SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

innohep 10,000 IU/ml

or

tinzaparin sodium 10,000 IU/ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Tinzaparin sodium 10,000 anti-Factor Xa IU/ml

Excipients with known effect:
Benzyl alcohol (10 mg/ml) and sodium (in total < 23 mg/ml).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Vials of 2 ml filled with a colourless to straw coloured liquid, free from turbidity and from matter that deposits on standing.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Prophylaxis of venous thromboembolism in adult patients undergoing surgery, particularly orthopaedic, general or oncological surgery.

Prophylaxis of venous thromboembolism in non-surgical adult patients immobilised due to acute medical illness including: acute heart failure, acute respiratory failure, severe infections, active cancer, as well as exacerbation of rheumatic diseases.

Prevention of clotting in extracorporeal circuits during haemodialysis and haemofiltration in adults.

4.2 Posology and method of administration

Posology

Prophylaxis of thromboembolic events in adults:

Administration is by subcutaneous injection.

Surgical patients at moderate risk of thromboembolic events:

3,500 anti-Xa IU given SC 2 hours before surgery and then once daily for as long as the patient is considered to be at risk of VTE.

Surgical patients at high risk of thromboembolic events e.g. undergoing orthopaedic or cancer surgery:

4,500 anti-Xa IU given SC 12 hours before surgery and then once daily for as long as the patient is considered to be at risk of VTE.

Non-surgical patients immobilised due to acute medical illness:

3,500 anti-Xa IU given SC once daily in patients at moderate risk of VTE, or 4,500 anti-Xa IU given SC once daily in patients at high risk of VTE. Administration should continue for as long as the patient is considered to be at risk of VTE.

Neuraxial anaesthesia

Caution is advised when performing neuraxial anaesthesia or lumbar puncture in patients receiving prophylactic doses of tinzaparin sodium, see section 4.4: Neuraxial anaesthesia. If neuraxial anaesthesia is planned, a minimum delay of 12 hours should be allowed between the last prophylactic dose and the needle or catheter placement. Tinzaparin sodium should not be resumed until at least 4-6 hours after the use of spinal anaesthesia or after the catheter has been removed. Thus, the 2 hours preoperative initiation of thromboprophylaxis with tinzaparin sodium is not compatible with neuraxial anaesthesia.

Haemodialysis and haemofiltration in adults:

Duration of 4 hours or less:

A bolus injection of 2,000 to 2,500 anti-Xa IU at the start of dialysis.

Duration of more than 4 hours:

A bolus injection of 2,500 anti-Xa IU at the start of dialysis/filtration, followed by 750 anti-Xa IU/hour as a continuous infusion.

Dose adjustment:

If necessary, the bolus dose may be increased or decreased gradually in increments of 500 anti-Xa IU until a satisfactory response is obtained. The usual dose is within 2,000–4,500 anti-Xa IU.

In case of concomitant transfusion of blood or concentrated red corpuscles, an extra bolus injection of 500–1,000 anti-Xa IU can be administered.

Dose monitoring:

Determination of plasma anti-Xa activity can be used to monitor the tinzaparin sodium dose during haemodialysis/haemofiltration. The plasma anti-Xa level should be approximately 0.5 anti-Xa IU/ml one hour after administration.

Interchangeability

For interchangeability with other LMWHs, see section 4.4.

Special populations

Paediatric population

The safety and efficacy of tinzaparin sodium in children below 18 years have not yet been established. Currently available data are described in section 5.2, but no recommendation on a posology can be made.

Renal impairment

If renal impairment is suspected, renal function should be assessed using a formula based on serum creatinine to estimate creatinine clearance level.

Use in patients with a creatinine clearance level < 30 ml/minute is not recommended, as dosage in this population has not been established. Available evidence demonstrates no accumulation in patients with creatinine clearance levels down to 20 ml/min. When required in these patients, tinzaparin sodium administration can be initiated with anti-Xa monitoring, if the benefit outweighs the risk (see section 4.4: Renal impairment).

Elderly

Tinzaparin sodium should be used in the elderly in standard doses. Precaution is recommended in the treatment of elderly patients with renal impairment. If renal impairment is suspected, see section 4.2: Renal impairment and section 4.4: Renal impairment.

Weight

For patients with very low or very high body weight, 50 anti-Xa IU per kg body weight once daily may be considered as an alternative to fixed dosing. For surgical patients, the first dose is given SC 2 hours before surgery. The administration should continue once daily for as long as the patient is considered to be at risk of VTE.

Method of administration

Parenteral products should be inspected visually prior to administration. Do not use if cloudiness or precipitate is observed. The liquid may turn yellow during storage but is still useable.

Administration is by subcutaneous injection when given as prophylaxis of thromboembolic events in adults. This can be done in abdominal skin, the outer side of the thigh, lower back, upper leg or upper arm. Do not inject in the area around the navel, near scars or in wounds.

For abdominal injections, the patient should be in a supine position, alternating the injections between the left and right side. The air-bubble within the syringe should not be removed. During the injection, the skin should be held in a fold.

For haemodialysis, the dose of tinzaparin sodium should be given into the arterial side of the dialyser or intravenously. The dialyser can be primed by flushing with 500-1,000 ml isotonic sodium chloride (9 mg/ml) containing 5,000 anti-Xa IU tinzaparin sodium per litre.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Current or history of immune-mediated heparin-induced thrombocytopenia (type II) (see section 4.4).
- Active major haemorrhage or conditions predisposing to major haemorrhage. Major haemorrhage is defined as fulfilling any one of these three criteria: a) occurs in a critical area or organ (e.g. intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, intra-uterine or intramuscular with compartment syndrome), b) causes a fall in haemoglobin level of 20 g/L (1.24 mmol/L) or more, or c) leads to transfusion of 2 or more units of whole blood or red blood cells.
- Septic endocarditis.
- The multidose vial formulations of tinzaparin sodium contain 10 mg/ml of the preservative benzyl alcohol. These formulations must not be given to premature babies or neonates due to the risk of gasping syndrome.

4.4 Special warnings and precautions for use

Neuraxial anaesthesia

Caution is advised when performing neuraxial anaesthesia or lumbar puncture in patients receiving prophylactic doses of tinzaparin sodium due to the risk of spinal haematomas resulting in prolonged or permanent paralysis. A minimum delay of 12 hours should be allowed between the last prophylactic dose of tinzaparin sodium and the needle or catheter placement. For continuous techniques, a similar delay should be observed before removing the catheter. Moreover, tinzaparin sodium should not be resumed until at least 4-6 hours after the use of spinal anaesthesia or after the catheter has been removed. Patients should be closely monitored for signs and symptoms of neurological injury.

Haemorrhage

Caution is advised when administering tinzaparin sodium to patients at risk of haemorrhage. For patients at risk of major haemorrhage see section 4.3. The combination with medicinal products affecting platelet function or the coagulation system should be avoided or carefully monitored (see section 4.5).

Intramuscular injections

Tinzaparin sodium should not be administered by intramuscular injection due to the risk of haematoma. Due to the risk of haematoma, concomitant intramuscular injections should also be avoided.

Heparin-induced thrombocytopenia

Platelet count should be measured before the start of treatment and periodically thereafter because of the risk of immune-mediated heparin-induced thrombocytopenia (type II). Tinzaparin sodium must be discontinued in patients who develop immune-mediated heparin-induced thrombocytopenia (type II) (see section 4.3 and 4.8). Platelet counts will usually normalise within 2 to 4 weeks after withdrawal.

Hyperkalaemia

Heparin products can suppress adrenal secretion of aldosterone, leading to hyperkalaemia. Risk factors include diabetes mellitus, chronic renal failure, pre-

existing metabolic acidosis, raised plasma potassium at pre-treatment, concomitant therapy with drugs that may elevate plasma potassium, and long-term use of tinzaparin sodium. In patients at risk, potassium levels should be measured before starting tinzaparin sodium and monitored regularly thereafter. Heparin-related hyperkalaemia is usually reversible upon treatment discontinuation, though other approaches may need to be considered if tinzaparin sodium treatment is considered lifesaving (e.g. decreasing potassium intake, discontinuing other drugs that may affect potassium balance).

Prosthetic heart valves

Therapeutic failures have been reported in patients with prosthetic heart valves on full anticoagulant doses of tinzaparin sodium and other low molecular weight heparins. Tinzaparin sodium is not recommended for use in this population.

Renal impairment

Use in patients with a creatinine clearance level < 30 ml/minute is not recommended, as dosage in this population has not been established. Available evidence demonstrates no accumulation in patients with creatinine clearance levels down to 20 ml/minute. When required in these patients, tinzaparin sodium administration can be used cautiously with anti-Xa monitoring, if the benefit outweighs the risk (see section 4.2). Although anti-Xa monitoring remains a poor predictor of haemorrhage risk, it is the most appropriate measure of the pharmacodynamic effects of tinzaparin sodium.

Elderly

Elderly are more likely to have reduced renal function (see section 4.4: Renal impairment); therefore caution should be exercised when prescribing tinzaparin sodium to the elderly.

Interchangeability

Low molecular weight heparins should not be used interchangeably because of differences in pharmacokinetics and biological activities. Switching to an alternative low molecular weight heparin, especially during extended use, must be exercised with particular caution and specific dosing instructions for each proprietary product must be followed.

Excipients warnings

The multidose vial formulations of tinzaparin sodium contain 10 mg/ml of the preservative benzyl alcohol. Benzyl alcohol may cause allergic reactions. Benzyl alcohol may cause toxic and anaphylactoid reactions in infants and children up to 3 years old. High volumes should be used with caution and only if necessary, especially in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis).

This medicinal product contains less than 1 mmol sodium (23 mg) per mL, i.e. essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

The anticoagulant effect of tinzaparin sodium may be enhanced by other drugs affecting the coagulation system, such as those inhibiting platelet function (e.g. acetylsalicylic acid and other non-steroidal anti-inflammatory drugs), thrombolytic agents, vitamin K antagonists, activated protein C, direct factor Xa and IIa inhibitors. Such combinations should be avoided or carefully monitored (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Anticoagulant treatment of pregnant women requires specialist involvement.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

A large amount of data on pregnant women (more than 2,200 pregnancy outcomes) indicate no malformative nor feto/neonatal toxicity of tinzaparin. Tinzaparin does not cross the placenta. Tinzaparin sodium can be used during all trimesters of pregnancy if clinically needed.

Epidural anaesthesia:

Due to the risk of spinal haematoma, treatment doses of tinzaparin sodium (175 IU/kg) are contraindicated in patients who receive neuraxial anaesthesia. Therefore, epidural anaesthesia in pregnant women should always be delayed until at least 24 hours after administration of the last treatment dose of tinzaparin sodium. Prophylactic doses may be used as long as a minimum delay of 12 hours is allowed between the last administration of tinzaparin sodium and the needle or catheter placement.

Pregnant women with prosthetic heart valves:

Therapeutic failures and maternal death have been reported in pregnant women with prosthetic heart valves on full anticoagulant doses of tinzaparin sodium and other low molecular weight heparins. In the absence of clear dosing, efficacy and safety information in this circumstance, tinzaparin sodium is not recommended for use in pregnant women with prosthetic heart valves.

Excipients:

Tinzaparin sodium vials contain benzyl alcohol. As this preservative may cross the placenta and may cause accumulation in toxicity (metabolic acidosis), tinzaparin sodium formulations without benzyl alcohol (syringes) should be used during pregnancy.

Breastfeeding

In patients at risk, the incidence of venous thromboembolism is particularly high during the first 6 weeks after child birth.

The passage of tinzaparin into human breast milk is expected to be very low. The oral absorption of any trace amount of tinzaparin sodium in the breast milk to the infant is very unlikely. Tinzaparin can be used during breastfeeding.

Excipients:

Tinzaparin sodium vials contain benzyl alcohol. Due to a risk of accumulation and toxicity (metabolic acidosis), tinzaparin sodium formulations without benzyl alcohol (pre-filled syringes) are the preferred choice during breastfeeding.

Fertility

There are no clinical studies with tinzaparin sodium regarding fertility.

4.7 Effects on ability to drive and use machines

Tinzaparin sodium has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

The most frequently reported undesirable effects are haemorrhage events, anaemia secondary to haemorrhage and injection site reactions.

Haemorrhage may present in any organ and have different degrees of severity. Complications may occur particularly when high doses are administered. Although major haemorrhages are uncommon, death or permanent disability has been reported in some cases.

Immune-mediated heparin-induced thrombocytopenia (type II) largely manifests within 5 to 14 days of receiving the first dose. Furthermore, a rapid-onset form has been described in patients previously exposed to heparin. Immune-mediated heparin-induced thrombocytopenia (type II) may be associated with arterial and venous thrombosis. Tinzaparin sodium must be discontinued in all cases of immune-mediated heparin-induced thrombocytopenia (see section 4.4).

In rare cases, tinzaparin sodium may cause hyperkalaemia due to hypoaldosteronism. Patients at risk include those with diabetes mellitus or renal impairment (see section 4.4).

Serious allergic reactions may sometimes occur. These include rare cases of skin necrosis, toxic skin eruption (e.g. Stevens-Johnson syndrome), angioedema and anaphylaxis. Treatment should be promptly discontinued at the slightest suspicion of such severe reactions.

The estimation of the frequency of undesirable effects is based on a pooled analysis of data from clinical studies and from spontaneous reporting.

Undesirable effects are listed by MedDRA SOC and the individual undesirable effects are listed starting with the most frequently reported. Within each frequency grouping, adverse reactions are presented in the order of decreasing seriousness.

Very common ≥1/10

Common ≥1/100 to < 1/10

Uncommon ≥1/1,000 to <1/100

Rare ≥1/10,000 to <1/1,000

Very rare <1/10,000

Not known (cannot be estimated from the available data)

Blood and lymphatic system disorders	
Common	Anaemia (incl. haemoglobin decreased)
Uncommon	Thrombocytopenia (type I) (incl. platelet count decreased)
Rare	Heparin-induced thrombocytopenia (type II) Thrombocytosis
Immune system disorders	
Uncommon	Hypersensitivity
Rare	Anaphylactic reaction
Metabolism and nutrition disorders	
Rare	Hyperkalaemia
Vascular disorders	

Common	Haemorrhage Haematoma
Uncommon	Bruising, ecchymosis and purpura
Hepatobiliary disorders	
Uncommon	Hepatic enzyme increased (incl. increased transaminases, ALT, AST and GGT)
Skin and subcutaneous tissue disorders	
Uncommon	Dermatitis (incl. dermatitis allergic and bullous) Rash Pruritus
Rare	Toxic skin eruption (including Stevens-Johnson syndrome) Skin necrosis Angioedema Urticaria
Musculoskeletal and connective tissue disorders	
Rare	Osteoporosis (in connection with long-term treatment)
Reproductive system and breast disorders	
Rare	Priapism
General disorders and administration site conditions	
Common	Injection site reaction (incl. injection site haematoma, haemorrhage, pain, pruritus, nodule, erythema and extravasation)

Paediatric population
Limited information derived from one study and postmarketing data indicates that the pattern of adverse reactions in children and adolescents is comparable to that in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Haemorrhage is the main complication of overdose. Due to the relatively short half-life of tinzaparin sodium (see section 5.2), minor haemorrhages can be managed conservatively following treatment discontinuation. Serious haemorrhage may require the administration of the antidote protamine sulfate. Patients should be carefully monitored.

Any hypovolaemia should be actively managed. Transfusion of fresh plasma may be used, if necessary. Plasma anti-Factor Xa and anti-Factor IIa activity should be measured during the management of overdose situations. Usually, the anticoagulant effects will have reduced to negligible levels after 24 hours, but treatment should be according to the patient's clinical condition.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antithrombotic agents, Heparin group, ATC code: B01AB10

Mechanism of action

Tinzaparin sodium is a low molecular weight heparin of porcine origin with an anti-Xa/anti-IIa ratio between 1.5 and 2.5. Tinzaparin sodium is produced by enzymatic depolymerisation of conventional unfractionated heparin. Like conventional heparin, tinzaparin sodium acts as an anticoagulant by potentiating antithrombin III's inhibition of activated coagulation factors, primarily factor Xa.

The biological activity of tinzaparin is standardised against the current "International standards for low molecular weight heparins", and expressed in anti-Xa international units (IU).

The anti-Xa activity of tinzaparin sodium is not less than 70 and not more than 120 IU/mg. The anti-IIa activity of tinzaparin sodium is approximately 55 IU/mg. The characteristic value of mass-average molecular mass of tinzaparin sodium is about 6,500 daltons.

Pharmacodynamic effects

Tinzaparin has a high antithrombin activity (anti-IIa), a low anti-Xa/anti-IIa ratio and an inhibition of thrombin formation with almost the same potency as unfractionated heparin. In addition to its anti-Xa/IIa activity, induction of TFPI (Tissue Factor Pathway Inhibitor) has been identified in patients.

Tinzaparin has a high average molecular weight (see Mechanism of action above).

Clinical efficacy and safety

Venous thromboembolism prophylaxis in moderate-risk surgery

In a double-blind, multi-centre study that included 1,290 patients who underwent general surgery, the patients were randomly assigned to groups that received either two doses of tinzaparin (2,500 IU; n = 431 or 3,500 IU; n = 430), or heparin 5,000 IU bolus dose (n = 429), to prevent deep vein thrombosis (DVT). The type of surgery was mostly abdominal (71%), gynaecological (13%) and urological (10%) and 57% of all patients were aged > 60 years. The treatments were administered subcutaneously 2 hours before surgery and continued for 7 to 10 days, and patients who required long-term prophylaxis continued with heparin after 10 days. The incidence of DVT before day 8 was 3.7% (2,500 IU), 1.6% (3,500 IU) and 1.6% (heparin). During the 1-month follow-up period, there was a significantly higher incidence of superficial and/or deep vein thrombosis in the 2,500 IU tinzaparin group (6%) compared with the 3,500 IU group (2.6%) and the heparin group (3.5%). All types of bleeding occurred in approximately 10% of each group during the hospital stay and in 3% from discharge and 1 month onwards, without statistically-significant differences between the three groups.

Venous thromboembolism prophylaxis in high-risk surgery

In a randomised, double-blind study that included 440 patients who underwent total hip replacement surgery, the patients were randomly assigned to groups that received either enoxaparin (4,000 IU once daily) or tinzaparin (4,500 IU once daily) for 15 days with the first injection 12 hours before surgery. The incidence of DVT was 20.1% (44/219) among the enoxaparin patients and 21.7% (48/221) among the tinzaparin patients. Proximal DVT occurred in 10.5% (23/219) of the enoxaparin patients and in 9.5% (21/221) of the tinzaparin patients. Severe bleeding was observed only in connection with the surgical wound (4 patients in the enoxaparin group and 2 in the tinzaparin group). Non-severe bleeding occurred in 21 patients in the enoxaparin group and 13 in the tinzaparin group.

Prophylaxis in haemodialysis patients

An open-label, long-term study that included 1,429 haemodialysis sessions with 52 patients showed no or minimal thrombosis, in 92.8% (1,326/1,429) and a satisfactory anticoagulation effect in 96% (1,370/1,427) of the sessions when tinzaparin was administered as a single bolus dose. The average dose of tinzaparin was 2,139 IU during the first sessions and 2,186 IU during the last sessions of the study. Haemorrhages in the skin or mucous membranes were observed in 27/1,408 (1.9%) of the dialysis sessions.

Special patient populations

Population with renal impairment

In an open-label, randomised, pharmacokinetic comparative study, it was investigated whether any accumulation occurred after repeated daily prophylactic doses of tinzaparin (4,500 IU) or enoxaparin (4,000 IU) over 8 days in elderly patients (> 75 years) with renal impairment (CrCl: 20 to 50 mL/min) and body weight < 65 kg. 55 patients were included in the analysis. The average anti-Xa activity increased significantly in the enoxaparin group (from 0.55 on day 1 to 0.67 on day 8; $p < 0.001$), but not in the tinzaparin group (from 0.44 on day 1 to 0.46 on day 8; $p = 0.296$). No VTE events occurred. Five cases of bleeding, two of which were severe, occurred in the tinzaparin group and four cases of bleeding, one of which was severe, occurred in the enoxaparin group.

In a prospective observational and multi-dose study, bioaccumulation of tinzaparin was evaluated. The study included 28 inpatients who were prescribed tinzaparin for non-surgical thrombosis prophylaxis and with an estimated glomerular filtration rate of ≤ 30 mL/min/1.73 m² (mean eGFR at baseline 20 mL/min/1.73 m²). Out of 28 enrolled patients, 14 completed a 5-day course of study treatment and 10 completed a 8-day course of study treatment. The patients received 3,500 IU once daily, with a decrease to 2,500 IU once daily if their body weight was < 40 kg, or increasing to 4,500 IU once daily with a BMI ≥ 30 kg/m². The median peak of the anti-Xa levels (range) was measured at the 4th hour on day 2 at 0.07 (0-0.24) IU/mL, 0.11 (0.07-0.25) IU/mL on day 5 and 0.09 (0.07-0.31) IU/mL on day 8. There was no statistically significant increase in the anti-Xa peak levels over time between day 2 and day 5. The range of variation for the anti-Xa peak levels was comparable with previously published data for surgical patients with normal renal function, receiving 3,500 IU tinzaparin. All anti-Xa peaks remained below 0.4 IU/mL and the anti-Xa trough levels

were not detectable, indicating the absence of bioaccumulation. No patient experienced thrombotic complications or severe bleeding events.

5.2 Pharmacokinetic properties

The absolute bioavailability based on anti-Xa activity after subcutaneous administration is approximately 90% and time to reach maximal activity is 4-6 hours.

Tinzaparin has a high, average molecular weight. Its elimination is dose-dependent and is a combination of a saturable elimination by the reticuloendothelial system and a non-saturable elimination via the renal route.

In healthy volunteers, the terminal elimination half-life following SC administration of tinzaparin at a dose of 4,500 IU or 175 IU/kg is approximately 3-4 hours based on anti-Xa activity.

Special patient populations

Pregnant women

The pharmacokinetic activity of tinzaparin has been studied in pregnant women. Data from sequential pharmacokinetic monitoring of 55 pregnant women who received tinzaparin at a dose of up to 175 IU/kg indicated that there was little or no influence of pregnancy on the pharmacokinetic properties of tinzaparin when compared with non-pregnant women.

Renal impairment

In patients treated with tinzaparin sodium (175 IU/kg), a population pharmacokinetic analysis showed no correlation between anti-Xa activity and creatinine clearance in moderate (30-50 mL/min) and severe (<30 mL/min) renal impairment. No clinically significant accumulation was observed in patients with creatinine clearance ≥20 mL/min.

The observed half-life of an intravenous bolus injection of 75 IU/kg that was administered just before dialysis was shorter (2.3 hours) than subcutaneous administration of the same dose on an off-dialysis day (3.9 hours).

Paediatric population
Preliminary data on the use of tinzaparin suggest that younger children including neonates and infants clear tinzaparin faster and therefore might require higher doses than older children. However, data are not sufficient to allow for dosing recommendations, see section 4.2.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol

Sodium acetate trihydrate

Sodium hydroxide

Hydrochloric acid, concentrated

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years.

Chemical and physical in use stability has been demonstrated for 28 days at 30°C.

From a microbiological point of view, once opened, the product may be stored for a maximum of 28 days at 30°C. Other in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

2 ml multi-dose glass vial containing 10,000 anti-Factor Xa IU/ml.

Pack sizes: 1, 2, 5 or 10 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 00043/0205

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

03/12/2025