The Christie NHS
NHS Foundation Trust

Title SHARED CARE PROTOCOL for Extended Treatment of symptomatic VTE and prevention of its recurrence in Cancer Patients with Solid and Haematological Tumours	**Unique Identifier**
Scope: Dalteparin (Fragmin ▼®) may be considered for shared care arrangements for the extended treatment of symptomatic venous thromboembolism (VTE) and prevention of its recurrence in patients with solid and haematological tumours.	**Classification SHARED CARE PROTOCOL**

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To be read in conjunction with the following documents: Fragmin ▼® Summary of Product Characteristics relating to the appropriate condition*, NICE clinical guidance Venous thromboembolism (VTE) reducing the risk**.** *** Note that dalteparin is not currently licensed for treatment and prophylaxis of VTE in patients with haematological tumours**	

Authorised by	Medicines Management Group	**Date**
Review Date September 2014		

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1.0 Introduction

Patients with cancer are at increased risk of VTEs due to increased blood coaguability, advanced age, recent surgery, immobilization, treatment with chemotherapy and hormones, and the use of indwelling central venous catheter devices.

Low molecular weight heparin represents the preferred agent for both the initial and continuing treatment of cancer patients with solid and haematological tumours with established VTE. Dalteparin is currently the only licensed low molecular weight heparin (LMWH) for use in patients with solid tumours and then only for a six month period. (It is not currently licensed for use in patients with haematological tumours). Patients who have active cancer remain at an increased risk of recurrent thrombosis after 6 months of therapy and further continuation of LMWH should be assessed on an individual patient basis.

2.0 Purpose

These guidelines look at the shared care management of patients for extended treatment and prophylaxis of VTE in patients with solid and haematological tumours.

3.0 Scope

Dalteparin (Fragmin ▼) may be considered for shared care arrangements for the extended treatment and prophylaxis of symptomatic VTE in patients with solid and haematological tumours. Patients < 40kg and who have had a stroke in the previous 3 months will be excluded from this SCP.

4.0 Review

2 years

5.0 Shared Care Protocol

5.1 Clinical Details

Dalteparin is indicated in patients with solid and haematological tumours (but not licensed in the latter) for the extended treatment of symptomatic venous thromboembolism and prevention of its recurrence.

Drugs affecting haemostasis should be discontinued prior to dalteparin therapy unless their use is essential, such as aspirin, dipyridamole, acetylsalicylic acid, NSAIDS, clopidrogel, prasugrel, ticagrelor, thrombolytics and anticoagulants.

Dalteparin may increase the risk of hyperkalaemia in patients on potassium-sparing drugs (e.g. ACE inhibitors) Serum potassium should be monitored at regular intervals e.g. monthly in these patients

Heparin can suppress adrenal secretion of aldosterone leading to hyperkalaemia, particularly in patients such as those with diabetes mellitus, chronic renal failure, preexisting 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 at monthly intervals thereafter

5.2 Product Information

- Treatment dose is based on patient's weight
- Prescribed as prefilled syringes containing the doses specified below
- Total recommended treatment period for shared care is six months
- For the first month of treatment, the dose, based on 200 iu/kg total body weight, administered once daily subcutaneously, (up to maximum of 18,000iu daily) is:

Body Weight (Kg)	Dose
<46	7,500 units
46-56	10,000 units
57-68	12,500 units
69-82	15,000 units
83 and over	18,000 units

- Months 2-6 administer daily subcutaneously at a dose of approximately 150iu/kg, once daily as follows:

Body Weight (kg)	
<56	7,500 units
57-68	10,000 units
69-82	12,500 units
83-98	15,000 units
≥99	18,000 units

Dalteparin should **not** be administered to patients with known hypersensitivity to this or other low molecular weight heparins and / or unfractionated heparin.
Dosage should be adjusted in the event of a reduction in platelet count. (Refer to consultant for advice).

5.3 Method of administration

Administration by subcutaneous injection, preferably into the abdominal subcutaneous tissue anterolaterally or posterolaterally, or into the lateral part of the thigh. Patients should be supine and the total length of the needle should be introduced vertically, not at an angle, into the thick part of a skin fold, produced by squeezing the skin between thumb and forefinger; the skin fold should be held throughout the injection.

5.4 Possible side effects of treatment

Clinical condition (reported frequency)	**Management**
Haemorrhage (Common in ≥ 1 in 100 to < 1 in 10)	Stop drug and seek urgent attention
Skin necrosis at the site of injection	Stop drug and discuss with Hospital team
(Rare ≥ 1 in 10,000) Uriticaria, pruritis	
Uncommon (≥ 1 in 1000 to < 1 in 100)	Stop drug and discuss with Hospital team
Immune system allergic reaction	Stop drug and discuss with Hospital team
(Rare ≥ 1 in 10,000)	
Pain (uncommon ≥ 1 in 1000 to < 1 in 100), haematoma (common ≥ 1 in 100 to < 1 in 10) at injection site	No need to discontinue therapy, may be self limiting

5.5 Aspects of care for which the Consultant is responsible

Assessing the patient and establishing a need for dalteparin therapy.
Establishing that the patient has adequate renal function (calculated creatinine clearance greater than 30ml/min).
Establishing baseline platelet count is adequate (>50,000/mm^3)
See SPC for dosing details if platelet count is between 50,000 and 100,000/mm^3
Ensuring that there are no contra-indications to therapy with dalteparin.

Plasma potassium should be measured in patients at risk before starting heparin therapy (see clinical information section 5.1) and monitored regularly e.g. at monthly intervals thereafter

Providing information for the patient, including adverse effects, unlicensed use (if applicable), obtaining consent and initiating treatment.
Prescribe the first month's treatment
Contacting the GP to invite / agree on shared care for the patient.
Assessing the continued appropriateness for dalteparin on a 3 monthly basis.
Reviewing any concerns regarding disease progression from the GP within 2

weeks.
Monitoring toxicity and reporting adverse events via the yellow card scheme
Ensuring that all other medical professionals in the shared care team are kept informed of any changes in the patient's circumstances.
Discontinuing therapy or **assuming responsibility** for prescribing at six months if treatment continues beyond licensed period.

5.6 Conditions of assuming responsibility by the GP

	Consultant	**Usual GP**
Renal function	Baseline	Not required routinely
Platelet count	Frequently during first 3 weeks, then regularly	Monthly: discuss need for dosage reduction if platelets <100,000mm^3 or drop in count more than 50%

5.7 Aspects of care for which the GP is responsible

Assessment of continued well being of the patient.
Monitoring toxicity and reporting adverse events to the consultant and via the yellow card scheme.
Providing the patient with repeat prescriptions for dalteparin for months 2-6.

Ensuring that all other medical professionals in the shared care team are kept informed of any changes in the patient's circumstances.

5.8 Individual consideration of each case between consultant and GP
Individual patients may require serum potassium levels monitoring on a monthly basis after initiating therapy, with parameters for referring back to the consultant established on a patient specific basis.

5.9 Product Patient Information Leaflet
See attached leaflet

5.10 References
Fragmin - Extended Treatment in Oncology (5000, 7500, 10000, 12500, 15000, 18000 I.U Syringes) Summary of Product Characteristics. Accessed at: http://www.medicines.org.uk/EMC/medicine/21706/SPC/Fragmin+-+Extended+Treatment+in+Oncology+(5000%2c+7500%2c+10000%2c+12500%2c+15000%2c+18000+I.U+Syringes)/ 29.06.2010
CG92 Venous thromboembolism reducing the risk: NICE Guideline. Accessed at http://www.nice.org.uk/nicemedia/live/12695/47195/47195.pdf 29.06.2010
Lee AYY, Levine MN, Baker RI et al. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. (CLOT study) N Engl J Med2003; 349: 146–153

6.0 Back up details available from hospital to General Practitioner and patient e.g. contact name and number, especially for out of hours problem.

Christie Hotline Number for 24hrs advice: 0161 446 3658

7.0 Statement of Agreement.

Shared care is an agreement between the GP and the Consultant. This form is a request by the consultant to share the suggested care pathway of your patient. If you are unable to agree to the sharing of care and initiating the suggested medication,

please make this known to the consultant within 14 days, ideally stating the nature of your concern

8.0 Written Information to be provided to the patient

To include advice and information regarding the treatment and medicines used.

Dalteparin (Fragmin) Patient information Leaflet

PACKAGE LEAFLET: INFORMATION FOR THE USER

Fragmin® 10,000 IU/0.4ml, 12,500 IU/0.5ml, 15,000 IU/0.6ml & 18,000 IU/0.72ml Solution for Injection

dalteparin sodium

Read all of this leaflet carefully before you start using this medicine

• Keep this leaflet. You may need to read it again.
• If you have any further questions, ask your doctor or pharmacist.
• This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Fragmin is and what it is used for

Fragmin is a solution for injection. Its active ingredient is dalteparin sodium.
Fragmin belongs to a group of medicines called low molecular weight heparins or antithrombotics, which help prevent the formation of blood clots by thinning the blood.
• Fragmin is used to treat blood clots (venous thromboembolism) and to prevent their recurrence.
• Venous thromboembolism is a condition where blood clots develop in the legs (deep vein thrombosis) or the lungs (pulmonary embolism), e.g. after surgery, prolonged bed-rest or pregnancy or in patients with certain types of cancer.
Ask your doctor if you are unsure why you have been given Fragmin.

2. Before you are given Fragmin

You should not be given Fragmin if you:

• are allergic (hypersensitive) to the active ingredient dalteparin sodium or a similar product or any of the other ingredients of Fragmin.
• have an active stomach ulcer or ulcer of the duodenum (small intestine).
• have suffered from a brain haemorrhage (bleeding in your brain).
• suffer from any condition which may cause you to bleed more easily (e.g. haemophilia, liver failure). Ask your doctor if you are unsure.
• have uncontrolled high blood pressure.
• have a condition called endocarditis (an inflammation of the lining of the heart and heart valves). Your doctor will have told you if you have this.
• have had a condition called "heparin-induced thrombocytopenia" (a decrease in the number of clotting cells (platelets) in your blood caused by heparin, which may cause you to bruise and bleed more easily). Your doctor will have told you if you have had this.
• have an injury to, or have had an operation involving your spine, head, eyes or ears.

If you are receiving Fragmin to treat blood clots, you should not have a spinal or epidural anaesthetic.

Take special care with Fragmin

Tell your doctor before you take Fragmin if you:
• have conditions which make you more susceptible to bleeding e.g:
- after an operation or trauma
- a stroke caused by a bleed
- severe liver or kidney failure
- abnormal or low numbers of platelets (clotting cells)
- eye disease caused by blood pressure or diabetes
- taking other medicines that thin the blood (e.g. aspirin, warfarin, dipyridamole).

• have been told by your doctor that you have a lot of potassium in your blood or have a low blood pH. Your doctor will monitor your blood regularly before and during treatment.
• have ever had an operation to insert an artificial heart valve.

You may need to have blood tests to monitor the effects of fragmin if you:
- have kidney failure
- are very thin or morbidly obese
- are pregnant
- are at increased risk of bleeding or rethrombosis (more blood clots)

Taking other medicines
Some medicines can affect the way Fragmin works, or Fragmin itself can reduce the effectiveness of other medicines taken at the same time.
Medicines that **increase** the effect of Fragmin include:
• Those used to thin your blood (e.g. aspirin, dipyridamole, Glycoprotein receptor antagonists and warfarin).
• Those used to reduce pain and inflammation (e.g. indometacin).
• Some medicines for gout, (e.g. sulfinpyrazone and probenecid).
• Etacrynic acid (a water retention tablet (diuretic)).
• Solutions given to increase the blood volume (e.g. dextrans).
• Medicines known as cytostatics (used in cancer treatment).
• Thrombolytic medications for treating transmural heart attack (e.g. TPA-tissue plasminogen activator).
Medicines that can **reduce** the effect of Fragmin, include:
• Those for allergy and hay fever (e.g. antihistamines).
• Those used for heart or circulation problems (e.g. digoxin or digitoxin).
• Antibiotics known as tetracyclines which are used to treat bacterial infections.
• Vitamin C (e.g. some vitamin supplements).
Other medicines that may interfere with fragmin include:

Those used to treat angina (intravenous nitroglycerine)

Antibiotics such as high dose penicillin which are used to treat bacterial infections.

Anti-malarials (e.g. quinine)

Tobacco smoking

Please note that if you are being treated with Fragmin for unstable coronary artery disease your doctor may adjust your dose of aspirin accordingly.
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
Pregnancy and Breast-feeding
Fragmin has not been found to cause harmful effects during pregnancy. The possibility of harm to the baby appears remote. Tell your doctor if you are pregnant and they will advise you.
Fragmin is not recommended for the prevention of blood clots on artificial valves during pregnancy.
Ask your doctor or pharmacist for advice before taking this medicine whilst breast-feeding.

Driving and using machines
Fragmin does not affect the ability to drive and operate machinery

3. How Fragmin is given to you
Your medicine will usually be administered by a doctor or nurse or you may be shown how to give the injection yourself at home (See Section on How to Inject Fragmin). The amount of Fragmin you receive will depend on your body weight.
Fragmin is given as a single, once daily, subcutaneous injection, which means it is injected beneath the skin. It is usually injected into a skin fold in your abdomen (stomach), or the upper part of your thigh. It should not be injected into your muscles.

Adults and the Elderly

To treat blood clots (venous thromboembolism)

The recommended doses depend on your body weight and will be calculated by your doctor. The usual dose used to treat venous thromboembolism is 200 IU (international units) for every kilogram you weigh once daily.The following table shows the dose you will receive depending on your body weight: **Body Weight (kg)**	**Dose (IU)**
< 46	7,500
46-56	10,000
57-68	12,500
69-82	15,000
83	18,000