East Lancashire Hospitals NHS Trust
A University Teaching Trust

BEST PRACTICE GUIDELINE

Use of Low Molecular Weight Heparins (LMWH) e.g. Enoxaparin (Inhixa™)

Purpose & Scope

This guideline aims to provide sufficient information to ensure LMWHs are used safely and appropriately. It is aimed at all healthcare professionals involved in the prescribing, dispensing or administration of LMWHs. It aims to cover all indications (licensed and unlicensed) for the prevention or treatment of venous thromboembolism. It is applicable to all patients who are to receive a LMWH and have been discharged from hospital, are still under the routine care of a hospital specialist through outpatient follow up, or who are being managed purely by a primary care clinician. It is not intended to guide management of inpatients in hospital or in a community hospital; the relevant Trust policies should be consulted in this instance.

Introduction & Background

Venous thrombosis is a condition in which a blood clot (thrombus) forms in a vein. Blood flow through the affected vein can be limited by the clot, causing swelling and pain in the affected limb or area. Venous thrombosis most commonly occurs in the 'deep veins' in the legs, thighs, or pelvis. This is known as a deep vein thrombosis. An embolism is created if a part or all of the blood clot in the deep vein breaks off from the site where it is created and travels through the venous system. If the clot lodges in the lung a very serious condition, pulmonary embolism (PE), arises, which can be life threatening. Venous thrombosis can form in any part of the venous system. However, deep vein thrombosis (DVT) and PE are the most common manifestations of venous thrombosis. DVT and PE are known as venous thromboembolism (VTE).

Low Molecular Weight Heparins (LMWHs)

LMWHs are used in the '**prevention**' of VTE (prophylaxis) in patients at moderate to high risk and are given in a low dose.

LMWHs are also used in the '**treatment**' of VTE in patients who develop a DVT or PE and are given in a higher dose.

As LMWHs work very quickly, they are used concurrently with warfarin in the first few days of treatment for patients with VTE and are continued until the INR is in the target range. Once the INR is in the target range for 24 hours (showing that the warfarin is working sufficiently) then the LMWH is stopped. However, not all patients can take warfarin and therefore LMWHs are sometimes used for longer periods of time instead of warfarin.
When used for prevention of VTE, LMWHs are given for as long as the patient is deemed to be at high risk, and then they are stopped. **Wider context**: Direct Oral Anticoagulants (DOAC's) are now used in many VTE management plans and have a rapid onset of action that does not require LMWH during initiation.

East Lancashire Health Economy Choices of LMWH

There are a number of LMWHs licensed for both prevention and treatment of DVT/PE in the UK. In East Lancashire Hospitals for medical, surgical and obstetric patients, the LMWH agreed for prophylaxis **and** treatment of VTE is **Enoxaparin (Inhixa™).**

For prophylaxis of PE/VTE use ENOXAPARIN (Inhixa™) Syringes
A dose of 40mg once daily is recommended for most adult medical and surgical patients, with dose adjustments for extremes of body weight and renal impairment.
Enoxaparin (Inhixa™) syringes are available in 20mg (0.2mL), 40mg (0.4mL) and 60mg (0.6mL) strengths.

For treatment of PE/VTE use ENOXAPARIN (Inhixa™) syringes.
It is vital that patients are weighed using appropriate equipment, that their weight is accurately recorded, and that the dose of enoxaparin is accurately calculated based on their weight.
For treatment dosing with enoxaparin the syringe choice will depend on the patient's body weight.
Enoxaparin (Inhixa™) syringes are available as 40mg (0.4mL), 60mg (0.6mL), 80mg (0.8mL), 100mg (1.0mL), 120mg (0.8mL) and 150mg (1.0mL) strengths.
The dose to be given, and the syringe to be prescribed should only be calculated by weighing the patient and using the charts inside.

In addition, **Enoxaparin (Inhixa™)** is used in acute coronary syndrome if fondaparinux is contra-indicated due to reduced renal function.
A dose of 1mg/kg every 24 hours is recommended for most patients (refer to SPC). ELHT vascular services also use therapeutic **doses** of **Enoxaparin** following embolectomy (Both indications RED traffic light).

How to use this guideline

Secondary Care Specialists Read the introduction above. Pages 2, 3 and 4 contain guidance for specific indications. Check whether prescribing for the whole course is your responsibility (i.e. via outpatient prescriptions) or whether the GP can be asked to prescribe. For treatment of VTE ensure the patient has been accurately weighed to calculate the correct rounded-up dose and if self-administering that the patient is trained. Communication to GP/primary care (discharge letter) must include the indication, dose, strength and volume of syringe (mL & units), monitoring requirements, renal status, patient weight and treatment duration. Where referral to district nurse / treatment room is required refer to page 6. Patients must be supplied with written information about their treatment that is understood.

Primary Care Prescribers Read the introduction above. Go to the central page relevant to the indication you have been asked to prescribe for. Check whether you should prescribe the remainder of the course, or whether the specialist should do so. Follow this advice. If a RED indication, refer back to the specialist. If an AMBER indication, prescribe including the Inhixa™ brand, indication, strength of syringe, dose and weight of patient on the FP10. The weight and indication will need to be added by hand, but are essential. Ensure the patient can self administer. Where district nursing (housebound patients) or treatment room referral required, refer to last page. Ensure patient written information in a suitable format has been supplied, and they understand how to manage their regimen.

Nursing or Pharmacy Staff involved in Dispensing or Administration Nursing and Community pharmacy staff should follow the guidance on the last page to facilitate the checking, dispensing and administration of enoxaparin prescriptions in primary care.

PREVENTION of DVT/PE in MEDICAL & SURGICAL PATIENTS

Prevention of VTE in patients at moderate to high risk

PLEASE NOTE THE DOSES USED IN ELHT FOR PROPHYLAXIS DIFFER FROM THE USUAL LICENSED DOSES

Patients on oral anticoagulation do not require prophylactic enoxaparin or may be bridged with therapeutic enoxaparin for surgical procedures – **see *The Peri-Procedural Management of Patients on Oral Anticoagulants and Antiplatelet medicines*** guidance.

Speciality	Indication	Licensed	Duration	Traffic Light
AMBER Traffic Light - For initiation by or on the recommendation of a specialist, and continuation by a primary care prescriber with the relevant competencies to do so. Nursing staff may still administer with written authorisation.				
General Surgery or Medicine	Immobile patients or those deemed to be at particularly high risk of DVT at home or in care situation.	No	For as long as patient is immobile and/or at higher risk of DVT/PE	AMBER
Haematology	Very high-risk patient, Pre-flight DVT/PE prophylaxis, Haematology advice only	No	Single dose 2-3 hours pre-flight outward and return (Ref: NHS CKS [Prodigy] Guideline)	AMBER
Assessment of risk should be made on an individual basis but it is likely that recent major surgery (within 1 month), active malignancy, previous unprovoked VTE, previous travel-related VTE with no associated temporary risk factor or presence of more than one risk factor identifies those travellers at highest thrombosis risk. Travellers at the highest risk of travel-related thrombosis undertaking journeys of >3 hours should wear well fitted below knee compression hosiery. In unusual circumstances where the patient is deemed to be at an additionally high risk, consultant haematologist advice is necessary to discern when pharmacological prophylaxis is considered appropriate using LMWH. Arrange for self-administration or district nurse (housebound patients) or treatment room nurse and consider need for compression hosiery. The person should be advised on the safe storage and disposal of 'sharps', and should be given a letter for security, immigration, and customs officials that explains why it is medically necessary for them to carry needles and syringes when travelling. **Ref. British Journal of Haematology, 152, 31–34**				
RED Traffic Light - Not for GP prescribing. Whole course supplied by hospital. Nursing staff may still administer with written authorisation. Prescribers should ensure adequate supplies for patients are prescribed as they will not be able to obtain via GP				
Vascular Surgery	High-risk patient: peri-operatively	Yes	Started the day prior to surgery	RED
Orthopaedics	Postoperatively: Hip Fracture/Replacement	Yes	Emergency surgery: 28 days following surgery Elective surgery: 10 days LMWH followed by 28 days aspirin * (*see ELHT guidance CP17a for full details)	RED
Orthopaedics	Postoperatively: Knee Replacement	Yes	14 days in total following surgery	RED
Orthopaedics	Lower limb cast immobilisation	Yes	Until cast removal/full mobility restored - review in Fracture Clinic	RED
All Surgical Specialities	Cancer: Abdominal Solid Tumour Patient Postoperatively	Yes	28 days in total after operation then stop	RED
All Surgical Specialities	High Risk Patient: Postoperatively	Yes	As directed by the surgeon Up to 28 days maximum	RED
Gynaecology	High Risk Patients: Postoperatively	Yes	7 days postoperatively	RED
Haematology	High Risk Patient: Treated with VTE inducing medicine such as lenalidomide	No	As long as receiving lenalidomide or equivalent	RED

Enoxaparin (Inhixa™) Dosing in VTE Prophylaxis for Surgical and Medical patients

VTE prophylaxis for medical and surgical patients		
Patient Weight	**Standard dose**	**Renal dose** (Creatinine clearance <30mL/min)
<50kg	Enoxaparin **20mg once** daily	Enoxaparin **20mg once** daily
50-120kg	Enoxaparin **40mg once** daily*	Enoxaparin **20mg once** daily
>120 – 150kg	Enoxaparin **40mg twice** daily	Enoxaparin **40mg once** daily
>150kg	Enoxaparin **60mg twice** daily	Enoxaparin **40mg once** daily

*May be given in two divided doses

PREVENTION of DVT/PE during PREGNANCY and following delivery

Prevention of DVT/PE in pregnant patients at moderate to very high risk

PLEASE NOTE THE DOSES USED IN PREGNANCY FOR PROPHYLAXIS DIFFER FROM THE USUAL LICENSED DOSES

This guidance below summarises the East Lancashire Hospitals Trust guidelines which are based upon the Royal College of Obstetrics & Gynaecology Guidelines for Thromboprophylaxis during pregnancy, labour and after vaginal delivery (April 2015, Green Top Guideline no. 37a). It does not address prophylaxis following caesarean section or the acute management of VTE in pregnancy, which is covered further on.

MODERATE TO HIGH RISK PATIENTS: NOT ON WARFARIN PRIOR TO PREGNANCY

Note: The table below is an abridged version of the full ELHT guideline which should be referred to for definitive guidance. This table is to give a quick reference guide to this complex area.

RED Traffic Light - Not for GP prescribing. Whole course supplied by hospital. Nursing staff may still administer with written authorisation. Prescribers should ensure adequate supplies for patients are prescribed as they will not be able to obtain via GP

Indication		Licensed	Duration	Traffic Light
Very high	Previous VTE on long-term warfarin Antithrombin deficiency Antiphospholipid syndrome with previous VTE	No	Recommend antenatal high-dose LMWH and at least 6 weeks postnatal LMWH/warfarin Requires specialist management by experts in haemostasis and pregnancy	RED
High Previous estrogen-provoked (pill or pregnancy) VTE	Previous recurrent or unprovoked VTE Previous VTE + thrombophilia Previous VTE + family history of VTE Asymptomatic thrombophilia (combined defects, homozygous factor V Leiden)	No	Recommend antenatal and 6 weeks postnatal prophylactic LMWH.	RED
Intermediate	Single previous VTE associated with transient risk factor no longer present without thrombophilia, family history or other risk factor Asymptomatic thrombophilia (except antithrombin deficiency, combined defects, homozygous factor V Leiden)	No	Consider antenatal LMWH (but not routinely recommended) Recommend 6 weeks postnatal prophylactic LMWH Recommend 10 days (or 6 weeks if family history or other risk factors) postnatal prophylactic LMWH	RED

Weight: Use pre-pregnancy or booking weight at approximately 16 weeks, NOT the current weight.

Enoxaparin (Inhixa™) Dosing in Prophylaxis of DVT and PE during PREGNANCY and following DELIVERY

Patient Weight	<50kg	50 - 90kg	>90 - 130kg	>130 - 170kg	>170kg
Standard Dose	20mg Once daily	40mg Once daily	60mg Once Daily*	80mg Once Daily	0.6mg/kg/day*
High-risk Dose		40mg Twice daily			

*may be given in two divided doses

IMPORTANT INFORMATION

Once the woman is in labour or thinks she is in labour, she should be advised not to inject any further LMWH. She should be reassessed on admission to hospital and further doses should only be prescribed by medical staff.

Regardless of their risk of VTE, immobilisation of women during pregnancy, labour and the puerperium should be minimised and dehydration should be avoided. Warfarin should usually be avoided during pregnancy. It can be used after delivery and during breastfeeding.

Treatment of DVT/PE in all patients managed with LMWH

Full anticoagulation of patients with a diagnosis (or working diagnosis) of DVT/PE

See pages 7 and 8 for dosing information for inpatients and outpatients.

Speciality	Indication	Licensed	Duration
AMBER Traffic Light - For initiation by or on the recommendation of a specialist, and continuation by a primary care prescriber with the relevant competencies to do so. Nursing staff may still administer with written authorisation			
General Medicine / Emergency Department	Treatment of suspected DVT only whilst awaiting scan or scan results, usually only over a weekend	Yes	Until warfarin is in range, or scan is negative
Oncology	Treatment of DVT/PE in an oncology patient with a solid tumour. Enoxaparin given first line (as is superior to warfarin) for the whole of the treatment course. Also given in place of warfarin for patients undergoing chemotherapy that interacts with warfarin	Yes	6 months – DVT and PE then review (NICE CG144)
General Medicine	Warfarin replacement. Full anticoagulation required but where warfarin is not appropriate or not tolerated, or where INR is out of range with warfarin. Including but not exclusively patients with NG/PEG tubes, hepatic failure, erratic lifestyle (e.g. IV drug abuser), unable to monitor INR, warfarin allergy	No	As per intended duration of warfarin treatment. Usually, 3 to 6 months – DVT 6 months - PE OR as stated by the specialist
All Surgical Specialities	Warfarin replacement. Given pre-operatively for up to 5 days up until the day of surgery instead of taking warfarin. Allows INR to fall before operation	No	As directed by the surgeon
RED Traffic Light - Not for GP prescribing. Whole course supplied by hospital. Nursing staff may still administer with written authorisation. Prescribers should ensure adequate supplies for patients, as they will not be able to get additional supplies from their GP.			
All Medical & Surgical Specialities	Given post-operatively in conjunction with warfarin whilst waiting for the INR to come into range	No	Until INR is in range, for a minimum of 6 days treatment with enoxaparin
Obstetrics & Gynaecology	Treatment of DVT/PE in pregnancy. First line treatment of choice.	No	During pregnancy and for at least 6 weeks postnatally, until at least 3 months is given in total
Obstetrics & Gynaecology	Patients with mechanical heart valves or those on long term warfarin prior to pregnancy should be discussed by obstetrics/gynaecology consultants with consultant cardiologists/haematologists, ideally before pregnancy	No	As advised by the specialist. Likely to be throughout pregnancy in place of warfarin.

Enoxaparin (Inhixa™) Strength	Syringe Colour	Graduations and Concentration
Inhixa™ 20mg (0.2mL)		No graduations available Not suitable for part dosing
Inhixa™ 40mg (0.4mL)		No graduations available Not suitable for part dosing
Inhixa™ 60mg (0.6mL)		Standard concentration of **100mg/mL** Each graduation of 0.025mL is equal to 2.5mg enoxaparin Suitable for part dosing
Inhixa™ 80mg (0.8mL)		Standard concentration of **100mg/mL** Each graduation of 0.025mL is equal to 2.5mg enoxaparin Suitable for part dosing
Inhixa™ 100mg (1.0mL)		Standard concentration of **100mg/mL** Each graduation of 0.025mL is equal to 2.5mg enoxaparin Suitable for part dosing
Inhixa™ 120mg (0.8mL) **High Strength**		High strength concentration of **150mg/mL** Each graduation of 0.025mL is equal to 3.75mg enoxaparin Suitable for part dosing
Inhixa™ 150mg (1.0mL) **High strength**		High strength concentration of **150mg/mL** Each graduation of 0.025mL is equal to 3.75mg enoxaparin Suitable for part dosing

Enoxaparin (Inhixa™) Dosing in Treatment of DVT or PE in all INPATIENTS

Enoxaparin can be administered subcutaneously (SC) either as a **ONCE DAILY** injection of 1.5mg/kg (150units/kg) or as **TWICE DAILY** injections of 1mg/kg (100units/kg). The regimen should be selected by the secondary care physician based on an individual assessment including evaluation of the thromboembolic risk and of the risk of bleeding. The dose regimen of 1.5mg/kg administered once daily should be used in uncomplicated patients with low risk of VTE recurrence.
The dose regimen of 1mg/kg administered twice daily should be used in all other patients such as those with obesity, with symptomatic PE, cancer, recurrent VTE or proximal (vena iliaca) thrombosis.

Lower risk of recurrence VTE

Renal dose (<30mL/min) 1mg/kg ONCE daily

Patient Weight	Dose (1.5mg/kg ONCE daily)	Enoxaparin (Inhixa™) Syringe(s) required	Injection volume required per dose
35-39	**50mg ONCE** daily	**60mg/0.6mL syringe**	**0.5 mL**
40-44	**60mg ONCE** daily		**0.6 mL**
45-49	**70mg ONCE** daily	**80mg/0.8mL syringe**	**0.7 mL**
50-54	**75mg ONCE** daily		**0.75 mL**
55-59	**80mg ONCE** daily		**0.8 mL**
60-64	**90mg ONCE** daily	**100mg/1mL syringe**	**0.9 mL**
65-69	**100mg ONCE** daily		**1 mL**
70-74	**105mg ONCE** daily	**120mg/0.8mL HIGH STRENGTH syringe**	**0.7 mL**
75-79	**112.5mg ONCE** daily		**0.75 mL**
80-84	**120mg ONCE** daily		**0.8 mL**
85-89	**131.25mg ONCE** daily	**150mg/1mL HIGH STRENGTH syringe**	**0.875 mL**
90-94	**135mg ONCE** daily		**0.9 mL**
95-99	**142.5mg ONCE** daily		**0.95 mL**
100-104	**150mg ONCE** daily		**1 mL**
105-109	**155mg ONCE** daily	**100mg/1mL syringe**	**1 mL**
		60mg/0.6mL syringe	**0.55 mL**
110-114	**165mg ONCE** daily	**100mg/1mL syringe**	**1 mL**
		80mg/0.8mL syringe	**0.65mL**
115-119	**170mg ONCE** daily	**100mg/1mL syringe**	**1 mL**
		80mg/0.8mL syringe	**0.7 mL**
120-124	**180mg ONCE** daily	**100mg/1mL syringe**	**1 mL**
		80mg/0.8mL syringe	**0.8 mL**
125-129	**185mg ONCE** daily	**2 x 100mg/1mL syringes**	**1 mL**
			0.85 mL
Dose dependant (Consultant discretion)	>130kg, BMI <40	**1mg/kg TWICE** daily, rounded to the nearest syringe	
	>130kg, BMI >40	**1.5mg/kg daily split into two divided doses**, rounded to the nearest syringe with **factor anti-Xa monitoring**	

Higher risk of recurrence VTE

Renal dose (<30mL/min) 1mg/kg ONCE daily

Patient Weight	Dose (1mg/kg TWICE daily)	Enoxaparin (Inhixa™) Syringe(s) required	Injection volume required per dose
35-39	**40mg TWICE** daily	**40mg (0.4mL)**	**0.4 mL**
40-44			
45-49	**50mg TWICE** daily	**60mg (0.6mL)**	**0.5 mL**
50-54			
55-59	**60mg TWICE** daily		**0.6 mL**
60-64			
65-69	**70mg TWICE** daily	**80mg (0.8mL)**	**0.7 mL**
70-74			
75-79	**80mg TWICE** daily		**0.8 mL**
80-84			
85-89	**90mg TWICE** daily	**100mg (1mL)**	**0.9 mL**
90-94			
95-99	**100mg TWICE** daily		**1 mL**
100-104			
105-109	**112.5mg TWICE** daily	**120mg (0.8mL) HIGH STRENGTH syringe**	**0.75 mL**
110-114			
115-119	**120mg TWICE** daily		**0.8 mL**
120-124			
125-129	**131.25mg TWICE** daily	**150mg/1mL HIGH STRENGTH syringe**	**0.875 mL**
>130kg	**150mg TWICE** daily **with anti-factor Xa monitoring**		**1 mL**

NICE Clinical Guideline (CG) 189 classifies obesity as a body mass index measurement (BMI) greater than 30.

Enoxaparin (Inhixa™) Dosing in Treatment of DVT or PE in all OUTPATIENTS using over-labelled packs

Clinical areas which keep stocks of over-labelled enoxaparin for use in treatment of DVT and PE will only stock **60mg/0.6mL**, **100mg/1mL** and **150mg/1mL** syringes. The information in the dosing table below gives information on which syringe(s) to select and associated volumes to be administered.

Lower risk of recurrence VTE

Renal dose (<30mL/min) 1mg/kg ONCE daily

Patient Weight	Dose (1.5mg/kg ONCE daily)	Enoxaparin (Inhixa™) Syringe(s) required	Injection volume required per dose
35-39	**50mg ONCE** daily	60mg/0.6mL syringe	0.5 mL
40-44	**60mg ONCE** daily		0.6 mL
45-49	**70mg ONCE** daily	100mg/1mL syringe	0.7 mL
50-54	**75mg ONCE** daily		0.75 mL
55-59	**80mg ONCE** daily		0.8 mL
60-64	**90mg ONCE** daily		0.9 mL
65-69	**100mg ONCE** daily		1 mL
70-74	**105mg ONCE** daily	150mg/1mL HIGH STRENGTH syringe	0.7 mL
75-79	**112.5mg ONCE** daily		0.75 mL
80-84	**120mg ONCE** daily		0.8 mL
85-89	**131.25mg ONCE** daily		0.875 mL
90-94	**135mg ONCE** daily		0.9 mL
95-99	**142.5mg ONCE** daily		0.95 mL
100-104	**150mg ONCE** daily		1 mL
105-109	**155mg ONCE** daily	100mg/1mL syringe	1 mL
		60mg/0.6mL syringe	0.55 mL
110-114	**165mg ONCE** daily	2 x 100mg/1mL syringes	1 mL
			0.65mL
115-119	**170mg ONCE** daily	2 x 100mg/1mL syringes	1 mL
			0.7 mL
120-124	**180mg ONCE** daily	2 x 100mg/1mL syringes	1 mL
			0.8 mL
125-129	**185mg ONCE** daily	2 x 100mg/1mL syringes	1 mL
			0.85 mL
Dose dependant (Consultant discretion)	>130kg, BMI <40	**1mg/kg TWICE** daily, rounded to the nearest syringe	
	>130kg, BMI >40	**1.5mg/kg daily split into two divided doses**, rounded to the nearest syringe with **factor anti-Xa monitoring**	

Higher risk of recurrence VTE

Renal dose (<30mL/min) 1mg/kg ONCE daily

Patient Weight	Dose (1mg/kg TWICE daily)	Enoxaparin (Inhixa™) Syringe(s) required	Injection volume required per dose
35-39	**40mg TWICE** daily	60mg/0.6mL syringe	0.4 mL
40-44			
45-49	**50mg TWICE** daily		0.5 mL
50-54			
55-59	**60mg TWICE** daily		0.6 mL
60-64			
65-69	**70mg TWICE** daily	1000mg/1mL syringe	0.7 mL
70-74			
75-79	**80mg TWICE** daily		0.8 mL
80-84			
85-89	**90mg TWICE** daily		0.9 mL
90-94			
95-99	**100mg TWICE** daily		1 mL
100-104			
105-109	**112.5mg TWICE** daily	150mg/1mL HIGH STRENGTH syringe	0.75 mL
110-114			
115-119	**120mg TWICE** daily		0.8 mL
120-124			
125-129	**131.25mg TWICE** daily		0.875 mL
>130kg	**150mg TWICE** daily **with anti-factor Xa monitoring**		1 mL

Weight

The patient's weight is required to calculate the appropriate dose of LMWH and should be recorded in the patient's record. Patients should be weighed at the start of therapy and, where applicable, during treatment. In exceptional circumstances, when a patient cannot be weighed, obtain the body weight from patients (or carers) as this is a more reliable source of information than estimates by healthcare staff. Patients who are morbidly obese (BMI >40 kg/m^2) may be considered for anti-factor Xa monitoring and dose adjustments made according to results.

Renal Impairment

The first dose administration should not be delayed; however, subsequent dosing must be based on renal function.

In patients with renal impairment, there is an increase in exposure of enoxaparin sodium which increases the risk of bleeding. In these patients, careful clinical monitoring is advised, and biological monitoring by anti-Xa activity measurement might be considered.

Creatinine Clearance	
<15 mL/min	Enoxaparin sodium is not recommended for patients with end stage renal disease (creatinine clearance <15 mL/min) due to lack of data in this population outside the prevention of thrombus formation in extra corporeal circulation during haemodialysis. However, the Renal Drug Database recommends a dose of 1mg/kg daily may be used with additional monitoring. Consider anti-factor Xa monitoring in patients with a creatinine clearance <15 mL/min.
15-30 mL/min	In patients with severe renal impairment (creatinine clearance 15-30 mL/min), exposure of enoxaparin sodium is significantly increased, therefore a dose adjustment is recommended for therapeutic and prophylactic dose ranges. A dose reduction of 1mg/kg daily may be used with additional monitoring. Consider anti-factor Xa monitoring in patients with a creatinine clearance <15 mL/min.
30-50 mL/min	No dose adjustment is recommended in patients with moderate (creatinine clearance 30-50 mL/min) and mild (creatinine clearance 50-80 mL/min) renal impairment.
50-80 mL/min	

Monitoring of anti-factor Xa concentrations can be considered in patients with renal impairment and in patients thought to be at risk of major bleeding. See ELHT SOP080 **Transporting & Processing Blood Samples and Communicating and Monitoring Results for Anti Xa Assays at ELHT during Treatment Dosing with LMWH** for more information.

- Take pre–dose (trough) and 4 hours post dose (peak) anti-factor Xa concentrations
- Aim for a trough less than 0.25iu/mL and peak of 0.5-1iu/mL

Results outside this range should be discussed with Haematology. Clinicians may choose to use unfractionated heparin if risk of bleeding is a particular concern, though this is much more complex in terms of administration and monitoring and this decision should be made at Consultant level.

Cautions

LMWH should be used with caution in patients with a history of asthma due to the presence of sodium bisulphite

Caution is recommended in the treatment of patients with renal impairment. In moderate renal impairment (eGFR <30mL/min) for treatment doses consider monitoring of anti-factor Xa. and in severe impairment (eGFR <15mL/min) seek urgent advice from hospital pharmacy/haematology. Note contraindication in patients over 90 years with renal impairment above.

Contraindications

- Recent cerebral haemorrhage or acute cerebral infarct
- Uncontrolled hypertension (BP > 210/120 mmHg)
- Active peptic ulcer disease or oesophageal varices
- Severe liver disease
- Thrombocytopenia (Platelets < 80 x 10^9/L)
- Active bleeding or raised BASELINE INR >1.5 - seek advice
- Previous heparin induced thrombocytopenia
- Prophylactic doses are not required if receiving therapeutic anticoagulation (e.g. Warfarin)
- Endocarditis
- Recent neurosurgery or eye / ear surgery
- Patients aged 90 years or over who have renal insufficiency
- Impending miscarriage or abortion
- Hypersensitivity to active ingredients

Treatment doses of low molecular weight heparin should not be given in conjunction with spinal or epidural anaesthesia.

Side Effects

Skin rashes / minor bruising: These can occur at the site of injection occasionally. Systemic allergic reactions have been reported extremely rarely.

Haemorrhage: LMWHs have been shown to increase the risk of haemorrhage. However, at the recommended dose this risk is low.

Thrombocytopenia: As with heparin, thrombocytopenia may occur rarely.

Skin necrosis: This has been reported. If this occurs treatment must be withdrawn immediately.

Priapism: This has been reported rarely.

Liver Function Tests: As for heparin, a transient increase in aminotransferase levels is frequently seen. Cessation of treatment is not usually required.

Hyperkalaemia: LMWHs can suppress adrenal secretion of aldosterone leading to hyperkalaemia, particularly in patients such as those with diabetes mellitus, chronic renal failure, pre-existing metabolic acidosis, raised plasma potassium or taking potassium sparing drugs. The risk of hyperkalaemia appears to increase with duration of therapy but is usually reversible. The SPC recommends that plasma potassium should be measured in patients at risk before starting LMWH therapy and monitored regularly thereafter particularly if treatment is prolonged beyond about 7 days. However, the British Society of Haematology takes a more pragmatic approach advising that the development of symptomatic hyperkalaemia appears to be unlikely in the absence of an additional cause of hyperkalaemia.

Osteoporosis: Long-term LMWH use can cause osteoporosis but the absolute risk of symptomatic osteoporosis is unknown. Several lines of evidence now suggest that LMWHs are associated with a lower risk of osteoporosis than heparin. The conclusion from the data at present is that

LMWH is preferred for long-term use and clinicians and patients should be aware of the risks of osteoporosis and consider this knowledge when determining the risk–benefit ratio of LMWH therapy.

Overdose: Emergency advice should be sought immediately Protamine reverses the anticoagulant effect of LMWHs incompletely (about 75-85%), although there is anecdotal evidence of clinical benefit in the bleeding patient. The risks and benefits of reversal should be weighed against the risks of overdose.

Monitoring of blood results

Heparin Induced thrombocytopenia (HIT)

• HIT is a possible complication of treatment with heparins. The immune-mediated type usually occurs 7-11 days (up to 20 days) after initiating treatment

• Patients who are to receive any type of heparin require a baseline platelet count

• No further monitoring is required during or following treatment unless clinically indicated (e.g. following cardiopulmonary bypass) or if the patient has received heparin in the preceding 100 days.

• Post-operative patients and cardiopulmonary bypass patients who have been exposed to heparin in the previous 100 days should have a platelet count 24 hours after starting heparin.

• Medical patients receiving heparin do not need routine platelet monitoring

• If the platelet count falls by 30% or more or the patient develops new thrombosis or skin allergy or any other of the rarer manifestations of HIT between Day 4 and 14 consider a diagnosis of
Heparin Induced Thrombocytopenia and discuss with a haematologist URGENTLY.

• There is NO need to monitor the anticoagulant activity of enoxaparin (e.g. INR or APTT).

Subcutaneous Administration

Prophylaxis and treatment dose enoxaparin (Inhixa™) is to be administered via **subcutaneous injection**. It is not necessary to remove the air bubble from the prefilled syringe before the injection as injection of the small air bubble is quite harmless. Avoiding the removal of the air bubble saves nursing time and helps avoid injection fluid on the tip of the needle, which might cause pain during injection.

It is recommended that LMWH should be injected into the abdominal fat layer. Other sites of injection can be used without problems. Administration should be avoided within 5cm of the umbilicus (belly button) and should be alternated between the left and right side.

A skin fold should be held between the thumb and forefinger and the entire length of the needle inserted at an angle of 90 degrees into the skin fold. The skin fold should be held during the injection and the solution slowly and fully injected. Enoxaparin (Inhixa™) syringes contain a plastic needle catch system which should be used directly after the injection needle is withdrawn from the injection site.

Patients should be taught how to self-administer LMWH injections, particularly if they are due to be discharged on them at home for a period. It is the responsibility of the prescriber initiating treatment to ensure patients and / or their carer(s) are adequately trained where they are to self-administer.

Provision of Patient Information

It is the responsibility of the initiating prescriber to give patients adequate information about their condition, and their treatment.

Although a patient information leaflet is included alongside any dispensed medication, patients should also be given additional information on what their LMWH is prescribed for.

It is the responsibility of the prescriber who initiates LMWH to arrange patients' attendance for any blood tests. Either directly at the hospital, or with prior agreement with the GP, in primary care.

Switching to enoxaparin (Inhixa™) from another LMWH

Patients initiated on another LMWH from other NHS hospitals or providers should be managed in line with this guidance. This may involve referring prescribing back to the original prescriber for advice depending on the indication of LMWH or consider switching the patient to enoxaparin (Inhixa™) at the appropriate equivalent dose.

Licensing of LMWHs

Enoxaparin (Inhixa™) has been recommended for use locally in some indications or at some doses which are not licensed, but where it is defined that it is best practice to use a LMWH or use of a particular dose of LMWH. Healthcare professionals are advised to follow normal procedures and adhere to their professional guidance when prescribing, dispensing, or administering a preparation in an indication/dose that is not licensed, as they would in any other similar situation.

Waste Disposal

Where people inject themselves, it is their responsibility to dispose of any used enoxaparin (Inhixa™) injections. Enoxaparin (Inhixa™) syringes come with the needle already attached to the syringe and contain a needle catch system which enables the needle to be covered safely after use to ensure needle stick injuries are avoided. However, patients should be supplied with a 1L yellow **SharpsSafe®**1L bin – these can be supplied by wards/clinical areas on discharge or can be prescribed in community on an FP10 prescription. Sharps boxes should only be filled to 2/3 full before replacing to ensure they are not overfilled. Yellow lidded bins are suitable for sharps that are contaminated with medicinal products, other than cytotoxic drugs. The sharps bin should be returned to the practice or selected community pharmacists for disposal.

Guidance for Nursing staff checking prescriptions for enoxaparin (Inhixa™)

Nursing staff should have access to the following information prior to dispensing or administering enoxaparin (Inhixa™). This can be obtained from the patient where possible, or confirmed with the prescriber where missing and this should be recorded:

- **Indication:** whether prophylaxis or treatment is intended (and whether the patient is pregnant where relevant). This is needed to be able to check the appropriate dose.
- **Strength of syringe required:** Note there are multiple strengths of enoxaparin (Inhixa™) syringe to enable accurate prophylactic and therapeutic dosing based on patient's body weight.
- **Volume of syringe required:** There are multiple injection volume syringes of the LMWH's available.
- **Weight of patient:** This is required to check that the appropriate dose has been prescribed.
- **Dose in mg for enoxaparin (Inhixa™):** The dosing charts on the inside of this guidance should be used to check the dose.
- **Frequency of administration:** Always given subcutaneously, usually self-administered.
- **Timing of administration:** LMWH should be given around the same time of day. In any single 24-hour period, the dose time may occasionally be varied by up to 2 hours before or after the dose time. However, where the dose timing for administering requires amending to facilitate administration (e.g. after hospital discharge), it is acceptable to move the dose time forwards or backwards on one occasion. As long as a dosing gap of at least 12 hours has occurred.

Guidance for Community Pharmacists dispensing Enoxaparin (Inhixa™)

Community pharmacists are advised to produce Standard Operating Procedures to govern the checking and dispensing of prescriptions for the LMWHs. It should be noted that the community pharmacist should have the relevant information outlined above prior to dispensing any prescription, and should obtain this from the patient, or from the GP where it is missing. Community pharmacists are advised to keep minimum stocks of enoxaparin (Inhixa™) where possible to ensure that patients do not miss doses. In addition, patients should be counselled to order prescriptions in advance of running out of stocks to prevent this.