# 13 Part VI: Summary of the risk management plan (RMP) – Apixaban*, 2.5 mg and 5 mg, Film-coated tablets

*Apixaban Sandoz 2,5 mg, filmomhulde tabletten
Apixaban Sandoz 5 mg, filmomhulde tabletten
Apixaban 1A Pharma 2,5 mg, filmomhulde tabletten
Apixaban 1A Pharma 5 mg, filmomhulde tabletten
Apixaban Hexal 2,5 mg, filmomhulde tabletten
Apixaban Hexal 5 mg, filmomhulde tabletten
ABATIXENT 2,5 mg, filmomhulde tabletten
ABATIXENT 5 mg, filmomhulde tabletten

This is a summary of the RMP for apixaban, 2.5 mg and 5 mg, Film-coated tablets. The RMP details important risks of apixaban, film-coated tablets, how these risks can be minimized, and how more information will be obtained about apixaban, film-coated tablets' risks and uncertainties (missing information).

Apixaban, film-coated tablets' summaries of product characteristics (SmPCs) and its package leaflets (PLs) give essential information to healthcare professionals (HCPs) and patients on how apixaban, film-coated tablets’ should be used.

Important new concerns or changes to the current ones will be included in updates of the apixaban, film-coated tablets' RMP.

## 13.1 Part VI: I. The medicine and what it is used for

**2.5 mg, Film-coated tablets:**

Prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery.

**2.5 mg and 5 mg, Film-coated tablets:**

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 ischemic attack (TIA); age ≥ 75 years; hypertension; diabetes mellitus; symptomatic heart failure [New York Heart Association (NYHA) Class ≥ II].

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

It contains apixaban as an active substance and is given orally as film-coated tablets (2.5 mg and 5 mg).

## 13.2 Part VI: II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of Apixaban, film-coated tablets, together with measures to minimize such risks are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PLs and SmPCs addressed to patients and HCPs;

- Important advice on the medicine's packaging;
- The authorized 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 minimize its risks.

Together, these measures constitute *routine risk minimization* measures.

In the case of apixaban, film-coated tablets, these measures are supplemented with *additional risk minimization measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including Periodic Safety Update Report (PSUR) assessment (if applicable) 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.

### 13.2.1 Part VI – 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 minimize 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, 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).

**Table 13-1 List of important risks and missing information**

| **List of important risks and missing information** | |
|---|---|
| Important identified risks | Bleeding |
| Important potential risks | Liver disorders |
| | Potential risk of bleeding or thrombosis due to overdose or underdose |
| Missing information | Use in patients with severe renal impairment |

### 13.2.2 Part VI – II.B: Summary of important risks

The safety information in the proposed Product Information is aligned to the innovator product.

**Table 13-2 Important identified risk: Bleeding**

| | |
|---|---|
| Risk minimization measures | **Routine risk minimization measures:**<br>SmPC sections 4.2,4.3, 4.4, 4.5, 4.8, 4.9, and 5.3<br>PL sections 2, 3, and 4<br>SmPC section 4.3 included following contraindications that increases the risk of bleeding:<br>• Active clinically significant bleeding. |

| | |
|---|---|
| | • Hepatic disease associated with coagulopathy and clinically relevant bleeding risk.<br>• Lesion or condition if considered a significant risk factor for major bleeding.<br>• Concomitant treatment with any other anticoagulant agent.<br>SmPC section 4.4 includes following recommendations:<br>• Apixaban to be used with caution in conditions with increased risk of hemorrhage, patients are to be carefully observed for signs of bleeding. Administration should be discontinued if severe hemorrhage occurs.<br>• Due to an increased bleeding risk, concomitant treatment with any other anticoagulants is contraindicated.<br>• Apixaban is not recommended for patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome due to the increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy.<br>Legal status: Prescription only<br>**Additional risk minimization measures:**<br>• Prescriber Guide<br>• Patient Alert Card |

**Table 13-3 Important potential risk: Liver disorders**

| | |
|---|---|
| Risk minimization measures | **Routine risk minimization measures:**<br>SmPC sections 4.2, 4.3, 4.4, and 4.8<br>PL Section 2 and 4<br>SmPC Section 4.3 includes contraindication of Hepatic disease associated with coagulopathy and clinically relevant bleeding risk.<br>SmPC sections 4.2, 4.4 includes the following recommendations:<br>- Apixaban is contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk.<br>- Apixaban not recommended in patients with severe hepatic impairment<br>  - Apixaban should be used with caution in patients with mild or moderate hepatic impairment (Child Pugh A or B) and patients with elevated liver enzymes alanine aminotransferase (ALT)/aspartate aminotransferase (AST) >2 x Upper Limit of Normal (ULN) or total bilirubin ≥ 1.5 x ULN<br>- Prior to initiating Apixaban, liver function testing should be performed<br>Legal status: Prescription only<br>**Additional risk minimization measures:** None |

**Table 13-4 Important potential risk: Potential risk of bleeding or thrombosis due to overdose or underdose**

| | |
|---|---|
| Risk minimization measures | **Routine risk minimization measures:**<br>SmPC sections 4.2, 4.4, and 4.9<br>PL section 3 |

| | |
|---|---|
| | SmPC sections 4.4, 4.9 and PL section 3 include recommendation of discontinuation of the treatment if hemorrhagic event occurs and treatment (e.g., surgical hemostasis, or the transfusion of fresh frozen plasma or the administration of a reversal agent for factor Xa inhibitors) should be considered.<br>Legal status: Prescription only<br>**Additional risk minimization measures:**<br>• Prescriber Guide |

**Table 13-5 Missing information: Use in patients with severe renal impairment**

| | |
|---|---|
| Risk minimization measures | **Routine risk minimization measures:**<br>SmPC sections 4.2 and 4.4<br>PL sections 2 and 3<br>Legal status: Prescription only<br>**Additional risk minimization measures:** None |

### 13.2.3 Part VI – II.C: Post-authorization development plan

#### 13.2.3.1 II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of apixaban, film-coated tablets.

#### 13.2.3.2 II.C.2. Other studies in post-authorization development plan

There are no studies required for apixaban, film-coated tablets.