

FRAGMIN® (dalteparin sodium)
ABBREVIATED PRESCRIBING INFORMATION
ALL PRESENTATIONS AND INDICATIONS

(See Fragmin Summary of Product Characteristics for full Prescribing Information).

Fragmin is administered by subcutaneous injection for all indications except for the prevention of clotting in the extracorporeal system during haemodialysis and haemofiltration where it is administered either intravenously or into the arterial side of the dialyzer.

Treatment of VTE

Fragmin 7,500 IU, 10,000 IU, 12,500 IU, 15,000 IU, 18,000 IU single-dose syringes containing dalteparin sodium 7,500 IU in 0.3 ml; 10,000 IU in 0.4 ml; 12,500 IU in 0.5 ml; 15,000 IU in 0.6 ml; 18,000 IU in 0.72 ml. **Indication:** Treatment of venous thromboembolism (VTE) presenting clinically as deep vein thrombosis (DVT), pulmonary embolism (PE) or both. **Dosage and Administration:** By subcutaneous (s.c.) injection. *Normal risk of bleeding:* single daily dose to match bodyweight: <46 kg — 7,500 IU; 46-56 kg — 10,000 IU; 57-68 kg — 12,500 IU; 69-82 kg — 15,000 IU; ≥83 kg — 18,000 IU. Single daily dose should not exceed 18,000 IU. **Fragmin 10,000 IU/1 ml Ampoules** containing 10,000 IU dalteparin sodium in 1 ml. **Fragmin 100,000 IU/4 ml Multidose Vial** containing 100,000 IU dalteparin sodium in 4 ml with benzyl alcohol. **Indication:** Treatment of venous thromboembolism (VTE) presenting clinically as deep vein thrombosis (DVT), pulmonary embolism (PE) or both. **Dosage and Administration:** By s.c. injection. *Normal risk of bleeding:* Fragmin 200 IU/kg s.c. once daily. Single daily dose should not exceed 18,000 IU. *Increased risk of bleeding:* Fragmin 100 IU/kg s.c. twice daily, up to a maximum total daily dose of 18,000 IU. For VTE treatment, anticoagulant monitoring is generally not necessary. Simultaneous anticoagulation with oral vitamin K antagonists can start immediately. Continue Fragmin until prothrombin complex levels have decreased to a therapeutic level – usually at least 5 days of combined treatment. **Legal Category:** POM. **Basic NHS Prices:** 10 prefilled syringes: 7,500 IU/0.3 ml £42.34; 5 prefilled syringes: 10,000 IU/0.4 ml £28.23; 12,500 IU/0.5 ml £35.29; 15,000 IU/0.6 ml £42.34; 18,000 IU/0.72 ml £50.82. For 10 ampoules: 10,000 IU/1 ml £51.22. For 1 Multidose Vial: 100,000 IU/4 ml £48.66. **PL Numbers:** 7,500 IU/0.3 ml 00057/0985. 10,000 IU/0.4 ml 00057/0976. 12,500 IU/0.5 ml 00057/0980. 15,000 IU/0.6 ml 00057/0981. 18,000 IU/0.72 ml 00057/0982. 10,000 IU/1 ml Ampoules 00057/0977. 100,000 IU/4 ml Multidose Vial 00057/0979.

Surgical Thromboprophylaxis

Fragmin 2,500 IU/0.2 ml or Fragmin 5,000 IU/0.2 ml single-dose syringes containing dalteparin sodium. **Indication:** Peri- and post-operative surgical thromboprophylaxis. **Dosage and Administration:** By s.c. injection. *Moderate risk of thrombosis:* Fragmin 2,500 IU s.c. 1-2 hours before surgery; thereafter 2,500 IU s.c. once daily in morning until full ambulation (usually 5-7 days). *High risk of thrombosis:* Fragmin 2,500 IU s.c. 1-2 hours before surgery; then again 8-12 hours later. Thereafter, 5,000 IU s.c. once daily in morning until full ambulation (usually 5-7 days). Alternatively, 5,000 IU Fragmin s.c. on evening before surgery, then 5,000 IU s.c. on each subsequent evening. Prolonged thromboprophylaxis in hip replacement surgery: 5,000 IU Fragmin s.c. on evening before surgery, then 5,000 IU s.c. on each subsequent evening up to 5 weeks post-operatively. If Fragmin is to be commenced post-operatively the first dose of Fragmin (2,500 IU) should be administered as soon as the perceived risk of bleeding is no longer present. **Legal Category:** POM. **Basic NHS Prices:** 10 prefilled syringes: 2,500 IU/0.2 ml £18.58; 5,000 IU/0.2 ml £28.23. **PL Numbers:** 2,500 IU/0.2 ml 00057/0983; 5,000 IU/0.2 ml 00057/0984.

Medical Thromboprophylaxis

Fragmin 5,000 IU/0.2 ml single-dose syringes containing dalteparin sodium. **Indication:** The prophylaxis of proximal DVT in patients bedridden due to a medical condition, including, but not limited to: congestive cardiac failure (NYHA class III or IV), acute respiratory failure or acute infection, who also have a predisposing risk factor for venous thromboembolism such as age over 75 years, obesity, cancer or previous history of VTE. **Dosage and Administration:** 5,000 IU s.c. once daily prescribed for up to 14 days. **Legal Category:** POM. **Basic NHS Prices:** 10 prefilled syringes 5,000 IU/0.2 ml: £28.23. **PL Number:** 00057/0984.

Haemodialysis or Haemofiltration

Fragmin 10,000 IU/1 ml or Fragmin 10,000 IU/4 ml Ampoules containing dalteparin sodium 10,000 IU in 1 ml and 10,000 IU in 4 ml. **Indication:** Prevention of clotting in the extracorporeal circulation during haemodialysis or haemofiltration, in patients with chronic renal insufficiency or acute renal failure. **Dosage and Administration:** Administer Fragmin into the arterial side of the dialyzer or intravenously. In chronic

renal insufficiency with no known additional bleeding risk: *Long-term haemodialysis or haemofiltration (more than 4 hours)*: Fragmin intravenous (i.v.) bolus injection 30-40 IU/kg body weight, followed by an infusion of 10-15 IU/kg body weight/hour. *Short-term haemodialysis or haemofiltration (less than 4 hours)*: A single bolus injection of 5000 IU can be administered, either intravenously or into the arterial side of the extracorporeal system, at the start of the procedure. Alternatively, an I.V. bolus injection of Fragmin 30-40 IU/kg body weight, followed by an infusion of 10-15 IU/kg bodyweight/hour.

The 5000 IU starting dose for the single bolus dosing regimen can be adjusted, session-to-session, based on the outcome of the previous dialysis; the dose may be increased or decreased in steps of 500 or 1000 IU (according to clinical judgement) until a satisfactory outcome is obtained. For both long and short-term haemodialysis and haemofiltration the plasma anti-Factor Xa levels should be within the range 0.5-1.0 IU/ml. *In acute renal failure, or patients at high risk of bleeding*: i.v. bolus injection of Fragmin 5-10 IU/kg body weight, followed by an infusion of 4-5 IU/kg body weight/hour and plasma anti-Factor Xa levels should be within the range 0.2-0.4 IU/ml. **Legal Category**: POM. **Basic NHS Prices**: For 10 ampoules: 10,000 IU/1 ml £51.22. 10,000 IU/4 ml £51.22. **PL Numbers**: 10,000 IU/1 ml 00057/0977. 10,000 IU/4 ml 00057/0978.

Unstable Angina

Fragmin Graduated Syringe 10,000 IU/ml Solution for Injection single-dose syringe containing dalteparin sodium 10,000 IU in 1 ml. **Fragmin 10,000 IU/1 ml Ampoules** containing 10,000 IU dalteparin sodium in 1 ml. **Fragmin 7,500 IU single-dose syringes** containing 7,500 IU in 0.3 ml. **Indication**: Unstable angina and non Q-wave myocardial infarction administered concurrently with aspirin. Extended Use – beyond 8 days in patients awaiting angiography/revascularisation. **Dosage and Administration**: Duration of therapy; acute phase: 120 IU/kg body weight administered s.c. 12 hourly for up to 8 days. Maximum dose is 10,000 IU/12 hours. Extended phase: beyond 8 days, for those awaiting revascularisation, treatment is recommended to be given until the day of the invasive procedure in a fixed dose of 5,000 IU (women <80 kg and men <70 kg) or 7,500 IU (women ≥80 kg and men ≥70 kg) 12 hourly. Treatment until the revascularisation procedure but not for more than 45 days. Maximum dose 10,000 IU/12 hours. **Legal Category**: POM. **Basic NHS Prices**: For 5 single-dose graduated syringes: 10,000 IU/1 ml £28.23. For 10 ampoules: 10,000 IU/1 ml £51.22. For 10 prefilled syringes: 7,500 IU/0.3 ml £42.34. **PL Numbers**: Graduated Syringe 10,000 IU/ml Solution for Injection single-dose syringe 00057/0986. 10,000 IU/1 ml Ampoules 00057/0977, 7,500 IU single-dose syringes 00057/0985.

Extended treatment of Symptomatic Venous Thromboembolism in patients with Solid Tumours

Fragmin 5,000 IU, 7,500 IU, 10,000 IU, 12,500 IU, 15,000 IU, 18,000 IU single-dose syringes containing dalteparin sodium 5,000 IU in 0.2 ml; 7,500 IU in 0.3 ml; 10,000 IU in 0.4 ml; 12,500 IU in 0.5 ml; 15,000 IU in 0.6 ml; 18,000 IU in 0.72 ml. **Indication**: Patients with solid tumours: Extended treatment of symptomatic VTE and prevention of its recurrence. **Dosage and Administration**: Administer Fragmin 200 IU/kg total body weight s.c. once daily for month 1 (first 30 days of treatment), followed by a Fragmin dose of approximately 150 IU/kg, s.c., once daily for months 2-6 using fixed-dose syringes. Maximum daily dose should not exceed 18,000 IU. In cancer patients with body weight <40 kg at time of venous thromboembolic event, Fragmin should not be used for extended treatment of symptomatic VTE and prevention of its recurrences due to lack of data (refer to SPC for dosing tables). *Renal failure*: In the case of significant renal failure, defined as a creatinine clearance <30 ml/min, the dose of Fragmin should be adjusted based on anti-Factor Xa activity (refer to SPC for further information). In the case of chemotherapy-induced thrombocytopenia, the Fragmin dose should be interrupted/reduced (refer to SPC for further information). **Legal Category**: POM. **Basic NHS Prices**: 10 prefilled syringes: 5,000 IU/0.2 ml £28.23; 7,500 IU/0.3 ml £42.34; 5 prefilled syringes: 10,000 IU/0.4 ml £28.23; 12,500 IU/0.5 ml £35.29; 15,000 IU/0.6 ml £42.34; 18,000 IU/0.72 ml £50.82. **PL Numbers**: 5,000 IU/0.2 ml 00057/0984. 7,500 IU/0.3 ml 00057/0985. 10,000 IU/0.4 ml 00057/0976. 12,500 IU/0.5 ml 00057/0980. 15,000 IU/0.6 ml 00057/0981. 18,000 IU/0.72 ml 00057/0982.

All Presentations

Use in Children: Safety and efficacy not established. **Use in Elderly**: No dose adjustment needed. **Contraindications**: Known hypersensitivity to Fragmin or other low molecular weight heparins and/or heparins; 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 or ears. Known hypersensitivity to benzyl alcohol for Multidose Vial presentation. In patients receiving Fragmin for treatment rather than prophylaxis, local and/or regional anaesthesia in elective surgical procedures is contra-indicated with the higher treatment doses of dalteparin. Dalteparin should not be used in patients who have suffered a recent (within 3 months) stroke unless due to systemic emboli. In cancer patients with body weight <40 kg at time of venous thromboembolic event, Fragmin should not be used for extended treatment of symptomatic VTE and prevention of its recurrences due to lack of data. **Warnings and Precautions:** Do not administer by intramuscular (i.m.) route. Due to risk of haematoma, other medicines given i.m. should be avoided for 24 hours if the dose of dalteparin exceeds 5,000 IU. Caution in conditions with increased risk of bleeding; 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 and in elderly patients ≥ 80 years may be at an increased risk of bleeding complications within therapeutic dosage ranges where careful clinical monitoring is required. Caution should also be observed at high dose treatment with dalteparin especially in patients treated for acute DVT, PE or unstable coronary artery disease. Monitoring of anti-Xa levels is not usually required but should be considered for certain special 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. Close monitoring is recommended in the case of low and changing physiologic renal function, e.g. neonates. 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. Monitor plasma potassium before and during Fragmin if risk of hyperkalaemia. Careful observation and care needed for patients having spinal or epidural anaesthesia. Not recommended for use in the prevention of valve thrombosis in patients with prosthetic heart valves. Limited data are available regarding the safety and efficacy of antithrombotic therapy in patients with primary or metastatic tumours of the brain who develop concurrent thromboembolic events. There is a risk of fatal intracranial bleeding with use of anticoagulation in this category of patients. Therefore, if treatment with Fragmin is considered it should be monitored closely with regular re-assessment of the status of tumour involvement of the brain and other individual risks. Thrombocytopenia, should it occur, usually appears within 3 weeks following the beginning of therapy. It is therefore recommended that the platelet counts are measured before starting treatment with Fragmin and monitored closely in the first 3 weeks and regularly thereafter during treatment (refer to SPC for more information). Patients with severely disturbed hepatic function, significant renal failure or chemotherapy-induced thrombocytopenia may need a dosage reduction and should be monitored accordingly. Dalteparin cannot be used interchangeably (unit for unit) with unfractionated heparin, other low molecular weight heparins, or synthetic polysaccharides. The 100,000 IU/4 ml Multidose Vial contains benzyl alcohol so must not be used in premature or newborn babies. Benzyl alcohol may cause toxic reactions in infants and children up to 3 years old. Other formulations without benzyl alcohol are available. The needle shield of Fragmin prefilled syringes may contain latex (natural rubber) which may cause severe allergic reactions in individuals with hypersensitivity to latex. **Drug Interactions:** Care with agents affecting coagulation/platelets and NSAIDs (refer to SPC for more information). **Pregnancy and Lactation:** Dalteparin should be used during pregnancy only if clearly needed, and caution should be exercised when prescribing to pregnant women (refer to SPC for more information). *The Multidose Vial contains benzyl alcohol therefore should not be used in pregnancy.* Epidural anaesthesia during childbirth is absolutely contraindicated in women who are being treated with high dose anticoagulants. Not recommended for use in pregnant women with prosthetic heart valves. Limited data are available for excretion of dalteparin in human milk. 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. **Side Effects:** Commonly reported side effects include reversible non-immunologically-mediated thrombocytopenia (Type I), haemorrhage, subcutaneous haematoma and pain at the injection site, transient elevation of liver transaminases. Other side effects include: anaphylactic reactions, hypersensitivity, skin necrosis, transient alopecia, immunologically mediated heparin-induced thrombocytopenia (Type II, with or without associated thrombotic complications), retroperitoneal and intracranial bleeds sometimes fatal, spinal or epidural haematoma, prosthetic cardiac valve thrombosis, hyperkalaemia, rash, osteoporosis (in connection with long-term treatment). (Refer to SPC for information on other side effects).

Marketing Authorisation Holder:

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Pfizer Medical Information on 01304 616161.