban Biogaran 20 mg film – coated tablets are indicated for the* 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.

Xiltess / Blomensy*// Rivaroxaban Biogaran 20 mg film – coated tablets are indicated for the* 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 administration.

Paediatric population:

Xiltess / Blomensy */ Rivaroxaban Biogaran 20 mg film-coated tablets are indicated for the* treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in children and adolescents aged less than 18 years and weighing more than 50 kg after at least 5 days of initial parenteral anticoagulation treatment.

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

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

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

If important information that may affect the safe use of rivaroxaban is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of rivaroxaban are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 (CrCI < 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

List of important risks and missing information	
	• 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)

II.B Summary of important risks

Haemorrhage **Important identified risk**	
Risk minimisation measures	Routine risk minimisation measures: SmPC (sections 4.3, 4.4, 4.5, 4.8 and 4.9) PIL (section "What you need to know before you take rivaroxaban Do not take rivaroxaban", "Possible side effects"). – Prescription only medicine. – Limited pack sizes Additional risk minimisation measures: • *Educational material for prescribers (Prescriber guide)* • *Patient alert cards*

Embryo-fetal toxicity **Important potential risk**	
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*

Patients with severe renal impairment (CrCI < 30 ml/min)

Missing information	
Risk minimisation measures	Routine risk minimisation measures: SmPC (sections 4.2 and 4.4) – Prescription only medicine. – Limited pack sizes Additional risk minimisation measures: *None*

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) **Missing information**	
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*

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

Pregnant or breast-feeding women **Missing information**	
Risk minimisation measures	Routine risk minimisation measures: SmPC (sections 4.3, 4.6 and 5.3)

	PIL (section "Pregnancy and breast-feeding"). – Prescription only medicine. – Limited pack sizes Additional risk minimisation measures: *None*

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

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

Patients with significant liver diseases (severe hepatic impairment/Child Pugh C) **Missing information**	
Risk minimisation measures	Routine risk minimisation measures: SmPC (section 4.2, 4.3 and 5.2): – 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.

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

There are no studies required for rivaroxaban.