Clinical guideline

Enoxaparin – prescribing, administration and monitoring

Enoxaparin is the low molecular weight heparin (LMWH) used at WUTH.
This guideline covers the following:

This document is a guideline and further information should be obtained from the relevant reference sources.

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1. Indications (see Table 1)

- Venous thromboembolism (VTE) prophylaxis
- Venous thromboembolism (VTE) treatment
- Acute coronary syndrome (ACS)

There are specific guidelines for managing VTE prophylaxis and treatment in:

- Maternity – for all patients who are pregnant and up to 6 weeks post-partum
- Trauma and Orthopaedics

2. Contraindications:

Enoxaparin is contraindicated in patients with:

- acute bacterial endocarditis
- active major bleeding and conditions with a high risk of uncontrolled haemorrhage, including recent haemorrhagic stroke;
- recent thrombotic stroke (should not be used for 14 days due to risk of haemorrhagic transfer)
- thrombocytopenia in patients with a positive in-vitro aggregation test in the presence of enoxaparin (heparin-induced thrombocytopenia [HIT]);
- active gastric or duodenal ulceration;
- hypersensitivity to either enoxaparin sodium, heparin or its derivatives — including other LMWHs;
- Platelet count less than 75 x 10^9/L (refer to haematology if platelets are below this level and treatment is deemed clinically essential)

3. Initiation

The dose and choice of drug is dependent on the patient's renal function (creatinine clearance [CrCl]) and weight. Check renal function using Cockcroft and Gault. Renal function using eGFR is not equivalent to CrCl and cannot be used for dose adjustment in renal impairment. A CrCl calculator is available on the intranet:
http://apps.wuth.nhs.uk/staff/formulary/calculators.aspx

Cockcroft and Gault equation for creatinine clearance:

Creatinine clearance (mL/min) = $\frac{\textbf{Y x (140-age) x weight (kg)}}{\textbf{Serum creatinine (µmol/L)}}$ Male Y= 1.23 Female Y=1.04

- Use ideal body weight (IBW) in patients unless over or under weight:
  IBW Females = [45.5kg + (2.3 x every inch over 5ft)] kg
  IBW Males = [50kg + (2.3 x every inch over 5ft)] kg
- Use adjusted body weight in obese patients = IBW + 0.4 x (actual body weight – IBW) kg
- Use actual body weight in underweight patients

VTE assessment to be completed on CERNER for all adult inpatients before enoxaparin prescribed for prophylaxis.

Table 1: **Indication for use of enoxaparin**
(For alternatives, see specific guidelines for 'Maternity' and 'Trauma and Orthopaedics')

Indication	Clinical situation	Dose drug and frequency	Renal dose and frequency
VTE prophylaxis (Also see specific VTE guidelines for 'Maternity' and 'Trauma and Orthopaedics')	Medical patient	Enoxaparin 40mg** **once** daily	CrCl<30ml/minute enoxaparin 20mg once daily
	Surgical patient high risk		
	Surgical patient moderate risk	Enoxaparin 20mg** **once** daily	
	Elective hip replacement	Rivaroxaban 10mg **once** daily for 35 days	CrCl<15ml/minute enoxaparin 20mg **once** daily for 35 days
	Elective knee replacement	Rivaroxaban 10mg **once** daily for 14 days	CrCl<15ml/minute enoxaparin 20mg **once** daily for 14 days
VTE treatment	All non-pregnant patients	Enoxaparin 1.5mg/kg‡ **once** daily*	CrCl<30ml/minute enoxaparin 1mg/kg‡ **once** daily
ACS	Prophylaxis	Fondaparinux 2.5mg **once** daily for 8 days then switch to enoxaparin	CrCl<20ml/minute enoxaparin 1mg/kg‡ **once** daily
	Full anticoagulation† in patients UNDER 75 years old	Enoxaparin 1mg/kg‡ **twice** daily	CrCl<30ml/minute enoxaparin 1mg/kg‡ **once** daily
	Full anticoagulation† in patients OVER 75 years old	Enoxaparin 0.75mg/kg‡ **twice** daily	CrCl<30ml/minute enoxaparin 1mg/kg‡ **once** daily

*For 5 days minimum and until INR in range for 2 consecutive days where warfarin is initiated.

****Extremes of actual body weight and VTE prophylaxis**:
<50kg – use 20mg enoxaparin once daily
100-150kg – use 80mg enoxaparin once daily
>150kg – use 120mg enoxaparin once daily

‡Actual body weight should be used for dose calculation. See Appendix 1 for dose banding.

†For example, full dosing is required for patients with atrial fibrillation, suspected venous thromboembolism, or a mechanical heart valve

4. Duration:

- VTE prophylaxis to continue for duration of inpatient stay unless VTE or bleeding risk changes. Repeat VTE assessment as per VTE policy
- VTE prophylaxis may continue on discharge for high risk patients
- VTE treatment when warfarin commenced — continue for a minimum of 5 days and until INR is above 2 for two consecutive days
- VTE treatment without warfarin commenced — continue for duration of treatment period
- VTE treatment when NOAC (apixaban, dabigatran, edoxaban, rivaroxaban) started — stop enoxaparin and replace with a NOAC when the next dose is due. If starting dabigatran or edoxaban, the patient must receive enoxaparin for at least 5 days before switching.

5. Administration

Subcutaneous administration. Self-administration of enoxaparin following discharge should be encouraged for patients who are capable; administration by a family member or carer may also be considered. If this happens, a sharps box needs to be supplied. Patients discharged to community care for administration of enoxaparin will need to have a Patient Medication Administration Chart (PMAC) completed prior to discharge.

6. Monitoring

As noted above the dose of enoxaparin needs to be reviewed when renal function is impaired. Enoxaparin can also cause hyperkalaemia and this is more likely to occur with prolonged duration of treatment and/or patients with diabetes mellitus, chronic renal failure, raised potassium levels or if taking potassium-sparing medicines.

Table 2: **Monitoring of enoxaparin**

<table>
<tr><th>Patient group</th><th>Parameter</th><th>Frequency</th><th>Action</th></tr>
<tr><td>All patients</td><td>FBC
U&E</td><td>• Baseline
• Daily for acutely unwell inpatients</td><td rowspan="2">If 30% or more reduction in platelets and patient develops new thrombosis or skin allergy between days 4 and 14 of heparin administration then HIT should be considered and investigated

If significant drop in Hb indicating bleeding, stop enoxaparin

Check creatinine clearance and amend dose as necessary</td></tr>
<tr><td>Post-operative patients including cardiopulmonary bypass patients who have been exposed to heparin in the previous 100 days and receiving any type of heparin</td><td>Platelets
U&E</td><td>• Baseline
• 24 hours after starting enoxaparin</td></tr>
<tr><td>Patients on LMWH >3 months.</td><td>FBC, U&E
Anti-Xa</td><td colspan="2"></td></tr>
</table>

	levels Bone densitometry	

7. Reversal

Within 5 minutes of being administered, protamine acts to neutralise the effects of enoxaparin. However, at maximum, it only neutralises 60% of enoxaparin's effect. The dose depends on the time since the enoxaparin was given:

- If enoxaparin given LESS than 5 hours ago, give 1mg protamine for every 1mg enoxaparin administered
- If enoxaparin given MORE than 5 hours ago, give 0.5mg protamine for every 1mg enoxaparin administered

Patients should be carefully monitored using either the activated partial thromboplastin time or the activated clotting time — carried out 5-15 minutes after protamine administration. Further doses may be needed because protamine is cleared from the blood more rapidly than heparin, especially low molecular weight heparin. In gross excess, protamine itself acts as an anticoagulant.

8. Discharge

Where enoxaparin is prescribed on discharge, the prescriber must provide clear instructions to the patient's GP regarding the dose of enoxaparin and the duration of treatment. Where treatment is intended to last longer than 6 weeks, a referral to haematology must be made to ensure ongoing monitoring.

When clinically checking the discharge prescription, at minimum, the ward pharmacist must ensure that the above information has been completed by the prescriber and is available on the discharge letter. The ward pharmacist should then complete the checklist below and endorse 'IDDAM' on the discharge prescription to indicate that the above checks are complete before any supplies of LMWH will be made on discharge. Up to 2 weeks' supply of LMWH will be made by the hospital at discharge and then this should be continued by the patient's GP.

- Appropriate **I**ndication (if on extended duration of LMWH due to poor compliance, must state in the notes that the decision has been approved by the senior medical staff)
- **D**ose – appropriate for the patient's renal function and weight
- **D**uration
- Appropriately trained person to **A**dminister the LMWH in the community if the patient is unable to self-administer.
- **M**onitoring. The patient has been referred to haematology by the clinician for ongoing monitoring for patient's receiving extended LMWH treatment

9. Other related trust guidance

Other guidelines relating to anticoagulation can be found under “anticoagulation” within the clinical guidelines section of the Medicines Management website.

10. References

1. National Institute for Health and Clinical Excellence (NICE) clinical guidelines 92: Venous thromboembolism: reducing the risk. Issue date: January 2010. Available at: www.nice.org.uk/guidance/index.jsp?action=byID&o=12695 (accessed 1/6/2015)
2. Department of Health. Venous thromboembolism risk assessment tool http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/documents/digitalasset/dh_113355.pdf (accessed 1/6/2015)
3. Summary of product characteristics. Clexane. http://www.medicines.org.uk/emc/medicine/12847 (accessed 1/6/2015)
4. British National Formulary May 2015 online https://www.medicinescomplete.com/mc/bnf/current/ (accessed 1/6/2015)
5. WUTH Maternity guidelines http://www.whnt.nhs.uk/document_uploads/Intranet-Pharmacy/VTE%20Guideline_(maternity)-clinical_guideline,v6.pdf
6. WUTH Trauma and Orthopaedic http://www.wuth.nhs.uk/media/1567932/VTE_prophylaxis_Trauma-and-orthopaedics_v23.pdf
7. WUTH http://www.wuth.nhs.uk/media/1567959/Heparin-induced-thrombocytopenia-HIT-Diagnosis-and-management-v1.pdf
8. Anticoagulant Guidelines Kings College Hospital http://www.kingsthrombosiscentre.org.uk/index.php/anticoagulation/anticoagulation-guidelines (accessed online 1/6/2015)
9. Summary of product characteristics protamine sulphate 1% http://www.medicines.org.uk/emc/medicine/10807/spc (accessed 8/6/2015)

Appendix: Dose banding for enoxaparin

Body weight (kg)	Dose at 1.5mg/kg (mg)		Body weight (kg)	Dose at 1mg/kg (mg)		Body weight (kg)	Dose at 0.75mg/kg (mg)
40-49	**60**		30-40	**30**		40-49	**30**
50-59	**80**		40-50	**40**		50-59	**40**
60-74	**100**		50-60	**50**		60-74	**50**
75-89	**120**		60-70	**60**		75-89	**60**
90-99	**140**		70-80	**70**		90-99	**70**
100-109	**150**		80-90	**80**		100-109	**75**
110-114	**160**		90-100	**90**		110-114	**80**
115-120	**180**		100-110	**100**		115-120	**90**
121-135	**200***		110-120	**110**		121-135	**100**
136-150	**220***		120-130	**120**		136-150	**110**
			130-140	**130**			
			140-150	**140**			
			150-160	**150**			

*Antifactor Xa levels need to be taken after the 3rd or 4th dose and doses adjusted accordingly after discussion with haematology when required.