SINTETICA

Summary of the Risk Management Plan for Heparin Sintetica

Heparin Sintetica, solution for infusion (Heparin sodium)

Marketing Authorization Holder: Sintetica SA

Document version: 0.2

Date: 20.04.2021

Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.
The RMP summary of HEPARIN SINTETICA is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.
Please note that the reference document which is valid and relevant for the effective and safe use of HEPARIN SINTETICA in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic.

Sintetica SA is fully responsible for the accuracy and correctness of the content of the published summary RMP of HEPARIN SINTETICA.

Summary of risk management plan for Heparin Sintetica (Heparin sodium)

This is a summary of the risk management plan (RMP) for Heparin Sintetica. The RMP details important risks of Heparin Sintetica, how these risks can be minimised, and how more information will be obtained about Heparin Sintetica's risks and uncertainties (missing information).

Heparin Sintetica's s package leaflet gives essential information to healthcare professionals and patients on how Heparin Sintetica should be used.

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

I. The medicine and what it is used for

Heparin Sintetica is authorised for the treatment of thrombotic conditions (see Information for healthcare professionals for the full indication). It contains heparin as the active substance and it is given by intravenous administration.

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

Important risks of Heparin Sintetica, together with measures to minimise such risks and the proposed studies for learning more about Heparin Sintetica '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 / Information for healthcare professionals addressed to 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*.

II.A List of important risks and missing information

Important risks of Heparin Sintetica 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 Heparin Sintetica. 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	• Hypersensitivity, including anaphylactic reactions • Haemorrhage • Heparin-induced thrombocytopenia and thromboembolic complications • Osteoporosis in pregnant women • Abortion or premature birth • Hyperkalaemia
Important potential risks	• Skin necrosis
Missing information	• Use in pediatric patients • Use in patients with hepatic impairment

II.B Summary of important risks

Hypersensitivity, including anaphylactic reactions	
Evidence for linking the risk to the medicine	Information for healthcare professionals, Literature reports
Risk factors and risk groups	Not known
Risk minimisation measures	Routine risk communication: Information for healthcare professionals sections 'Contraindications', 'Warnings and precautions' and 'Undesirable effect' Contraindication to patients with known hypersensitivity to heparins or any of the excipients Other routine risk minimisation measures beyond the Product Information: *Legal status*: Prescription-only medicinal product Targeted follow up questionnaire

Haemorrhage	
Evidence for linking the risk to the medicine	Information for healthcare professionals, Literature reports
Risk factors and risk groups	Hypersensitivity to heparin
Risk minimisation measures	Routine risk communication: Information for healthcare professionals sections 'Contraindications', 'Warnings and precautions', 'Interactions', 'Undesirable effect' and 'Overdose' Contraindication to patients with conditions associated with an increased susceptibility or with suspected lesions of the vascular system Recommendation to avoid heparin therapy in patients with risk of hematoma Monitoring and control of coagulation parameters required for infants, children and patients with impaired renal and / or hepatic function Other routine risk minimisation measures beyond the Product Information: *Legal status*: Prescription-only medicinal product

Heparin-induced thrombocytopenia and thromboembolic complications	
Evidence for linking the risk to the medicine	Information for healthcare professionals, Literature reports
Risk factors and risk groups	Patients with positive platelet aggregation test
Risk minimisation measures	Routine risk communication: Information for healthcare professionals sections 'Contraindications', 'Warnings and precautions' and 'Undesirable effect Contraindication to patients with past history of heparin-induced thrombocytopenia Recommendation to administer heparin in patients who develop clinically relevant thrombocytopenias with heparin only if

	platelet aggregation test provides a negative result Recommendation to use danaparoid (a heparinoid) and lepirudin (a direct inhibitor of thrombin) as therapeutic alternatives Other routine risk minimisation measures beyond the Product Information: *Legal status*: Prescription-only medicinal product Targeted follow up questionnaire

Osteoporosis in pregnant women	
Evidence for linking the risk to the medicine	Information for healthcare professionals, Literature reports
Risk factors and risk groups	Not known
Risk minimisation measures	Routine risk communication: Information for healthcare professionals sections 'Undesirable effect' and 'Pre-clinical data' Other routine risk minimisation measures beyond the Product Information: *Legal status*: Prescription-only medicinal product

Abortion or premature birth	
Evidence for linking the risk to the medicine	Information for healthcare professionals, Literature reports
Risk factors and risk groups	Pregnant women at risk of imminent abortion
Risk minimisation measures	Routine risk communication: Information for healthcare professionals sections 'Contraindications', 'Warnings and precautions', 'Pregnancy / Breastfeeding' and 'Undesirable effect' Contraindication to pregnant women in risk of imminent abortion Contraindication of epidural anaesthesia to pregnant women treated with heparin

	Medical supervision recommended during pregnancy, in particular when used for long-term Other routine risk minimisation measures beyond the Product Information: *Legal status*: Prescription-only medicinal product

Hyperkalaemia	
Evidence for linking the risk to the medicine	Information for healthcare professionals, Literature reports
Risk factors and risk groups	Patients at risk of hyperkalaemia include: • With baseline condition susceptible of increasing serum levels of potassium (e.g. diabetes, renal impairment…) • Intake drugs that increase potassium levels in the blood
Risk minimisation measures	Routine risk communication: Information for healthcare professionals sections 'Warnings and precautions', 'Interactions' and 'Undesirable effect' Medical monitoring required when using drugs that increase the serum potassium levels Recommendation to control serum potassium in patients at risk (e.g. diabetic patients, with limited renal function, on drugs that increase potassium levels) Other routine risk minimisation measures beyond the Product Information: *Legal status*: Prescription-only medicinal product

Important Potential Risks

Skin necrosis	
Evidence for linking the risk to the medicine	Information for healthcare professionals, Literature reports
Risk factors and risk groups	Not known

Risk minimisation measures	Routine risk communication: Information for healthcare professionals sections 'Undesirable effect' Other routine risk minimisation measures beyond the Product Information: *Legal status*: Prescription-only medicinal product

Missing information

Use in paediatric patients	Routine risk communication**:** Info. Prof. sections 'Warnings and precautions' Routine risk minimisation activities recommending specific clinical measures to address the risk**:** Medical monitoring and control of coagulation parameters are necessary in children. Other routine risk minimisation measures beyond the Product Information**:** *Legal status*: Prescription-only medicinal product
Use in patients with hepatic impairment	Routine risk communication**:** Info. Prof. sections 'Contraindications', 'Warnings and precautions' Routine risk minimisation activities recommending specific clinical measures to address the risk**:** Heparin Sintetica is contraindicated in conditions associated with an increased tendency to haemorrhages, such as hepatic disease. Careful monitoring and control of coagulation is necessary in patients with reduced hepatic function. In patients with reduced hepatic function, treatment with Heparin Sintetica should be

	carried out according to the results of the coagulation tests. Other routine risk minimisation measures beyond the Product Information**:** *Legal status*: Prescription-only medicinal product

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 Heparin Sintetica.

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

There are no studies required for Heparin Sintetica.