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To view details for **FRAGMIN 10 000 IU/1ML SOLUTION FOR INJECTION**, please read and accept the disclaimer or go back to product listing for DALTEPARIN SODIUM.

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Product Name: **FRAGMIN 10 000 IU/1ML SOLUTION FOR INJECTION**

1. **LEAFLET MAH BRAND_PL 00057-0977.PDF** (99KB)

2. **SPC-DOC_PL 00057-0977.PDF** (68KB)

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Medicines & Healthcare products Regulatory Agency

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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Fragmin 10,000 IU/1 ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient

Dalteparin sodium (INN)
Quality according to Ph Eur and in-house specification.

Potency is described in International anti-factor Xa units (IU) of the 1st International Standard for Low Molecular Weight Heparin.

Content of the active ingredient
Ampoules containing dalteparin sodium, 10,000 IU (anti-factor Xa) in 1ml.

3 PHARMACEUTICAL FORM

Solution for injection for intravenous or subcutaneous administration.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Prevention of clotting in the extracorporeal circulation during haemodialysis or haemofiltration, in patients with chronic renal insufficiency or acute renal failure.

Treatment of venous thromboembolism (VTE) presenting clinically as deep vein thrombosis (DVT), pulmonary embolism (PE) or both.

Unstable angina and non-Q wave myocardial infarction (unstable coronary artery disease-UCAD), administered concurrently with aspirin.

Extended Use

Fragmin may be used beyond 8 days in patients awaiting angiography/ revascularisation procedures (see Section 5.1)

4.2 Posology and method of administration

Recommended dosage for adults

(i) Prevention of clotting during haemodialysis and haemofiltration

In chronic renal insufficiency for patients with no known additional bleeding risk, the dosage is:

(a) Long-term haemodialysis or haemofiltration - duration of haemodialysis/haemofiltration more than 4 hours;

An I.V. bolus injection of Fragmin 30-40 IU (anti-Factor Xa)/kg bodyweight, followed by an infusion of 10-15 IU (anti-Factor Xa)/kg bodyweight/hour.

(b) Short-term haemodialysis or haemofiltration - duration of haemodialysis/haemofiltration less than 4 hours:

Either as above, or, a single IV. bolus injection of Fragmin 5000 IU (anti-Factor Xa).

Both for long and short-term haemodialysis and haemofiltration, the plasma anti-Factor Xa levels should be within the range 0.5-1.0 IU (anti-Factor Xa)/ml.

In acute renal failure, or chronic renal failure in patients with a high risk of bleeding, the dosage is:

An I.V. bolus injection of Fragmin 5-10 IU (anti-Factor Xa)/kg bodyweight, followed by an infusion of 4-5 IU (anti-Factor Xa)/kg bodyweight/hour.

The plasma anti-Factor Xa levels should be within the range 0.2-0.4 IU (anti-Factor Xa)/ml.

When considered necessary, it is recommended that the antithrombotic effect of Fragmin be monitored by analysing anti-Factor Xa activity using a suitable chromogenic substrate assay. This is because Fragmin has only a moderate prolonging effect on clotting time assays such as APTT or thrombin time.

(ii) Treatment of venous thromboembolism (VTE).

Fragmin can be administered subcutaneously either as a single daily injection or as twice daily injections.

(a) Once daily administration

200 IU/kg body weight is administered sc. once daily. Monitoring of the anticoagulant effect is not necessary. The single daily dose should not exceed 18,000 IU.

(b) Twice daily administration

A dose of 100 IU/kg body weight administered sc. twice daily can be used for patients with increased risk of bleeding. Monitoring of the treatment is generally not necessary but can be performed with a functional anti-Factor Xa assay. Maximum plasma levels are obtained 3-4 hours after sc. injection, when samples should be taken. Recommended plasma levels are between 0.5-1.0 IU (anti-Factor Xa)/ml.

Simultaneous anticoagulation with oral vitamin K antagonists can be started immediately. Treatment with Fragmin is continued until the prothrombin complex levels (factor II, VII, IX and X) have decreased to a therapeutic level. At least five days of combined treatment is normally required.

(iii) Unstable coronary artery disease

120 IU/kg body weight are administered subcutaneously twelve hourly for up to 8 days if considered of benefit by the physician . The maximum dose is 10,000 IU/12 hours

Patients needing treatment beyond 8 days, while awaiting angiography/revascularisation, should receive a fixed dose of either 5,000 IU (women < 80 kg and men <70 kg) or 7,500 IU (women ≥80 kg and men ≥70 kg) 12 hourly. Treatment is recommended to be given until the day of the revascularisation procedure (PTCA or CA BG) but not for more than 45 days.

Paediatric population

The safety and efficacy of dalteparin sodium in children has not been established. Currently available data are described in sections 5.1 and 5.2 but no recommendation on a posology can be made.

Monitoring Anti-Xa levels in children

Measurement of peak anti-Xa levels at about 4 hours post-dose should be considered for certain special populations receiving Fragmin, such as children. For therapeutic treatment with doses administered once daily, peak anti-Xa levels should generally be maintained between 0.5 and 1.0 IU/mL measured at 4 hours post-dose. In the case of low and changing physiologic renal function such as in neonates, close monitoring of anti-Xa levels is warranted. For prophylaxis treatment the anti- Xa levels should generally be maintained between 0.2-0.4 IU/mL.

As with all antithrombotic agents, there is a risk of systemic bleeding with Fragmin administration. Care should be taken with Fragmin use in high dose treatment of newly operated patients. After treatment is initiated patients should be carefully monitored for bleeding complications. This may be done by regular physical examination of the patients, close observation of the surgical drain and periodic measurements of hemoglobin, and anti-Xa determinations.

Elderly

Fragmin has been used safely in elderly patients without the need for dosage adjustment.

4.3. Contraindications

Known hypersensitivity to Fragmin or other low molecular weight heparins and/or heparins e.g. history of confirmed or suspected immunologically mediated heparin induced thrombocytopenia (type II); acute gastroduodenal ulcer; cerebral haemorrhage; known haemorrhagic diathesis or other active haemorrhage; serious coagulation disorders; acute or sub-acute septic endocarditis; injuries to and operations on the central nervous system, eyes and ears.

In patients receiving Fragmin for treatment rather than prophylaxis, local and/or regional anaesthesia in elective surgical procedures is contra-indicated with high doses of dalteparin (such as those needed to treat acute deep-vein thrombosis, pulmonary embolism, and unstable coronary artery disease).

4.4. Special warnings and precautions for use

Do not administer by the intramuscular route. Due to the risk of haematoma, intramuscular injection of other medical preparations should be avoided when the twenty-four hour dose of dalteparin exceeds 5,000 IU.

Caution should be exercised in patients in whom there is an increased risk of bleeding complications, e.g. following surgery or trauma, haemorrhagic stroke, severe liver or renal failure, thrombocytopenia or defective platelet function, uncontrolled hypertension, hypertensive or diabetic retinopathy, patients receiving concurrent anticoagulant/antiplatelet agents (see interactions section). Caution shall also be observed at high-dose treatment with dalteparin (such as those needed to treat acute deep-vein thrombosis, pulmonary embolism, and unstable coronary artery disease).

It is recommended that platelets be counted before starting treatment with Fragmin and monitored regularly. Special caution is necessary in rapidly developing thrombocytopenia and severe thrombocytopenia (<100,000/µl) associated with positive or unknown results of in-vitro tests for anti-platelet antibody in the presence of Fragmin or other low molecular weight (mass) heparins and/or heparin

Fragmin induces only a moderate prolongation of the APTT and thrombin time. Accordingly, dosage increments based upon prolongation of the APTT may cause overdosage and bleeding. Therefore, prolongation of the APTT should only be used as a test of overdosage.

Monitoring Anti-Xa Levels
Monitoring of Anti-Xa Levels in patients using Fragmin is not usually required but should be considered for specific patient populations such as paediatrics, those with renal failure, those who are very thin or morbidly obese, pregnant or at increased risk for bleeding or rethrombosis

Where monitoring is necessary, laboratory assays using a chromogenic substrate are considered the method of choice for measuring anti-Xa levels. Activated partial thromboplastin time (APTT) or thrombin time should not be used because these tests are relatively insensitive to the activity of dalteparin. Increasing the dose of dalteparin in an attempt to prolong APTT may result in bleeding (see section 4.9).

Patients under chronic haemodialysis with dalteparin need as a rule fewer dosage adjustments and as a result fewer controls of anti-Xa levels. Patients undergoing acute haemodialysis may be more unstable and should have a more comprehensive monitoring of anti-Xa levels (see section 5.2).

Patients with severely disturbed hepatic function may need a reduction in dosage and should be monitored accordingly.

If a transmural myocardial infarction occurs in patients where thrombolytic treatment might be appropriate, this does not necessitate discontinuation of treatment with Fragmin but might increase the risk of bleeding.

As individual low molecular weight (mass) heparins have differing characteristics, switching to an alternative low molecular weight heparin should be avoided. The directions for use relating to each specific product must be observed as different dosages may be required.

Interchangeability with other anticoagulants
Dalteparin cannot be used interchangeably (unit for unit) with unfractionated heparin. Other low molecular weight heparins, or synthetic polysaccharides. Each of these medicines differ in their starting raw materials, manufacturing process, physico-chemical, biological, and clinical properties, leading to differences in biochemical identity, dosing, and possibly clinical efficacy and safety. Each of these medicines is unique and has its own instructions for use.

Heparin can suppress adrenal secretion of aldosterone leading to hyperkalaemia, particularly in patients such as those with diabetes mellitus, chronic renal failure, pre-existing metabolic acidosis, a raised plasma potassium or taking potassium sparing drugs. The risk of hyperkalaemia appears to increase with duration of therapy but is usually reversible. Plasma potassium should be measured in patients at risk before starting heparin therapy and monitored regularly thereafter particularly if treatment is prolonged beyond about 7 days.

When neuraxial anaesthesia (epidural/spinal anaesthesia) or spinal puncture is employed, patients are at risk of developing an epidural or spinal hematoma, which can result in long-term or permanent paralysis. The risk of these events is increased by the use of indwelling epidural catheters or by the concomitant use of drugs affecting hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants. The risk also appears to be increased by traumatic or repeated epidural or spinal puncture. Patients should be monitored frequently for signs and symptoms of neurological impairment when anticoagulation is given in connection with epidural/spinal anaesthesia.

Insertion or removal of the epidural or spinal catheter should be postponed to 10-12 hours after dalteparin doses administered for thrombosis prophylaxis, while in those receiving higher therapeutic dalteparin doses (such as 100 IU/kg -120 IU/kg every 12 hours or 200 IU/kg once daily), the interval should be a minimum of 24 hours.

Should a physician, as a clinical judgement, decide to administer anticoagulation in the context of epidural or spinal anaesthesia, extreme vigilance and frequent monitoring must be exercised to detect any signs and symptoms of neurologic impairment such as back pain, sensory or motor deficits (numbness and weakness in lower limbs) and bowel or bladder dysfunction. Nurses should be trained to detect such signs and symptoms. Patients should be instructed to inform immediately a nurse or a clinician if they experience any of these.

If signs or symptoms of epidural or spinal haematoma are suspected, urgent diagnosis and treatment may include spinal cord decompression.

There have been no adequate studies to assess the safe and effective use of Fragmin in preventing valve thrombosis in patients with prosthetic heart valves. Prophylactic doses of Fragmin are not sufficient to prevent valve thrombosis in patients with prosthetic heart valves. The use of Fragmin cannot be recommended for this purpose.

At long-term treatment of unstable coronary artery disease, such as e.g., before revascularisation, dose reduction should be considered at reduced kidney function (S-creatinine > 150 μmol/l).

Paediatric population:
Clinical experience of treatment of children is limited. If dalteparin is used in children the anti-Xa levels should be monitored.

The administration of medications containing benzyl alcohol as a preservative to premature neonates has been associated with a fatal "Gasping Syndrome" (see section 4.6).

Elderly patients (especially patients aged eighty years and above) may be at an increased risk for bleeding complications within the therapeutic dosage ranges. Careful clinical monitoring is advised.

4.5 Interaction with other medicinal products and other forms of interaction

The possibility of the following interactions with Fragmin should be considered:

i) An enhancement of the anticoagulant effect by anticoagulant/antiplatelet agents e.g. aspirin/dipyridamole, GP IIb/IIIa receptor antagonists, Vitamin K antagonists, NSAIDs e.g. indometacin, cytostatics, dextran, thrombolytics, sulfinpyrazone, probenecid, and etacrynic acid.

ii) A reduction of the anticoagulant effect may occur with concomitant administration of antihistamines, cardiac glycosides, tetracycline and ascorbic acid.

Because NSAIDs and ASA analgesic/anti-inflammatory doses reduce production of vasodilatatory prostaglandins, and thereby renal blood flow and the renal excretion, particular care should be taken when administering dalteparin concomitantly with NSAIDs or high dose ASA in patients with renal failure.

However, if there are no specific contraindications, patients with unstable coronary artery disease (unstable angina and non-Q-wave infarction) can be treated with low doses of acetylsalicylic acid.

As heparin has been shown to interact with intravenous nitroglycerine, high dose penicillin, quinine and tobacco smoking interaction cannot be ruled out for dalteparin.

Paediatric population

Interaction studies have only been studied in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy
Dalteparin does not pass the placenta. A large amount of data on pregnant women (more than 1000 exposed outcomes) indicate no malformative nor feto/ neonatal toxicity. Fragmin can be used during pregnancy if clinically needed.

If dalteparin is used during pregnancy, the possibility of foetal harm appears remote. However, because the possibility of harm cannot be completely ruled out, dalteparin should be used during pregnancy only if clearly needed.

There are more than 2,000 published cases (studies, case series and case reports) on administration of dalteparin in pregnancy. As compared with unfractionated heparin, a lower bleeding tendency and reduced risk of osteoporotic fracture was reported. The largest prospective study "Efficacy of Thromboprophylaxis as an Intervention during Gravidity" (EThIG), involved 810 pregnant women and investigated a pregnancy-specific scheme for risk stratification (low, high, very high risk of venous thromboembolism) with daily doses of dalteparin between 50 – 150 IU/kg body weight (in single cases up to max. 200 IU/kg body weight). However, only limited randomised controlled studies are available on the use of low molecular weight heparins in pregnancy.

Animal experiments did not show any teratogenic or fetotoxic properties of dalteparin (see section 5.3).

Epidural anaesthesia during childbirth is absolutely contraindicated in women who are being treated with high-dose anticoagulants (see section 4.3). Caution is recommended when treating patients with an increased risk of haemorrhage, such as perinatal women (see section 4.4). In pregnant women during the last trimester, dalteparin anti-Xa half-lives of 4 to 5 hours were measured.

Fragmin 100,000 IU/4ml multidose vial contains benzyl alcohol as a preservative. As benzyl alcohol may cross the placenta, Fragmin without preservative should therefore be used during pregnancy.

Therapeutic failures have been reported in pregnant women with prosthetic heart valves on full anti-coagulant doses of low molecular weight heparin. In the absence of clear dosing, efficacy and safety information in this circumstance, Fragmin is not recommended for use in pregnant women with prosthetic heart valves.

Breast-feeding
Limited data are available for excretion of dalteparin in human milk. One study in 15 women (between day 3 and 5 of lactation and 2 to 3 hours after receiving prophylactic doses of dalteparin detected small amounts of anti- factor Xa levels of 2 to 8% of plasma levels in breast milk, equivalent to a milk/plasma ratio of <0.025-0.224. An anticoagulant effect on the infant appears unlikely.

A risk to the suckling child cannot be excluded. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with

Fragmin should be made taking into account the benefit of breast-feeding to the child and the benefit of Fragmin therapy to the woman.

Fertility
Based on current clinical data there is no evidence that dalteparin sodium effects fertility. No effects on fertility, copulation or peri- and postnatal development were noted when dalteparin sodium was tested in animals.

4.7 Effects on ability to drive and use machines

Fragmin does not affect the ability to drive or operate machinery.

4.8 Undesirable effects

About 3% of the patients having had prophylactic treatment reported side-effects.

The reported adverse reactions, which may possibly be associated to dalteparin sodium, are listed in the following table by system organ class and frequency group: *common* (≥1/100, <1/10), *uncommon* (≥1/1000, <1/100), *rare* (≥1/10 000).

System Organ Class	*Frequency*	*Adverse reactions*
Blood and lymphatic system disorders	Common	Mild thrombocytopenia (type I), which usually is reversible during the treatment
	Not Known*	Immunologically-mediated heparin-induced thrombocytopenia (type II, with or without associated thrombotic complications)
Immune system disorders	Uncommon	Hypersensitivity
	Not Known*	Anaphylactic reactions
Nervous system disorders	Not Known*	Intracranial bleeds have been reported and some have been fatal
Cardiac disorders	Not Known*	Prosthetic cardiac valve thrombosis
Vascular disorders	Common	Haemorrhage
Gastrointestinal disorders	Not Known*	Retroperitoneal bleeds have been reported and some have been fatal
Hepatic and biliary disorders	Common	Transient elevation of transaminases
Skin and subcutaneous tissue disorders	Uncommon	Urticaria, pruritus
	Rare	Skin necrosis, transient alopecia
	Not Known*	Rash
General disorders and administration site conditions	Common	Subcutaneous haematoma at the injection site Pain at the injection site
Injury, Poisoning and	Not Known*	Spinal or epidural hematoma

Procedural Complications		

*(cannot be established from available data)

The risk of bleeding is depending on dose. Most bleedings are mild. Severe bleedings have been reported, some cases with fatal outcome.

Heparin products can cause hypoaldosteronism which may result in an increase in plasma potassium. Rarely, clinically significant hyperkalaemia may occur particularly in patients with chronic renal failure and diabetes mellitus (see section 4.4).

Long term treatment with heparin has been associated with a risk of osteoporosis. Although this has not been observed with dalteparin, the risk of osteoporosis cannot be excluded.

Paediatric population
Frequency, type and severity of adverse reactions in children are expected to be the same as in adults. The safety of long term dalteparin administration has not been established.

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.

4.9 Overdose
The anticoagulant effect (i.e. prolongation of the APTT) induced by Fragmin is inhibited by protamine. Since protamine itself has an inhibiting effect on primary haemostasis it should be used only in an emergency.

The prolongation of the clotting time induced by Fragmin may be fully neutralised by protamine, but the anti-Factor Xa activity is only neutralised to about 25-50%. 1 mg of protamine inhibits the effect of 100 IU (anti-Factor Xa) of Fragmin.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Dalteparin sodium is a low molecular weight heparin fraction (weight average molecular weight of 6000 Daltons (range between 5,600 and 6,400 Daltons)) produced from porcine-derived heparin sodium.

Mechanism of action
Dalteparin sodium is an antithrombotic agent, which acts mainly through its ability to potentiate the inhibition of Factor Xa and thrombin by antithrombin. It

has a relatively higher ability to potentiate Factor Xa inhibition than to prolong plasma clotting time (APTT).

Pharmacodynamic effects
Compared with standard, unfractionated heparin, dalteparin sodium has a reduced adverse effect on platelet function and platelet adhesion, and thus has only a minimal effect on primary haemostasis. Some of the antithrombotic properties of dalteparin sodium are thought to be mediated through the effects on vessel walls or the fibrinolytic system.

Clinical efficacy and safety
In a prospectively randomised study in 3489 patients (FRISC II) with acute coronary syndromes, early invasive strategy was clearly superior to non – invasive strategy.

In a post-hoc analysis, the extended use of Fragmin, up to Day 45 reduced the incidence of death and/or MI compared with placebo in the non-invasive group (revascularisation only if necessary).

The use of Fragmin beyond 8 days did not significantly reduce the incidence of death and/or MI, compared to placebo, in patients who were contraindicated to early angiography and revascularisation.

Paediatric population

There is limited safety and efficacy information on the use of dalteparin in paediatric patients. If dalteparin is used in these patients, anti-Xa levels should be monitored.

The largest prospective study investigated the efficacy, safety and relation of dose to plasma anti-Xa activity of dalteparin in prophylaxis and therapy of arterial and venous thrombosis in 48 paediatric patients (Nohe et al, 1999).

Nohe et al (1999) Study Demographics and Trial Design

Trial design	**Patients**	**Diagnosis**	**Indication, Fragmin Dose, Target anti-Xa, Duration**		
Single-center, open label trial; (n = 48)	Age: 31 week preterm to 18 years Gender: 32 males, 16 females	Arterial or venous thrombosis; PVOD; PPH	Prophylaxis: (n = 10) 95 ± 52 anti-Xa IU/kg sc qd; 0.2 to 0.4 IU/mL 3-6 months	Primary Therapy: (n = 25) 129 ± 43 anti-Xa IU/kg sc qd; 0.4 to 1.0 IU/mL 3-6 months	Secondary Therapy: (n = 13) 129 ± 43 anti-Xa IU/kg sc qd; 0.4 to 1.0 IU/mL 3-6 months

In this study, no thromboembolic events occurred in the 10 patients receiving dalteparin for thromboprophylaxis. In the 23 patients given dalteparin for primary antithrombotic therapy of arterial or venous thrombosis, complete recanalization was seen in 7/23 (30%), partial recanalization in 7/23 (30%) and no recanalization in 9/23 (40%). In the 8 patients administered dalteparin for secondary antithrombotic therapy following successful thrombolysis, recanalisation was maintained or improved. In the 5 patients receiving dalteparin for secondary therapy following failed thrombolysis, no recanalization was seen. Minor bleeding, reported in 2/48 children (4%), resolved after dose reduction. Patient platelet counts ranged from 37,000/μl to 574,000/μl. The authors attributed platelet counts below normal (150,000/μl) to immunosuppressive therapy. A reduction in platelet count ≥ 50% of the initial value, a sign of heparin-induced thrombocytopenia type 2 (HIT 2), was not observed in any patient. For both prophylaxis and therapy groups, the dalteparin doses (anti-Xa IU/kg) required to achieve target anti-Xa activities (IU/ml) were inversely related to age ($r^2 = 0.64$, P = 0.017; $r^2 = 0.13$, P = 0.013). The predictability of the anticoagulant effect with weight-adjusted doses appears to be reduced in children compared to adults, presumably due to altered plasma binding (see section 5.2).

5.2 Pharmacokinetic properties

Elimination
The half life following i.v. and s.c. administration is 2 hours and 3.5 - 4 hours respectively, twice that of unfractionated heparin.

Bioavailability
The bioavailability following s.c. injection is approximately 87 per cent and the pharmacokinetics are not dose dependent. The half life is prolonged in uraemic patients as dalteparin sodium is eliminated primarily through the kidneys.

Special Populations

Haemodialysis:
In patients with chronic renal insufficiency requiring haemodialysis, the mean terminal hal-life of anti-Factor Xa activity following a single intravenous dose

of 5000 IU dalteparin was 5.7 ± 2.0 hours, i.e. considerably longer than values observed in healthy volunteers, therefore, greater accumulation can be expected in these patients.

*Paediatric Populatio*n:
Infants less than approximately 2 to 3 months of age or <5kg have increased LMWH requirements per kg likely due to their larger volume of distribution. Alternative explanations for the increased requirement of LMWH per body weight in young children include altered heparin pharmacokinetics and/or a decreased expression of anticoagulant activity of heparin in children due to decreased plasma concentrations of antithrombin.

5.3 Preclinical safety data

The acute toxicity of dalteparin sodium is considerably lower than that of heparin. The only significant finding, which occurred consistently throughout the toxicity studies after subcutaneous administration of the higher dose levels was local haemorrhage at the injection sites, dose-related in incidence and severity. There was no cumulative effect on injection site haemorrhages.

The haemorrhagic reaction was reflected in dose related changes in the anticoagulant effects as measured by APTT and anti-Factor Xa activities.

It was concluded that dalteparin sodium did not have a greater osteopenic effect than heparin since at equivalent doses the osteopenic effect was comparable.

The results revealed no organ toxicity irrespective of the route of administration, doses or the duration of treatment. No mutagenic effect was found. No embryotoxic or teratogenic effects and no effect on fertility reproductive capacity or peri- and postnatal development was shown.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium chloride (Ph. Eur.)
Water for Injections (Ph. Eur.)

6.2 Incompatibilities

The compatibility of Fragmin with products other than those mentioned under 6.6 has not been investigated.

6.3. Shelf life

3 years

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

Clear glass ampoules (Ph Eur Type 1) containing dalteparin sodium, 10,000 IU (anti-factor Xa) in 1ml

6.6 Special precautions for disposal

Fragmin solution for injection is compatible with isotonic sodium chloride (9 mg/ml) or isotonic glucose (50 mg/ml) infusion solutions in glass bottles and plastic containers for up to 24 hours. Compatibility between Fragmin and other products has not been studied.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 00057/0977

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05 April 2002

10 DATE OF REVISION OF THE TEXT

10/05/2016