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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 venous thromboembolism (VTE) in adults with enoxaparin (Inhixa®)

Enoxaparin sodium is the Low Molecular Weight Heparin (LMWH) of choice in OUH. Enoxaparin is a biological medicine and as such should be prescribed by brand; Inhixa® will be supplied for all enoxaparin prescriptions. Each reference to enoxaparin in this document relates to Inhixa®. Enoxaparin is 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.

Starting LMWH therapy

Prior to starting treatment, a baseline coagulation screen, full blood count and U&Es (including renal function and liver function) must be performed.

Dose of enoxaparin

Doses differ according to indication and are outlined in tables 1, 2 and 3.

- Standard dose for treatment of VTE = 1.5mg/kg daily (table 1)
- Dose for treatment of VTE in high-risk patients = 1mg/kg twice daily (table 2)
- Dose of treatment of VTE in presence of renal impairment = 1mg/kg once daily (table 3)

To minimise risk, pre-filled syringes of enoxaparin are recommended. Please utilise Powerplans within ePMA to aid safe prescribing.

Weight of patient

Doses of enoxaparin are weight-based. It is imperative that the patient is weighed and that the weight is documented on the patient's electronic record. In exceptional circumstances, when weighing the patient is not possible, the estimated weight must be documented. For patients with known fluid overload (e.g. those requiring dialysis, nephrotic syndrome, liver or heart failure), dry weight should be used to dose the LMWH. **Pharmacy will not dispense enoxaparin and nursing staff are at liberty to refuse to administer enoxaparin if there is no documented weight.** Patients who weigh less than 40kg should be discussed with a Haematology SpR before treatment is initiated. Also consider discussing treatment with Haematology if the patient's weight exceeds 180kg.

Use in renal impairment

Anticoagulation with heparins in the presence of significant renal impairment is not straightforward due to risk of accumulation. In addition, bleeding complications are likely to be more severe in patients with renal impairment because platelet function is impaired. The dose of enoxaparin is dependent upon renal function (see below).
When checking anti-Xa in patients with renal impairment, trough levels are recommended.

Contraindications

- Known hypersensitivity to enoxaparin, heparin or its derivatives including other LMWHs
- Current or recent GI ulceration
- Presence of malignant neoplasm at high risk of bleeding
- Recent brain or spinal injury
- Recent brain, spinal or ophthalmic surgery
- Recent intracranial haemorrhage
- Known or suspected oesophageal varices
- Arteriovenous malformation
- Vascular aneurysms, major intraspinal or intracerebral vascular abnormalities
- Acute stroke (contact stroke team)
- Uncontrolled severe hypertension
- Regional anaesthesia is a relative contra-indicated in patients receiving enoxaparin
- History of Heparin-Induced Thrombocytopenia (HIT)

Risk factors for bleeding include:

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

Table 1: Standard dose for treatment of VTE 1.5mg/kg daily – Creatinine Clearance above 30ml/min

A switch from once daily to twice daily dosing is required from 110kg due to availability of syringes.

Weight *	Dose of enoxaparin by subcutaneous injection using a pre-filled syringe
39kg or less	speak to haematology
40-47kg	60mg once daily
48-59kg	80mg once daily
60-73kg	100mg once daily
74-88kg	120mg once daily
89-109kg	150mg once daily
110-125kg	100mg morning and 80mg evening
126-139kg	100mg twice daily
140-154kg	120mg morning and 100mg evening
155-162kg	120mg twice daily
163-176kg	150mg morning and 100mg evening
177-190kg	150mg morning and 120mg evening
191kg or more	150mg twice daily

Table 2: Treatment of VTE in high-risk patients 1mg/kg twice daily – Creatinine Clearance above 30ml/min

High risk is defined as:

1. recurrent episode of VTE whilst on therapeutic anticoagulation
2. new diagnosis of VTE in a patient known to have triple positive antiphospholipid syndrome
3. new diagnosis of iliofemoral DVT under active review by vascular for early surgical intervention duration to be directed by the vascular team.

Weight *	Dose of enoxaparin by subcutaneous injection using a pre-filled syringe
39kg or less	speak to haematology
40-44kg	40mg twice daily
45-54kg	60mg morning and 40mg evening
55-64kg	60mg twice daily
65-74kg	80mg morning and 60mg evening
75-84kg	80mg twice daily
85-94kg	100mg morning and 80mg evening
95-104kg	100mg twice daily
105-114kg	120mg morning and 100mg evening
115-122kg	120mg twice daily
123-132kg	150mg morning and 100mg evening
133-142kg	150mg morning and 120mg evening
143kg or more	150mg twice daily

Table 3: Treatment of VTE in renal impairment 1mg/kg daily – Creatinine Clearance 30ml/min or less including dialysis (for acute kidney injury or maintenance)

A switch from once daily to twice daily dosing is required from 165kg due to availability of syringes.

Weight *	Dose of enoxaparin by subcutaneous injection using a pre-filled syringe
39kg or less	Speak to haematology
40-49kg	40mg once daily
50-69kg	60mg once daily
70-89kg	80mg once daily
90-109kg	100mg once daily
110-134kg	120mg once daily
135-164kg	150mg once daily
165-189kg	100mg morning and 80mg evening
190-209kg	100mg twice daily
210-229kg	120mg morning and 100mg evening
230- 244kg	120mg twice daily
245-259kg	150mg morning and 100mg evening
260-284kg	150mg morning and 120mg evening
285kg or more	150mg twice daily

* Doses of enoxaparin are weight-based. It is imperative that the patient is weighed and that the weight is documented on the patient's electronic record. In exceptional circumstances, when weighing the patient is not possible, the estimated weight must be documented. For patients with known fluid overload (e.g. those requiring dialysis, nephrotic syndrome, liver or heart failure), dry weight (known or estimated) should be used to dose the LMWH.

Monitoring

Plasma anti-Xa concentration can be used to monitor the anticoagulant effect of enoxaparin. For patients with renal impairment (CrCl 30ml/min or less), it is recommended to check anti-Xa levels after 7 days. Patients at extremes of weight (less than 40kg or more than 150kg) can be considered for anti-Xa levels if treatment with enoxaparin is likely to exceed 7 days. This must be done in secondary care.

	Anti-Xa target range Enoxaparin ONCE daily	Anti-Xa target range Enoxaparin TWICE daily
Peak	1.0-2.0 units/ml	0.6-1.0 units/ml
Trough	0.4 units/ml or less	

(Take the peak level 3-4 hours after dose and trough immediately prior to dose).

If the anti-Xa level is out of the range, contact haematology for advice. Patients with anti-Xa levels in range, do not require repeat monitoring unless their clinical situation changes.

Inhibition of aldosterone secretion by LMWH can 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 enoxaparin for longer than 7 days potassium should be monitored.

All patients who are to receive enoxaparin 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 (see below).

Patients with platelet counts which are less than 50 or expected to fall to less than 50

Therapeutic anticoagulation is not generally used in patients who have platelet counts less than 50 due to the risk of bleeding. If patients have an acute VTE then anticoagulation should be carefully considered. Please consider discussing with the Haemostasis SpR Bleep 5529 or Consultant.

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 enoxaparin 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, enoxaparin should be stopped and an alternative anticoagulant, such as fondaparinux, argatroban, danaparoid or bivalirudin 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).

Adverse effects

- Commonly reported adverse effects include subcutaneous haematomas at the site of injection
- Systemic bleeding is a rare complication of treatment with enoxaparin

Patients with cancer

Randomised controlled trials have recently evaluated the use of DOACs in patients with active cancer. When compared directly with LMWH, DOACs are as effective at treating VTE as LMWH. Please see MIL Vol 8, No 1 for more details.

Pregnancy and lactation

Enoxaparin 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 enoxaparin in pregnancy. Separate guidance is available from the Women's Services Directorate.

Oral anticoagulation with warfarin

Warfarin should be started concurrently if deemed appropriate for ongoing therapy. Treatment with enoxaparin should continue in parallel with oral anticoagulation for five days or until the patient's INR has been greater than or equal to 2 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.*

Overdose / reversal

In an emergency the anticoagulant effect of enoxaparin can be partially reversed by protamine sulphate (60-75% of anti-Xa activity). The is determined by the time elapsed since the enoxaparin dose:

Time since enoxaparin dose	Dose of protamine
8hrs or less	1mg for every 1mg enoxaparin
More than 8hrs	0.5mg for every 1mg enoxaparin
More than 12 hrs	Protamine may not be required

The Haemophilia and Thrombosis Centre can be contacted for further advice. (Out of hours, contact the on-call haematology registrar via switchboard)

Enoxaparin

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

Enoxaparin 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.

Safe medication practice

- 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.
- Enoxaparin doses are weight-based. Ensure that the patient's weight is documented.

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