Gwent Shared Care Protocol

DALTEPARIN (▼Fragmin®) for extended treatment and prophylaxis of VTE in patients with solid tumours

Protocol No. 19	✶PLEASE CHECK http://www.gpmtc.wales.nhs.uk FOR THE LATEST VERSION OF THIS PROTOCOL✶
General guidance	This protocol outlining the shared care arrangements for patients with solid tumours receiving **dalteparin (▼Fragmin®)** for the extended treatment and prophylaxis of venous thromboembolism (VTE). The *Gwent Partnership Medicines and Therapeutics Committee* have endorsed its use on the understanding that: 1. The shared care arrangements only cover 6 months, which is currently the licensed duration of treatment/prophylaxis for dalteparin. This protocol should be read in conjunction with the: 1. *Shared Care Agreement Form* (see below) 2. Summary of Product Characteristics (SPC or Data Sheet) for dalteparin – available at: http://emc.medicines.org.uk/medicine/21706/SPC/Fragmin+-+Extended+Treatment+in+Oncology+(5000%2c+7500%2c+10000%2c+12500%2c+15000%2c+18000+I.U+Syringes)/
1. Licensed indication	Patients with solid tumours: Extended treatment of symptomatic venous thromboembolism (VTE) and prevention of its recurrence.
2. Therapeutic use & Background information	VTE is a major complication of cancer (occurring in 4% to 20% of patients) and is one of the leading causes of death in patients with cancer. The risk appears to be greater for those patients who are hospitalised and/or receiving active treatment; certain newer treatment regimens that include thalidomide, lenalidomide, or bevacizumab have reported very high rates of VTE. Low molecular weight heparin (LMWH) represents the preferred agent for both the initial and continuing treatment of cancer patients with established VTE.[1] Dalteparin is currently the only licensed LMWH for these indications and then only for a 6 month period. For certain patients i.e. those with progressive disease this duration needs to be life long however, there is no trial evidence to support this. Dalteparin cannot be used interchangeably with other LMWHs.
3. Contra-indications	Patients with the following conditions are **excluded** from this protocol: ➢ Known or suspected hypersensitivity to dalteparin or other LMWHs and/or heparins. ➢ History of immunologically mediated Heparin Induced Thrombocytopenia. ➢ Renal impairment (calculated creatinine clearance < 30ml/min). ➢ Significant hepatic impairment. ➢ Active gastric/duodenal ulceration or oesophageal varices. ➢ Haemophilia and other inherited/major bleeding disorders or any unusual susceptibility to bleeding or haemorrhagic pericardial/ pleural effusion. ➢ Thrombocytopenia with platelets < 50. ➢ Recent (within 3 months) cerebral haemorrhage (stroke due to systemic emboli excepted). ➢ Severe hypertension. ➢ Recent neurosurgery or eye/ear surgery and injuries to the central nervous system, eyes and ears - *expert opinion suggests that provided there is no active bleeding, LMWHs (dalteparin) may be used in this patient group outside the acute healing phase post eye or ear surgery/injury. Therefore it is recommended that LMWH may be used 3 months after eye/ear surgery.* ➢ Subacute endocarditis.

[1] http://jco.ascopubs.org/cgi/content/abstract/JCO.2007.14.1283v1

	➢ Children under 16 years. ➢ Low body weight (< 40kg at time of venous thromboembolic event). ➢ Body weight >90 kg. ➢ Pregnancy. In patients receiving dalteparin for treatment (rather than prophylaxis), local and/or regional anaesthesia in elective surgical procedures is contra-indicated.
4. Typical dosage regimen (adults)	**Month 1** Administer dalteparin 200 IU/kg total body weight subcutaneously (SC) once daily for the first 30 days of treatment. Dalteparin should not be administered by the intramuscular route. ***Body weight*** / ***Dose (IU)*** < 46kg: 7500 46kg to 56kg: 10000 57kg to 68kg: 12500 69kg to 82kg: 15000 83kg and over: 18000 The total daily dose should not exceed 18,000 IU daily. Maximum dose of 18, 000 IU was used in patient weighing up to 132 kg in the CLOT study. **Months 2-6** Dalteparin should be administered at a dose of approximately 150 IU/kg, sc, once daily using fixed dose syringes and the table shown below. ***Body weight*** / ***Dose (IU)*** ≤ 56kg: 7500 57kg to 68kg: 10000 69kg to 82kg: 12500 83kg to 98kg: 15000 ≥ 99kg: 18000 Recommended duration of treatment is 6 months (first month of dalteparin treatment is included). Relevance of continuing treatment beyond this period will be evaluated according to individual risk/benefit ratio, taking into account particularly the progression of cancer. No data is available with dalteparin beyond 6 months of treatment in the CLOT study. In practice an individual specialist clinician may choose to extend the duration beyond six months, however this shall be in the context of an off licence prescription and it would be appropriate for the prescribing to be continued by the specialist (in Secondary/Tertiary care) making such a decision.
5. Drug interactions Check *BNF* Appendix 1 before co-prescribing any other drug.	➢ Drugs affecting haemostasis should be discontinued prior to dalteparin therapy unless their use is essential, such as aspirin, dipyridamole, acetylsalicylic acid, NSAIDS, clopidogrel, thrombolytics and anticoagulants. ➢ Dalteparin may increase the risk of hyperkalaemia in patients on potassium-sparing drugs (e.g. ACE inhibitors).
6. Adverse drug reactions All healthcare professionals have a responsibility to patients in advising/acting on suspected bleeds related to dalteparin.	***Clinical condition (reported frequency)*** / ***Management*** Major haemorrhage (<1%): **Stop drug and seek urgent attention** Skin necrosis usually at the site of injection (<1%): **Stop drug and discuss** Cutaneous or systemic allergic reaction (>1%; <10%): **Stop drug and discuss** Pain, haematoma and mild local irritation at injection site (>1%; <10%): **No need to discontinue therapy** common, may be self-limiting **Other side effects:** 1. Long term heparin treatment has been associated with a risk of osteoporosis. Although this has not been observed with dalteparin the risk cannot be excluded. 2. Heparin products can increase the levels of plasma potassium, clinically significant

	hyperkalaemia may occur in patients with chronic renal failure and diabetes mellitus. **Patients should be particularly warned to report <u>any bleeding</u>.** All serious adverse events should be reported to MHRA/CHM.
7. Baseline investigations	**To be undertaken by specialist centre***:* FBC, Differential white cell count and platelet count Clotting screen (PT and APTT) U&Es, creatinine (including eGFR measurement) LFTs
8. Monitoring	**Patients requiring monitoring of the drug level by anti Xa activity are excluded from this protocol.** In certain patients there is a need to monitor dalteparin by measuring the anti Xa level 4 hours post the last dose, these patients will be followed up regularly by the anticoagulant clinic. ***Ongoing Monitoring by Primary Care:***

Monitoring	*Result*	*Action*
FBC monthly to monitor platelets count	Platelets < 150 or drop in count of more than 50%.	***Discuss with the consultant haematologist.***
U & E monthly if high risk of hyperkalaemia *i.e. those with diabetes mellitus, chronic renal failure, acidosis, raised potassium concentrations or those taking potassium-sparing drugs /potassium supplements.*	K > 5.5mmol/L	***Repeat the U & E test and seek haematology advice if K still > 5.5mmol/L***

9. Pharmaceutical aspects	Single dose syringes: Do not store above 25°C. Dalteparin pre-filled syringes are single dose containers - discard any unused product
10. Specialist centre contact information	**If stopping the medication or needing advice please contact** **Dr Sarah Lewis 01873 732259** **Dr Simon Noble 01633 234934**
11. Criteria for shared care	Prescribing responsibility will only be transferred when: • Treatment is for a specified indication and duration. • Treatment has been initiated and established by the Specialist Centre. • The patient's initial reaction to and progress on the drug is satisfactory. • The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements.
12. Responsibilities of initiating consultant	1. To ensure patient has a basic understanding of what risks and benefits are associated with dalteparin therapy, to provide a patient information leaflet and to inform the patient of what action to take in the event adverse effects (particularly any unexplained bleeding). 2. To confirm the patient's understanding and consent to treatment and to inform the patient of the need for blood monitoring. 3. To undertake baseline monitoring (detailed above). 4. To discontinue any drugs affecting haemostasis as required (e.g. NSAIDs). 5. Initiate treatment with dalteparin and to inform the patient of the dose reduction from month 2 and **provide the first 40 days of treatment** (labelled appropriately with directions to cover the dose reduction) and to inform the patient of arrangements for obtaining further prescriptions. 6. Instruct patient or carer on administration (or arrange for district nurse to be involved in the administration). 7. Monitor for heparin-induced thrombocytopenia (HIT) or hyperkalaemia if required for the first 14 days of treatment. It is the responsibility of the initiating physician to ensure that the patient has received clear advice and blood test form regarding necessary monitoring within the first 40 days and to ensure a safe mechanism for prompt action on the result.

	Where it is inconvenient or inappropriate for the patient to attend the specialist centre for a blood test to monitor for HIT, the patient will be issued with a haematology form to take to their GP along with a '*Patient Letter*' explaining the process to the patient, and a '*GP letter*' which the patient will hand to their GP surgery explaining the process to the GP, it will still be the specialist centre's responsibility to follow up and action the initial (within 14-day) platelet level. 8. To send the Shared Care Agreement Form to the GP (attached below). 9. Initiating consultant to keep patient under clinical review, assessing need for ongoing dalteparin treatment at 6 months. Where the risk/benefit to the patient favours continuation beyond the licensed 6 month duration then, with the patient's acceptance, further consent should be sought from the GP in writing for the continued unlicensed prescribing beyond 6 months. 10. Provide advice and support if problems occur during treatment using the contact details provided 11. Give direction as to when treatment should be discontinued in all cases as appropriate.
13. Responsibilities of Primary Care	1. To respond to the Shared Care Agreement Form (attached below). 2. To monitor and prescribe dalteparin in collaboration with the specialist and follow these guidelines. 3. Whenever practicable, to reaffirm with the patient the importance of reporting any unexplained bleeding. 4. Monitor for hyperkalaemia in those patients at higher risk of raised plasma-potassium concentrations. 5. Discontinuation of treatment if patient is experiencing severe side effects and specialist advice is not immediately available. 6. To give a timely response to any further specialist request to continue prescribing dalteparin beyond the licensed 6 month duration. Clinicians should use their discretion to avoid any interruptions in treatment. 7. To send confirmation letter to patient and/or carer if treatment is discontinued.
14. Responsibilities of patients/carer	1. To attend hospital and GP clinic appointments. 2. Failure to attend will result in medication being stopped on specialist advice. 3. To report adverse effects to their specialist or GP (particularly any unexplained bleeding).
15. Responsibilities of all prescribers	**As dalteparin is a Black Triangle drug (▼) for this indication <u>all</u> suspected adverse reactions (including any considered not to be serious) should be reported to MHRA via the "yellow card scheme." http://yellowcard.mhra.gov.uk/**
16. Responsibilities of pharmacists	➢ Whenever practicable, to reaffirm with the patient the importance of reporting any unexplained bleeding.
17. Supporting documentation / information	**Other information:** NPSA/2010/RRR014 states: *Essential information such as dose, weight, renal function, indication and duration of treatment is communicated at transfers of care (e.g. by discharge letters) and used to ensure that future doses are safe*. http://www.nrls.npsa.nhs.uk/resources/?entryid45=75208 In 2010 (April & December) the All Wales Medicines Strategy Group (AWMSG) considered issues relating to LMWH and has produced documents to promote uptake of best practice and to reduce avoidable harm, waste and variation in NHS Wales: http://www.wales.nhs.uk/sites3/page.cfm?orgid=371&pid=46618 **Patient information leaflet** http://emc.medicines.org.uk/medicine/14282/PIL/Fragmin%2010000,%2012500,%2015000,%2018,000%20I.U.%20Syringes/
18. GP request letter	**Shared Care Agreement Form – Attached below**

Shared Care Agreement Form

CONSULTANT REQUEST

To: Dr.

Your patient:	**NHS No. (10digit):**
was seen on:	
with a diagnosis of:	
I recommend that the following drug is initiated:	

This drug has been accepted as suitable for shared care by the *GPMTC*. I agree to the responsibilities set out in the protocol SCP No. 19 (*copy attached*). This should be read in conjunction with the definition of shared care at: **http://www.wales.nhs.uk/sites3/Documents/371/Doc%202%20Defining%20shared%20care.pdf**

I am requesting your agreement to sharing the care of this patient. The preliminary tests set out in the protocol have been carried out. I am currently prescribing the stabilising treatment. **Please note that the dalteparin dose was reduced after the first month of treatment**

I would like you to undertake treatment from:		
The required dose from this date will be:		
The baseline tests are:		
Monitoring for hyperkalaemia **Note this should be reconsidered if the patient's condition changes** (*see section 8 of the protocol*)	❑Required	❑NOT required

If you undertake treatment I will reassess the patient in ____ weeks. You will be sent a written summary within 14 days. I will accept referral for reassessment at your request.

The medical staff of the department are available at all times to give you advice.

Consultant Name:	**Signature:**
Department:	
Hospital:	**Date:**
Contact Telephone Nos:	

GP RESPONSE (*Please circle the appropriate number below detailing your response*)

1. I am willing to undertake shared care as set out in SCP No. _____ for this patient.
2. I would like further information. Please contact me on: _____
3. I am unable to undertake shared care for this patient because: (*Please state*)

_____

G.P. Signature _____ Date _____

Practice Address/Stamp _____

PLEASE RETURN WHOLE COMPLETED FORM OR TO THE REQUESTING CONSULTANT WITHIN 1 WEEK

This Shared Care Protocol should be read in conjunction with the Summary of Product Characteristics