Part VI: Summary of the risk management plan

Summary of risk management plan for Edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets

This is a summary of the risk management plan (RMP) for edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets. The RMP details important risks of edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets, how these risks can be minimized, and how more information will be obtained about edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets' risks and uncertainties (missing information).

Edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets should be used.

Important new concerns or changes to the current ones will be included in updates of edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets' RMP.

I. The medicine and what it is used for

Edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets is authorized for:

- Prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (NVAF) with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischemic attack (TIA).
- Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and for the prevention of recurrent DVT and PE in adults.

It contains edoxaban tosylate monohydrate as the active substance and it is given by oral route of administration as 15 mg, 30 mg, and 60 mg film-coated tablets.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets, together with measures to minimize such risks and the proposed studies for learning more about edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets' 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 package leaflet and SmPC addressed to patients and healthcare professionals;
- 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 edoxaban 15 mg, 30 mg, and 60 mg 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 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 edoxaban 15 mg, 30 mg, and 60 mg 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 edoxaban 15 mg, 30 mg, and 60 mg 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 administered or 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 edoxaban 15 mg, 30 mg, and 60 mg 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);

List of important risks and missing information	
Important identified risks	Bleeding or Bleeding due to: • Drug interaction in combination with other drugs known to increase the risk of bleeding e.g., aspirin, NSAIDs. • Inappropriate administration of 60 mg dose/inadvertent overdose by use of 60 mg dose, e.g., in combination with use of strong P-gp inhibitors; in patients with low body weight ≤ 60 kg; and in patients with moderate to severe renal impairment (CrCl 15 - 50 mL/min).
Important potential risks	Hepatic dysfunction.
	Trend toward decreasing efficacy in nonvalvular atrial fibrillation (NVAF) subjects with high CrCl.
Missing information	Lack of reversal agent.
	Reproductive and development toxicity (Pregnancy and breastfeeding).
	Patients with hepatic impairment.
	Patients with severe renal impairment (CrCl < 30 mL/min) or end-stage renal disease (CrCl < 15 mL/min or on dialysis).
	Patients with mechanical heart valves.
	Combination with dual antiplatelet therapy.
	Off-label use in Europe in populations or indications outside the approved indications per European SmPC.

II.B Summary of important risks

The safety information in the proposed product information is aligned to the reference medicinal product.

Important identified risk: Bleeding	
Risk minimization measures	**Routine risk minimization measures:** SmPC Sections 4.2 to 4.5 and 4.9. PL Sections 2 and 4. **Routine risk minimization activities recommending specific clinical measures to address the risk:** Increase awareness of the risk of bleeding and provide guidance on how to manage the risk of bleeding in SmPC Sections 4.2, 4.3, 4.4, 4.5, 4.8 and 4.9. **Other routine risk minimization measures beyond the Product Information:** Legal status: Prescription-only medicine. **Additional risk minimization measures:** Educational Materials: Prescriber guide Patient alert card.

II.C Post-authorization development plan

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 edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets.

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

There are no studies required for edoxaban 15 mg, 30 mg, and 60 mg film-coated tablets.