Summary of risk management plan for
Inhixa
2,000 IU (20 mg)/0,2 ml,
4,000 IU (40 mg)/0,4 ml,
6,000 IU (60 mg)/0,6 ml,
8,000 IU (80 mg)/0,8 ml,
10,000 IU (100 mg)/1 ml,
12,000 IU (120 mg)/0,8 ml,
15,000 IU (150 mg)/1 ml,
30,000 IU (300 mg)/3 ml,
50,000 IU (500 mg)/5 ml,
solution for injection (*Enoxaparinum sodium*)

This is a summary of the risk management plan (RMP) for Inhixa 2,000 IU (20 mg)/0,2 ml, 4,000 IU (40 mg)/0,4 ml, 6,000 IU (60 mg)/0,6 ml, 8,000 IU (80 mg)/0,8 ml, 10,000 IU (100 mg)/1 ml, 12,000 IU (120 mg)/0,8 ml, 15,000 IU (150 mg)/1 ml, 30,000 IU (300 mg)/3 ml, 50,000 IU (500 mg)/5 ml, solution for injection (hereinafter referred to as Inhixa products). The RMP details important risks of Inhixa products, how these risks can be minimised, and how more information will be obtained about Inhixa's risks and uncertainties (missing information).

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

This summary of the RMP for Inhixa products should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

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

I. The medicine and what it is used for

Inhixa is authorised for:

Prophylaxis of venous thromboembolic disease in moderate and high risk surgical patients, in particular those undergoing orthopaedic or general surgery including cancer surgery.

Prophylaxis of venous thromboembolic disease in medical patients with an acute illness (such as acute heart failure, respiratory insufficiency, severe infections or rheumatic diseases) and reduced mobility at increased risk of venous thromboembolism.

Treatment of deep vein thrombosis and pulmonary embolism, excluding pulmonary embolism likely to require thrombolytic therapy or surgery.

Prevention of thrombus formation in extra corporeal circulation during haemodialysis.

Acute coronary syndrome:

- Treatment of unstable angina and Non ST-segment elevation myocardial infarction (NSTEMI), in combination with oral acetylsalicylic acid,
- Treatment of acute ST-segment elevation myocardial infarction (STEMI) including patients to be managed medically or with subsequent percutaneous coronary intervention (PCI).

Further information about the evaluation of Inhixa’s benefits can be found in Inhixa’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/inhixa

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

Important risks of Inhixa products, together with measures to minimise such risks and the proposed studies for learning more about Inhixa'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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment 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 Inhixa products is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Inhixa products 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 Inhixa. 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	• Major haemorrhages • Heparin induced thrombocytopenia
Important potential risks	• Medication error
Missing information	• Use in patients with hepatic impairment • Use un pregnant women and lactating women • Use in children and adolescents

II.B Summary of important risks

Important identified risk: Major haemorrhages	
Evidence for linking the risk to the medicine	In clinical studies, haemorrhages were the most commonly reported reaction.
Risk factors and risk groups	Active major bleeding and conditions with a high risk of uncontrolled haemorrhage, including recent haemorrhagic stroke, renal

	impairment, elderly and extremes of weight, impaired haemostasis, history of peptic ulcer, recent ischaemic stroke, uncontrolled severe arterial hypertension, diabetic retinopathy, recent neuro- or ophthalmologic surgery, organic lesions liable to bleed, invasive procedures or the concomitant use of medications affecting haemostasis such as systemic salicylates, acetylsalicylic acid at anti-inflammatory doses, NSAIDs including ketorolac, other thrombolytics, e.g. alteplase, reteplase, streptokinase, tenecteplase, urokinase and anticoagulants.
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections 4.2, 4.3, 4.4, 4.8 and 4.9* *PL sections 2 and 4* *SmPC section 4.4 where advice is given on monitoring of platelet counts*
Additional pharmacovigilance activities	Not applicable.
Important identified risk: Heparin induced thrombocytopenia	
Evidence for linking the risk to the medicine	Frequency not known. The sharp drop in platelet count is caused by antibodies binding to a complex of PF4 and heparin. Since LMWHs generally display less interaction with PF4 it could be that they may give rise to a lower incidence of HIT; this was indeed found to be the case in a prospective study of unfractionated heparin versus enoxaparin. The incidence is difficult to estimate and depends on the type of clinical indication and the duration of therapy, but is generally thought to be around 1–3%.
Risk factors and risk groups	Enoxaparin is to be used with extreme caution in patients with a history of heparin-induced thrombocytopenia with or without thrombosis.
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections 4.3, 4.4 and 4.8* *PL sections 2 and 4* *SmPC section 4.4 where advice is given on monitoring of platelet counts* *Targeted follow-up questionnaire*
Additional pharmacovigilance activities	Not applicable.

Important potential risk: Medication error	
Evidence for linking the risk to the medicine	The majority (47.6%) of heparin errors originate in administering the medication, followed by 18.8% in transcribing the order, 14.1% in prescribing the product, 13.9% in dispensing functions and 5.4% in

	patient/laboratory monitoring activities. Nursing staff were most frequently involved with heparin errors (60%), followed by pharmacy staff (14%) and prescribers (13%).
Risk factors and risk groups	All patients under heparin treatment are potentially at risk.
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections 2, 4.2, 4.3 and 4.4* *PL section 2, 3 and 6*
Additional pharmacovigilance activities	Not applicable.

Missing information: Use in children and adolescents	
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections 4.2 and 4.8* *PL section 2 and 3*
Missing information: Use in patients with hepatic impairment	
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections 4.2 and 4.4* *PL section 2*
Missing information: Use un pregnant women and lactating women	
Risk minimisation measures	Routine risk minimisation measures: *SmPC sections 4.4, 4.6 and 5.3* *PL section 2*

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 Inhixa products.

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

There are no studies required for Inhixa products.