MIL

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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Treatment of VTE with dalteparin (Fragmin®) in adult patients with cancer

Evidence has shown that patients with active cancer, or patients undergoing cancer treatment have lower rates of VTE recurrence when treated with low molecular weight heparin (LMWH) instead of warfarin, without increasing the risk of bleeding.

This document focuses on the doses of subcutaneous dalteparin for cancer patients, and which patients should be excluded from this regimen. For all other clinical information with respect to dalteparin for the treatment of VTE, please see MIL Vol 2 No 2 *Treatment of venous thromboembolism (VTE) in adults with dalteparin (Fragmin®).*

Patient exclusions

For patients to be considered for extended treatment with dalteparin, they must be able to self-inject, or have a carer who can inject for them. If they are not able to, they will be treated as for non-cancer patients.

Patients with significant renal impairment (creatinine clearance less than 30mL/min) should be discussed with a Haematology SpR (bleep 5529).

Patients who weigh less than 40kg are excluded from the product license and should be discussed with a Haematology SpR before extended treatment is initiated. Also consider discussing treatment with Haematology if the patient's weight exceeds 180 kg.

Dose and administration

Month 1

Body weight (kg)	Dose of dalteparin by subcutaneous injection using a pre-filled syringe (units)
Less than 46 Consider discussing with haem SpR if less than 40kg	7,500 once daily
46-56	10,000 once daily
57-68	12,500 once daily
69-82	15,000 once daily
83-98	18,000 once daily
99-112	10,000 **twice daily**
113-137	12,500 **twice daily**
138-165	15,000 **twice daily**
166 or more Consider discussing with haem SpR if greater than 180kg	18,000 **twice daily**

Single doses should not exceed 18,000 units.

The license for dalteparin states to give 18,000 units to all patients 83kg and above. However, British and American guidelines as well as local expert opinion recommend dosing based on actual body weight in patients who are 83kg and above.

Pharmacy will not dispense dalteparin and nursing staff are at liberty to refuse to administer dalteparin from a prescription on which the weight is not documented.

In the case of chemotherapy-induced thrombocytopenia, the dose should be adopted as follows:

For platelet counts **below** 50 x 10^9/L, the manufacturer suggests that dalteparin should be withheld until the platelet count recovers to greater than or equal to 50 x 10^9/L. However, a risk benefit assessment may favour continuing a 50% dose of dalteparin for counts between 25 and 50 x 10^9/L. If anticoagulation is discontinued an IVC filter should be considered. Consider discussing management of these patients with haematology (bleep 5529).

Month 2 onwards- Ensure patient is reweighed

Body weight (kg)	Dose of dalteparin by subcutaneous injection using a pre-filled syringe (units)
Less than 57	7,500 once daily
57-68	10,000 once daily
69-82	12,500 once daily
83-98	15,000 once daily
99-112	18,000 once daily
113-137	10,000 **twice daily**
138-165	12,500 **twice daily**
166 or more	15,000 **twice daily**

In the case of chemotherapy-induced thrombocytopenia in the extended treatment phase (after month 1), consult product literature or contact Haematology for advice on bleep 5529.

Duration of treatment

Licensed duration of treatment is 6 months. This is based on Lee et al (2003) who performed their trial when six months was standard for all acute VTE. VTE patients are now usually reviewed at 3 months to decide on subsequent management. If cancer is not cured some form of long-term anticoagulation is usually

recommended. If this is with LMWH there are no data as to whether the dose can be reduced to a prophylactic dose. Patients can be referred to the Oxford Haemophilia and Thrombosis Centre for review. A local shared-care agreement exists between primary and secondary care for supplying dalteparin.

Data are emerging from clinical trials around the use of DOACs (in particular for Rivaroxaban and Edoxaban) as treatment for cancer related VTE. At present LMWH remains the standard of care although there are advantages of using oral medications. The current DOAC trial data suggest that clinically relevant bleeding is more likely with a DOAC, particularly for patients with gastrointestinal cancer, and VTE recurrence is less likely with a DOAC when compared to LMWH. Please contact haematology (bleep 5529) to discuss if considering using a DOAC.

References

1. Lee AYY *et al* (2003) Low molecular weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. *NEJM **349** 146-153*
2. Summary of Product Characteristics (SPC) for dalteparin (Fragmin®). Accessed via www.medicines.org.uk 17th April 2019
3. British National Formulary (BNF) 76th Ed. *British Medical Association and the Royal Pharmaceutical Society of Great Britain, London, UK. September 2018- March 2019*
4. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing *NICE **CG144**, June 2012*
5. Antithrombotic Therapy for VTE Disease (2016) 10th Ed. *Chest **149** (2): 315-352*
6.Witt et al (2018) American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. *Blood Advances **2** 3257-3291*
7. Young et al (2018) Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D). *J Clin Onc **36**(20) 2017-2023*
8. Raskob et al (2018) Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism *NEJM; **378** 615-624*

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