Dalteparin is a low molecular weight heparin (LMWH) indicated for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) (collectively known as venous thromboembolism (VTE)) in adults. The diagnosis should be confirmed radiologically (e.g. ultrasound, CTPA) since clinical diagnosis alone is inaccurate. Treatment should be started if imaging is delayed (for more than 1 hour for suspected PE or for more than 4 hours for suspected DVT) unless the risk of therapy is felt to outweigh the benefit, in which case this should be documented in the medical notes. Once the diagnosis is confirmed treatment should be continued or started immediately. When dalteparin is contraindicated, consider using unfractionated heparin (UFH) (see MIL Vol.5 No.6 Guidelines on when to use and how to monitor unfractionated heparin in adults) or fondaparinux (contact the on call haematology registrar for advice).

Advantages of dalteparin over UFH
- Dalteparin produces reliable anticoagulation rapidly, without the need for routine monitoring in most patients
- Dalteparin is convenient to administer and is as effective as UFH
- The dose of dalteparin is calculated from the patient’s weight
- Dalteparin is administered subcutaneously
- The use of the subcutaneous route allows patients to be more mobile and self-caring and facilitates outpatient treatment and faster discharge

Mode of action
Dalteparin potentiates action of antithrombin; compared with UFH it results in less anti IIa (thrombin) and more anti-Xa activity.

Dose & administration
Patients starting full dose anticoagulation should have a FBC, U&E and coagulation screen. In order to minimise the risk associated with complicated dose calculations and to reduce drug wastage, the Medicines Management & Therapeutics Committee (MMTC) has recommended that wherever possible pre-filled syringes of dalteparin are used. Various pre-filled syringes are available. Each syringe corresponds to a weight band (see Table 1). It is advisable to use the Powerplans within ePMA to aid safe prescribing. 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.

Weight
It is imperative that the patient is weighed and that the weight is documented on the drug chart. In exceptional circumstances, when weighing the patient is not possible, the estimated weight must be documented on the drug chart. Patients who weigh less than 40kg are excluded from the product license and should be discussed with a Haematology SpR on bleep 5529 before extended treatment is initiated. Also consider discussing treatment with Haematology if the patient’s weight exceeds 180 kg.

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.

Table 1: Standard dalteparin dose recommendations for treatment of VTE: Should be used in all cases except where there is risk of bleeding (see recommendations below).

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

Single doses should not exceed 18,000 units
Table 2. Month 2 onwards standard dalteparin dose recommendations for treatment of VTE.
If patients are to remain on dalteparin beyond the first month as treatment for a VTE, ensure the patient is reweighed and dose reduce according to the table below:

<table>
<thead>
<tr>
<th>Month 2 onwards: Ensure patient is reweighed</th>
<th>Body weight (kg)</th>
<th>Dose of dalteparin by subcutaneous injection using a pre-filled syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>Dose of dalteparin by subcutaneous injection using a pre-filled syringe</td>
<td></td>
</tr>
<tr>
<td>Less than 57</td>
<td>7,500 once daily</td>
<td></td>
</tr>
<tr>
<td>57-68</td>
<td>10,000 once daily</td>
<td></td>
</tr>
<tr>
<td>69-82</td>
<td>12,500 once daily</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>166 or more</td>
<td>15,000 twice daily</td>
<td></td>
</tr>
</tbody>
</table>

Patients with cancer
Evidence suggests that patients with cancer have lower VTE recurrence rates when treated with LMWH instead of warfarin. Please see MIL Vol.7 No.10 for full guidance.

Risk factors for bleeding include:
- Liver disease
- Renal impairment
- History of peptic ulcer disease
- Concomitant medicines that may enhance anticoagulant effect
- Alcohol abuse
- Severe hypertension (systolic greater than 180mmHg, diastolic greater than 110mmHg)
- Congestive heart failure
- Doses based on incorrect patient weight

Note, in patients who are considered to be at an increased risk of bleeding, administration of dalteparin in divided daily doses of 100 units per kg subcutaneously twice daily may be safer.

Contra-indications (principally as for UFH)
- Known hypersensitivity to dalteparin
- Cerebral haemorrhage, acute gastric or duodenal ulceration, known haemorrhagic diathesis
- Uncontrolled severe hypertension
- Injuries to or recent operations to the ears/eyes or central nervous system
- Infective endocarditis
- Severely disturbed liver or renal function
- Regional anaesthesia is contra-indicated in patients receiving dalteparin
- History of Heparin-Induced Thrombocytopenia (HIT)

Oral anticoagulation with warfarin
Warfarin should be started concurrently. Treatment with dalteparin should continue in parallel with oral anticoagulation for five days or until the patient’s INR has been greater than or equal to 2.0 for at least 24 hours (two consecutive days), whichever is longer. For more information, please see MIL Vol.5 No.8 Initiating Oral Anticoagulation in Adult Patients.

Monitoring
A baseline coagulation screen and platelet count should be taken in all cases. Monitoring of the anticoagulant effect is not normally necessary for dalteparin prescriptions. However, for certain patients (see HIT, below) monitoring of platelet counts is recommended every 2-4 days from days 4 to 14 of treatment.

Inhibition of aldosterone secretion by unfractionated or low molecular weight heparin can cause result in hyperkalaemia in susceptible patients (e.g. patients with diabetes, chronic renal failure, or acidosis, or those taking potassium sparing drugs). If such patients are given dalteparin for longer than 7 days potassium should be monitored.

Plasma anti-Xa concentration can be used to monitor the anticoagulant effect of dalteparin, such as in patients with renal impairment or if abnormal coagulation parameters or bleeding should occur during therapy. Maximum plasma concentration is obtained 3-5 hours after subcutaneous injection, when samples should be taken. For patients on once daily dosing, the expected peak plasma concentration is about 1.0 anti-Xa unit per mL with a range of 0.5 – 1.5 (and 0.5-1.0 anti-Xa units per mL for twice daily dosing).

Use in renal impairment
Anticoagulation with heparins in the presence of significant renal impairment is not straightforward as both low molecular weight heparin and unfractionated heparin are likely to accumulate when the CrCl falls below 20 ml/min. In addition bleeding complications are likely to be more severe in patients with renal impairment because platelet function is impaired. For these reasons if treatment dosages of heparin are required in patients with a CrCl less than 20 ml/min there are two options:

- Use subcutaneous dalteparin with 2/3 of the normal weight adjusted dosage (see Table 3 for dose banding recommendations) and monitoring of anti-Xa plasma concentration may be considered, although the correlation between anti-Xa level and bleeding risk is very weak. The advantage of this is that the response is more predictable, but the disadvantage is that initially monitoring is still required and LMWH is not readily reversible.

OR
- Use intravenous UFH and monitor the APTT appropriately. The advantage of UFH is that it can easily be stopped if necessary and its effects wear off rapidly. It can also be easily reversed with protamine. The disadvantage is that achieving adequate anticoagulation is unpredictable and dosage adjustments based on appropriately timed APTT measurements require careful management. For more information, see MIL Vol.5 No.6 Guidelines on when to use and how to monitor Unfractionated Heparin in adults.
**Adverse effects**
- Commonly reported adverse effects include subcutaneous haematoma at the site of injection
- Systemic bleeding is a rare complication of treatment with dalteparin.
- Heparin-induced thrombocytopenia (HIT) has been reported in association with low molecular weight heparins and is an indication for immediate cessation of treatment.

Heparin products can cause hypoaosmeteronism which may result in an increase in plasma potassium. Rarely, clinically significant hyperkalaeemia may occur, particularly in patients with chronic renal failure and diabetes mellitus.

**Pregnancy and lactation**
Dalteparin has been assessed in pregnant women and no harmful effects are known with respect to the course of pregnancy and the health of the unborn and neonate. Dosing in pregnant patients may vary from those quoted above due to differences in the volume of distribution of dalteparin in pregnancy. Separate guidance is available from the Women’s Services Directorate.

**Overdose / reversal**
In an emergency the anticoagulant effect of dalteparin can be partially reversed by protamine sulphate. One mg of protamine sulphate inhibits the effect of 100 units (anti-Xa) of dalteparin. The usual maximum dose is 50 mg given by slow IV injection (rate not exceeding 5 mg per minute). The Haemophilia and Thrombosis Centre can be contacted for further advice. (Out of hours, contact the on call haematology registrar via switchboard).

**Dalteparin and intramuscular injections**
Intramuscular injections should be avoided in patients receiving anticoagulants, except for adrenaline in severe anaphylaxis.

**Dalteparin and surgery**
Separate guidelines are available for the peri-operative management of anticoagulation (see MIL Vol.10 No.5 for full guidance). If necessary, contact the on call haematology registrar for advice.

**Heparin-induced thrombocytopenia (HIT)**
Clinically important HIT is rare with LMWH except in patients receiving the drug in some post-operative settings. Evidence suggests the risk of developing HIT with LMWH is greatest in patients who have undergone cardiac surgery, and that other patients do not require monitoring. The more common type of HIT is immune-mediated and does not normally develop until 5-10 days after starting unless the patient has been exposed to heparins in the previous 100 days. All patients who are to receive dalteparin should have a platelet count on the day of starting therapy. For patients receiving the drug after cardiac surgery, check the platelet count every 2-4 days between days 4 to 14 (or from day 1 if the patient has been exposed to heparins in the previous 100 days). All other patients do not require platelet count monitoring unless they show signs of HIT such as thrombosis or skin allergy. If HIT is strongly suspected or confirmed, dalteparin should be stopped and an alternative anticoagulant, such as danaparoid, lepirudin, bivalirudin, argatroban or fondaparinux should be given (see MIL Vol. 5 No. 10 Alternative Anticoagulants for use in Heparin-Induced Thrombocytopenia in Adults or contact the on call haematology registrar for advice).

**Safe medication practice**
- Dalteparin should always be prescribed with "UNITS" written in full.
- When using pre-filled single dose syringes, to ensure delivery of the full dose, do not expel the air bubble from the pre-filled syringe before injection
- Dalteparin doses are weight-based. Ensure that the patient’s weight is documented on ALL prescriptions for dalteparin.

**References**
4. Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing. NICE CG144, June 2012

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