PART VI. SUMMARY OF THE RISK MANAGEMENT PLAN

According to the *Guidance on the format of the risk management plan (RMP) in the EU integrated format (EMA/PRAC/613102/2015 Rev 2)*, a separate RMP Part VI should be provided for each product in the RMP.

However, we have considered to prepare a unique Summary of RMP for all strengths of Apixaban film-coated tablets as the risks are the same for all products and the information provided by the different strengths of the originator in the EMA website *EPAR: Summary for the public* is also common.

Summary of risk management plan for Apixaban film-coated tablets

I. The medicine and what is used for

Apixaban 2.5 mg film-coated tablets is indicated for:

- Prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery.
- Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); age ≥ 75 years; hypertension; diabetes mellitus; symptomatic heart failure (NYHA Class ≥ II).
- Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults (see Section 4.4 from the SmPC for haemodynamically unstable PE patients).

Apixaban 5 mg film-coated tablets is indicated for:

- Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); age ≥ 75 years; hypertension; diabetes mellitus; symptomatic heart failure (NYHA Class ≥ II).
- Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults (see Section 4.4 from the SmPC for haemodynamically unstable PE patients).

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

Important risks of Apixaban 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;
- The medicine´s legal status - the way a medicine is supplied to the patient (only with medical prescription) can help to minimise the risks.

Together, these measures constitute routine risk minimisation measures,

In the case of Apixaban film-coated tablets, 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 Apixaban 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 Apixaban 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.

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 Apixaban. 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 yet 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.

Summary of safety concerns	
Important identified risks	- Bleeding
Important potential risks	- Liver Injury - Potential risk of bleeding or thrombosis due to overdose or underdose
Missing information	- Use in patients with severe renal impairment

II.B Summary of important risks

Important identified risk: Bleeding	
Risk minimisation	Routine risk minimisation measures:

measures	SmPC section 4.2 "*Posology and method of administration*" Contraindication in SmPC section 4.3 "*Contraindication*" Warning in SmPC section 4.4 "*Special warnings and precautions for use*" Warning in SmPC section 4.5 "*Interaction with other medicinal products and other forms of interactions*" • Cyp 3A4 and P-gp inhibitors • Anticoagulants • NSAIDS/platelet aggregation inhibitors • SSRIs/SNRIs Haemorrhage is listed in SmPC section 4.8 "*Undesirable effects*" SmPC section 4.9 "*Overdose*" <u>Additional risk Minimisation measures:</u> • Prescriber Guide • Patient Alert Card

II.C Post-authorisation development plan

Not applicable.