Low Molecular Weight Heparins (LMWHs) Summary Prescribing Guide

Sharon Andrew
Midlands & Lancashire CSU
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Version Control

Version Number	Date	Amendments made
1.1	12.2.15	Prescribing checklist updated, check for contraindications added.
1.2	14.7.16	Table 1. updated with local decisions regarding colour classification & information on bridging therapy
1.3	30.11.17	Updated therapeutic indications and associated dosing regimens. Updated monitoring requirements.
1.4	23.9.19	Updated RAG ratings for GP/CSR

Contents

1. INTRODUCTION

Historically, patients requiring subcutaneous anticoagulation have received treatment in secondary care. In recent years, Low Molecular Weight Heparins (LMWHs) have effectively replaced the routine use of unfractionated heparin in the majority of patients; and the potential for self-administration has led to an increased volume of prescribing in primary care.

2. PURPOSE AND SUMMARY

This guidance has been produced to facilitate the safe prescribing of LMWHs in primary care. It provides an overview of points to be considered when initiating LMWHs and when transferring prescribing responsibilities to or from another organisation.

3. SCOPE

This is a summary guidance document. It outlines general LMWH prescribing considerations and monitoring requirements. It also outlines points which should be communicated and agreed; when transferring prescribing responsibilities and the associated patient care between organisations.

This document does not provide guidance on the inpatient use of LMWHs or specific guidance on use in paediatrics or other specialist patient groups. For more information, prescribers should refer to the individual organisation's policy.

Any decision around how a service operates and whether shared care is part of that commissioned service will be led by the commissioning organisation; clinicians should follow their locally agreed arrangements and not undertake in shared care unless a process has been defined.

NB. For the purpose of this guidance the term Venous Thrombo Embolism (VTE) covers **both** Deep Vein Thrombosis (DVT) **and** Pulmonary Embolism (PE)

4. GUIDANCE

4.1. Table 1. Overview of LMWH indications, locally agreed Colour Classifications, duration of treatment & licensing status[1-3,6]

Speciality	Indication	Duration of treatment	Licensed Indication ✓or ✖			
			Dalteparin Fragmin®	Enoxaparin Clexane ®	Tinzaparin Innohep ®	LMMG Colour Classification
General Medical	Treatment of VTE or suspected VTE in patients unable to stabilise on warfarin or DOACs or with a contraindication to warfarin or DOACs (For treatment of suspected VTE or for confirmed VTE whilst waiting for an oral vitamin K antagonist to be established – see miscellaneous below).	• 1st DVT/PE: 3-6 months • Previous DVT/PE: Lifelong If VTE confirmed:	x	x	x	Amber 1
	Prophylaxis of DVT or PE when unable to stabilise on warfarin or DOACs, with an allergy or with contra-indication to warfarin and/or DOACs. (This includes IVDU patients)	Lifelong with review of the need for anticoagulation at least annually (or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk)	x	x	x	Amber 1
	Extended prophylaxis of high risk patients in the primary care setting e.g. Immobile patients or those deemed to be at particularly high risk of DVT at home or in a care situation and who are unable to tolerate/take warfarin or DOACs	As per specialist advice, treatment should be reviewed if mobility improves and at least annually. (or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk)	x	x	x	Amber 1
Oncology	Patients with solid tumours: Extended treatment of symptomatic venous thromboembolism (VTE) and prevention of its recurrence. Note: LMWHs are used in preference to oral anticoagulation for the whole treatment course.	Recommended duration of treatment is 6 months	√	x Approved for off-label use by some local organisations	√	Amber 1
	Prophylaxis of VTE in oncology patients on VTE inducing therapy	As per chemotherapy protocol/specialist advice	x	x	x	Red
Obstetrics & Gynae[13]	Pregnancy: Treatment of VTE (pre and post-partum)	As per specialist advice	x	x	x	Red **Please note: Amber** in Fylde Coast **Amber 1** in Greater Preston and Chorley & South Ribble – **post-partum only**)
	Pregnancy: Prevention of VTE (High risk patients- pre and post-partum)	As per specialist advice	x	x	x	Red (Amber in Fylde Coast)

Speciality	Indication	Duration of treatment	Licensed Indication ✓or ✖			
			Dalteparin Fragmin®	Enoxaparin Clexane ®	Tinzaparin Innohep ®	LMMG Colour Classification
	Use by fertility clinics, and also to prevent miscarriage	As per specialist advice	x	x	x	Red
Surgical	VTE Prophylaxis Post-operative use [e.g. hips, knees, general surgical]	Dependant on type of surgery and patient factors- follow local protocols/specialist advice	√	√	√	Red
	All Surgical Specialities: Post-operative use in conjunction with warfarin whilst waiting for the INR to come into range	Until INR is in target range for at least 2 consecutive days If INR not in range at point of discharge follow-advice on bridging therapy below	√	√	√	Red
	Extended Thromboprophylaxis of VTE for High Risk Patients with History of Thrombosis associated with central venous access	On-going whilst central venous access required (For review if clinically events occur affecting anticoagulation relevant bleeding risk)	x	x	x	Red
Travel[11,12]	Suggested for travel prophylaxis where travelling time is over 6 hrs in high-risk patients, i.e. patients with surgery in the previous 4 weeks requiring more than 30mins general anaesthesia, patients with known thrombophilia and patients with cancer	As per specialist advice	x	x	x	Amber 0
Cardiology	Unstable coronary artery disease (including non – ST segment elevation myocardial infarction)	For up to 8 days	√	√	x	Red
	Unstable coronary artery disease (including non – ST segment elevation myocardial infarction) awaiting angiography or revascularisation and having already had 8 days of treatment of dalteparin	Every 12 hours until the day of the procedure	√	x	x	Red
	Treatment of acute ST segment elevation myocardial infarction (patients **not** undergoing percutaneous coronary intervention)	Different treatment schedules dependent on patient age– see table 4.4	x	√	x	Red
	Treatment of acute ST segment elevation myocardial infarction (patients undergoing percutaneous coronary intervention)	Different treatment schedules dependent on patient age – see table 4.4	x	√	x	Red
Miscellaneous	'Bridging' therapy for sub-therapeutic INRs It is expected that the organisation which initiates treatment or identifies the sub therapeutic INR, arranges for follow up INR testing and provides sufficient supply of LMWH and Warfarin to provide treatment until the follow up appointment. The place of follow up will be determined by locally commissioned pathways, but where a secondary care organisation has provided the initial supply of LMWH and Warfarin it is anticipated that the on-going care and follow up will be transferred to a primary care organisation, unless otherwise inappropriate.	Until INR is in target range for at least 2 consecutive days Dose and Licensing as per main Indication	√	√	√	Amber 0

Speciality	Indication	Duration of treatment	Licensed Indication ✓or ✖			
			Dalteparin Fragmin®	Enoxaparin Clexane ®	Tinzaparin Innohep ®	LMMG Colour Classification
	For suspected VTE or for confirmed VTE whilst waiting for an oral vitamin K antagonist to be established. At least five days of combined treatment is normally required. It is expected that the organisation which initiates treatment will continue to provide treatment until VTE has been excluded. Where VTE is confirmed, as outlined above re: bridging therapy the initiating organisation should provide the initial supply of LMWH and Warfarin and arrange for follow up INR testing (ensuring that the patient has sufficient supply of LMWH and Warfarin to provide the minimum treatment course and until the follow up appointment).	**Until VTE excluded or if VTE confirmed:** **Dalteparin & Enoxaparin**: At least **5 days** and until an oral vitamin K antagonist has been established & the INR is in range for 2 days **Tinzaparin:** At least **6 days** and until an oral vitamin K antagonist has been established & the INR is in range for 2 days	√	√	√	Amber 0 (Amber 1 in Greater Preston and Chorley & South Ribble)

4.2 LMWH Prescribing Checklist

When LMWH prescribing responsibility is being transferred from one organisation to another, it is essential that the points below are considered and supporting information is made available to the new organisation. Clinicians should follow their locally agreed arrangements and not undertake in shared care unless a process has been defined.

LMWH Prescribing Checklist [4]	Tick when complete
1. **Indication:** The indication for LMWH use is clear. e.g. There is no ambiguity regarding use for prophylaxis or treatment of VTE.	
2. **Contraindications:** The patient has been assessed for pharmacological and clinical contraindications to the use of LMWHs. LMWHs are only continued where the benefits of treatment outweigh the risks. Contra-indications include but are not limited to; active bleeding, thrombocytopenia, acquired bleeding disorders (e.g. liver failure), severe hypertension, major trauma, concurrent use of interacting medicines, anticoagulants or antiplatelets. (See the SPCs for further information)	
3. **Licensing status of the medication/dose:** The licensing status of the LMWH and prescribed dose has been considered. Where a medication is being used for an unlicensed indication or unlicensed dose, the rationale for use has been provided (e.g. Ease of dosing/self-administration) or there is an organisational agreement to use 'off license' preparations or doses.	
4. **Duration of treatment:** The duration of treatment is known, this has been recorded and a system has been put in place to ensure that once the course is complete no further prescriptions are issued. It is good practice to put the stop-date on the prescription. If the course length is dependent on the outcome of a clinical review, the prescription should be endorsed with the date of clinical review.	
5. **Dose:** The dose is appropriate for the indication, weight and renal function; and is measurable. It is good practice to write the dose on the prescription as the number of units or mg and to state the strength/volume to be injected, along with the size of syringe or vial to be supplied. (See dosing charts or the SPCs for further information)	
6. **Weight:** The patient has been weighed and this weight has been used to accurately calculate the dose. The weight should be recorded in kilograms (kg)[4], documented in the patient notes and on the prescription. Patients should be weighed periodically throughout treatment as appropriate[4]; for example if they are on prolonged treatment or if it is expected that their weight may fluctuate. Specialist advice should be sought regarding dosing and monitoring of patients at extremes of weight. (See monitoring section for more information).	
7. **Renal function:** The patient's renal function has been checked and documented. Dose adjustment may be required, in patients with CrCl <30mls/min. (See dosing charts and monitoring information or SPC for further information)	
8. **Baseline bloods:** Base line bloods have been checked and are available. (See monitoring requirements for more information)	
9. **Follow up/monitoring:** Arrangements have been made for any follow-up/monitoring required. (See monitoring requirements for more information)	
10. **Quantity of supply:** The quantity supplied at any one time should not exceed one month's supply[5].	
11. **Administration:** The patient/carer has received training on how to self-administer the LMWH or appropriate alternative arrangements have been made. e.g. district nurse administration	
12. **Disposal:** Arrangements have been made for the safe disposal of used syringes. i.e. A sharps bin has been prescribed/supplied and the patient/carer has been told what to do when it is full/how to obtain replacements	

4.3 Dalteparin (Fragmin®) Dosing Chart

Dosing information has been provided to minimise the risk of calculation errors. Where local organisation dosing charts exist, prescribers should refer to these, as they may not directly correlate with the information provided below.

Dalteparin Maximum single daily dose= 18 000 units regardless of body weight (If CrCl< 30 ml/min, adjust dose based on anti-Factor Xa activity as per SPC)					
Indication	**Weight (Kg)**	**If CrCL <30 ml/min**: Adjust dose based on anti-Factor Xa activity. **Dose (Units)**	**Frequency**	**Each Dose Supplied As** **Volume**	**Syringe used**
Treatment of VTE Licensed Indication	<46kg	7500 units	Once Daily	0.3ml	0.3ml syringe (25000 units/ml)
	46-56kg	10000 units	Once Daily	0.4ml	0.4ml syringe (25000 units/ml)
	57-68kg	12500 units	Once Daily	0.5ml	0.5ml syringe (25000 units/ml)
	69-82kg	15000 units	Once Daily	0.6ml	0.6ml syringe (25000 units/ml)
	83kg and over	18000 units	Once Daily	0.72ml	0.72ml syringe (25000 units/ml)
Treatment of VTE in Pregnancy Unlicensed Indication (Dosing information is as per BNF.	**Weight (Kg) Based on early pregnancy weight**	**Dose (Units)**	**Frequency**	**Each Dose Supplied As** **Volume**	**Syringe used**
	Under 50kg	5000 units	Twice Daily	0.5 ml	1ml syringe (10,000 units/ml)
	50- 69 kg	6000 units	Twice Daily	0.6 ml	1ml syringe (10,000 units/ml)
	70- 89kg	8000 units	Twice Daily	0.8 ml	1ml syringe (10,000 units/ml)
	90kg and over	10000 units	Twice Daily	1.0ml	1ml syringe (10,000 units/ml)
Unstable coronary artery disease (including non – ST segment elevation myocardial infarction) Licensed Indication		**Dose (Units)** 120 units / kg For up to 8 Days Max dose 10000units	**Frequency** Twice Daily Twice Daily		
Unstable coronary artery disease (including non – ST segment elevation myocardial infarction) awaiting angiography or revascularisation and having already had 8 days of dalteparin Licensed Indication	**Weight (Kg)**	Treatment is recommended to be given until the day of the revascularisation procedure (PTCA or CABG) but not for more than 45 days. **Dose (Units)**	**Frequency**	**Each Dose Supplied As** **Volume**	**Syringe used**
	Male Up to 70kg	5000 units	Twice Daily	0.2ml	0.2ml syringe (25,000 units/ml)
	Male 70kg and above	7500 units	Twice Daily	0.3ml	0.3ml syringe (25000 units / ml)
	Female Up to 80kg	5000 units	Twice Daily	0.2ml	0.2ml syringe (25,000 units/ml)
	Female 80kg and above	7500 units	Twice Daily	0.3ml	0.3ml syringe (25000 units / ml)

Extended treatment & prophylaxis of VTE in patients with solid tumours Licensed Indication	**First 30 days' treatment:** 200units/Kg daily (max dose 18 000units) or as per dose bands below. (For patient at increased risk of haemorrhage the dose can be divided into two i.e. 100 units/kg twice daily)				
	Weight (Kg)	**Dose (Units) & Frequency** See below for dose adjustments in chemotherapy-induced thrombocytopenia.		**Each Dose Supplied As** **Volume**	**Syringe used**
	<46kg	7500 units	Once Daily	0.3ml	0.3ml syringe (25000 units/ml)
	46-56kg	10000 units	Once Daily	0.4ml	0.4ml syringe (25000 units/ml)
	57-68kg	12500 units	Once Daily	0.5ml	0.5ml syringe (25000 units/ml)
	69-82kg	15000 units	Once Daily	0.6ml	0.6ml syringe (25000 units/ml)
	83kg and over	18000 units	Once Daily	0.72ml	0.72ml syringe (25000 units/ml)
	Then for a further 5 months dose: 150units/Kg daily or as per dose bands below.				
	≤56kg	7500 units	Once Daily	0.3ml	0.3ml syringe (25000 units/ml)
	57-68kg	10000 units	Once Daily	0.4ml	0.4ml syringe (25000 units/ml)
	69-82kg	12500 units	Once Daily	0.5ml	0.5ml syringe (25000 units/ml)
	83-98kg	15000 units	Once Daily	0.6ml	0.6ml syringe (25000 units/ml)
	99 kg and over	18000 units	Once Daily	0.72ml	0.72ml syringe (25000units/ml)

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

Platelets<50,000/mm^3 (or 50x10^{9}L): refer back to the specialist initiating treatment and hold treatment until platelets recover.
Platelets = 50,000-100,000mm^3 or (50-100x10^{9}L): refer back to the specialist initiating treatment and reduce dose as per table below.

Body Weight (kg)	**Reduced Dose**	
≤56kg	5000 units	Once Daily
57-68kg	7500 units	Once Daily
69-82kg	10000 units	Once Daily
83-98kg	12500 units	Once Daily
≥99kg	15000 units	Once Daily

Once the platelet count has recovered to ≥100,000mm^3 (or ≥ 100 x 10^{9}L): treatment can be re-started at full dose
In cancer patients with body weight < 40kg at time of venous thromboembolic event, Dalteparin should not be used for extended treatment of symptomatic VTE and prevention of its recurrences due to lack of data.

4.4 Enoxaparin (Clexane®) Dosing Chart

Dosing information has been provided to minimise the risk of calculation errors. Where local organisation dosing charts exist, prescribers should refer to these, as they may not directly correlate with the information provided below.

Enoxaparin (If eGFR less than 30mls/min, reduce dose as per SPC)					
Indication	**Weight (Kg)***	**Dose (mg & Units) Frequency** Dose = 1.5mg/kg (150units/kg) every 24hr until adequate oral anticoagulation established *When the quantity of drug to be injected requires to be adjusted based on the patient's body weight, use the graduated pre-filled syringes to reach the required volume by discarding the excess before injection. Please be aware that in some cases it is not possible to achieve an exact dose due to the graduations on the syringe, and in such case the volume shall be rounded **up** to the nearest graduation.*[2] **If CrCL <30mls/min:** Reduce to 1mg/Kg		**Each Dose Supplied As**	
				Volume	**Syringe used**
Treatment of VTE Licensed Indication	40Kg	60mg (6000 units)	Once Daily	0.6ml	0.6ml (100mg/ml Orange)
	45Kg	67.5mg (6750 units)	Once Daily	0.675ml	0.8ml (100mg/ml Brown)
	50Kg	75mg (7500 units)	Once Daily	0.75ml	0.8ml (100mg/ml Brown)
	55Kg	82.5mg (82500 units)	Once Daily	0.825ml	1ml (100mg/ml Grey)
	60Kg	90mg (9000 units)	Once Daily	0.9ml	1ml (100mg/ml Grey)
	65Kg	97.5mg (97500 units)	Once Daily	0.975ml	1ml (100mg/ml Grey)
	70Kg	105mg (10500 units)	Once Daily	0.7ml	0.8ml (120mg/0.8ml Pink)
	75kg	112.5mg (11250 units)	Once Daily	0.75ml	0.8ml (120mg/0.8ml Pink)
	80Kg	120mg (12000 units)	Once Daily	0.8ml	0.8ml (150mg/ml Blue)
	85kg	127.5mg (12750 units)	Once Daily	0.85ml	1ml (150mg/ml Blue)
	90Kg	135mg (13500 units)	Once Daily	0.9ml	1ml (150mg/ml Blue)
	95kg	142.5mg (14250 units)	Once Daily	0.95ml	1ml (150mg/ml Blue)
	100Kg	150mg (15000 units)	Once Daily	1ml	1ml (150mg/ml Blue)
Treatment of VTE in pregnancy Unlicensed Indication (Dosing information is as per BNF)	**Weight (Kg)*** **Based on early pregnancy weight**	**Dose (mg & Units)**	**Frequency**	**Each Dose Supplied As**	
				Volume	**Syringe used**
	Up to 50Kg	40mg (4000 units)	Twice Daily	0.40ml	0.4ml (100mg/ml Yellow)
	50-69Kg	60mg (6000 units)	Twice Daily	0.60ml	0.6ml (100mg/ml Orange)
	70- 89Kg	80mg (8000 units)	Twice Daily	0.80ml	0.8ml (100mg/ml Brown)
	90Kg and above	100mg (10000 units)	Twice Daily	1ml	1ml (100mg/ml Grey)

Enoxaparin (If eGFR less than 30mls/min, reduce dose as per SPC)			
Unstable angina / Non ST segment elevation myocardial infarction Licensed Indication		**Dose (mg)** **Frequency** 1mg / kg Twice Daily Usually for 2-8 days (minimum of 2 days)	
Treatment of acute ST segment elevation myocardial infarction (patients not undergoing percutaneous coronary intervention) **Licensed Indication**		<u>Adults 18-74 years</u> Initially 30mg (by intravenous injection) followed by 1mg/kg (by subcutaneous injection) for 1 dose then 1mg/kg (by subcutaneous injection) every 12 hours (max per dose 100mg for first two subcutaneous injections) for up to 8 days. <u>Adults 75 years and over</u> 0.75mg/kg every 12 hours (by subcutaneous Injection). Max per dose 75mg, for first two doses only.	
Treatment of acute ST segment elevation myocardial infarction (patients undergoing percutaneous coronary intervention) **Licensed Indication**		<u>Adults 18-74 years</u> Initially 30mg (by intravenous injection) followed by 1mg/kg (by subcutaneous injection) for 1 dose then 1mg/kg (by subcutaneous injection) every 12 hours (max per dose 100mg for first two subcutaneous injections) for up to 8 days. Then 0.3mg/kg (by intravenous injection) for 1 dose (dose to be given at time of procedure if the last subcutaneous dose was given more than 8 hours previously. <u>Adults 75years and over</u> 0.75mg/kg every 12 hours (by subcutaneous Injection). Max per dose 75mg, for first two doses only. Then 0.3mg/kg (by intravenous injection) for 1 dose (dose to be given at time of procedure if the last subcutaneous dose was given more than 8 hours previously.	
Extended treatment & prophylaxis of VTE in patients with solid tumours	This is an unlicensed indication; dosing information is not available in the BNF. Prescribers should ensure that they are working under their locally agreed protocols.		

***Dosing information has been provided for patients up to 100kg, this is the maximum weight, which can be dosed using a single pre-filled syringe. For patients above this weight please liaise with secondary care to confirm the appropriate dosing schedule.**

4.5 Tinzaparin (Innohep®) Dosing Chart

Dosing information has been provided to minimise the risk of calculation errors. Where local organisation dosing charts exist, prescribers should refer to these, as they may not directly correlate with the information provided below.

Tinzaparin (If eGFR less than 20mls/min, reduce dose as per SPC)					
Indication	**Weight (Kg)***	**Dose (Units) & Frequency** Dose = 175 units/Kg **If CrCl< 30ml/min**: Monitoring of anti Xa activity should be considered		**Each Dose Supplied As** (Doses should be rounded to the nearest 10000 units to allow accurate measurement). **Volume**	**Syringe used**
Treatment of VTE (175 units/kg daily until adequate oral anticoagulation established) Licensed indication	40kg	7000 units	Once Daily	0.35ml	0.5ml syringe (20 000 unit/ml)
	45kg	8000 units	Once Daily	0.40ml	0.5ml syringe (20 000 unit/ml)
	50kg	9000 units	Once Daily	0.45ml	0.5ml syringe (20 000 unit/ml)
	55kg	10000 units	Once Daily	0.50ml	0.5ml syringe (20 000 unit/ml)
	60kg	11000 units	Once Daily	0.55ml	0.7ml syringe (20 000 unit/ml)
	65kg	11000 units	Once Daily	0.55ml	0.7ml syringe (20 000 unit/ml)
	70kg	12000 units	Once Daily	0.60ml	0.7ml syringe (20 000 unit/ml)
	75kg	13000 units	Once Daily	0.65ml	0.7ml syringe (20 000 unit/ml)
	80kg	14000 units	Once Daily	0.70ml	0.7ml syringe (20 000 unit/ml)
	85kg	15000 units	Once Daily	0.75ml	0.9ml syringe (20 000 unit/ml)
	90kg	16000 units	Once Daily	0.80ml	0.9ml syringe (20 000 unit/ml)
	95kg	17000 units	Once Daily	0.85ml	0.9ml syringe (20 000 unit/ml)
	100kg	18000 units	Once Daily	0.90ml	0.9ml syringe (20 000 unit/ml)
	105kg	18000 units	Once Daily	0.90ml	0.9ml syringe (20 000 unit/ml)
Treatment of VTE in Pregnancy (based on early pregnancy weight) Unlicensed Indication (Dosing information is as per BNF)	As above, Dose = 175 units/kg daily				
Extended treatment / Prophylaxis of VTE in patients with active cancer	As above, Dose = 175 units/kg daily (for up to 6 months)				

*Dosing information has been provided for patients up to 105kg, this is the maximum weight, which can be dosed using a single pre-filled syringe. For patients above this weight please liaise with secondary care to confirm the appropriate dosing schedule.

4.6 LMWH Monitoring Requirements

<table>
<tr><th>Parameter</th><th>Monitoring Requirements. [1-4,6]</th></tr>
<tr><td>Full Blood Count</td><td>Check at baseline, then as clinically indicated.</td></tr>
<tr><td>Platelets</td><td>Check at baseline, then regularly thereafter during the treatment (as advised by secondary care or outlined in the local shared care protocol).

Heparin induced thrombocytopenia (HIT) is a rare side effect of LMWHs, it usually but not always happens within the first 21 days of treatment.
Signs of HIT include a reduction in platelet count of 30% or more, thrombosis & skin allergy[6]. If HIT is confirmed/strongly suspected, stop treatment and discuss with haematologist/responsible secondary care clinician (within 24hrs).

Regular monitoring of platelet count also applies to extended treatment for cancer-associated thrombosis, especially during the first month, considering that cancer and its treatments such as chemotherapy may also cause thrombocytopenia</td></tr>
<tr><td>Renal Function</td><td>Renal function should be checked on initiation then a minimum of every 6 months, dependent on the patient’s risk of deterioration.

LMWHs are renally excreted, if creatinine clearance is 30-50ml/min check renal function more frequently, as clinically indicated. Dose adjustment may be required in renal impairment as per the SPC, see below for a summary of manufacturers’ recommendations.
<table>
<tr><th>LMWH</th><th>Manufacturers’ recommendations in renal impairment (RI) [1,2,3,8]</th></tr>
<tr><td>Dalteparin</td><td>Monitoring of anti-factor Xa levels should be considered in RI. Use with caution in patients with RI who have an increased risk of bleeding complications.
In patients with significant renal failure i.e. CrCl <30 ml/min, the dose should be adjusted based on anti-Factor Xa activity[1].
For patients with an increased risk of bleeding, it is recommended that dalteparin is administered according to the twice daily regimen. (See SPC for more details).</td></tr>
<tr><td>Enoxaparin</td><td>It is recommended that Enoxaparin is avoided in patients with CrCl <15ml/min. A dose reduction is advised in patients with severe RI (CrCl <30ml/min). The manufacturers advise that in patients with a CrCl of 15-30ml/min that the dose should not exceed 20mg daily. However no trials testing the efficacy and safety of this reduced dose (where a 40mg dose would normally be indicated) have yet been identified.[9] No dosage adjustments are recommended in patients with a CrCl >30ml/min, but careful clinical monitoring is advised. Monitoring of anti-factor Xa levels should be considered in patients with RI.
(Please see SPC for Dosage table for patients with severe renal impairment (creatinine clearance [15-30] ml/min)</td></tr>
<tr><td>Tinzaparin</td><td>Use with caution in all patients with RI. Use in patients with a creatinine clearance level < 30 ml/minute is not recommended, as dosage in this population has not been established. Available evidence demonstrates no accumulation in patients with creatinine clearance levels down to 20 ml/ min. If the benefit outweighs the risk, tinzaparin treatment can be initiated / used cautiously with anti-Xa monitoring in these patients. In this situation, the dose of tinzaparin should be adjusted, if necessary, based on anti-factor Xa activity. No specific guidance is provided regarding the dose reduction required in patients with a CrCl <20ml/min.</td></tr>
</table></td></tr>
<tr><td>Potassium</td><td>Check on initiation, then periodically, dependent on the patient’s risk of hyperkalaemia[6].

LMWHs can inhibit aldosterone secretion, resulting in hyperkalaemia. Patients with diabetes mellitus, chronic renal failure, acidosis, raised plasma potassium or taking potassium-sparing drugs are more susceptible. The risk appears to increase with duration of treatment.</td></tr>
</table>

Anti-factor Xa	Anti-factor Xa is a surrogate marker of anticoagulant effect. Routine monitoring is not recommended, however it may be of benefit in certain patient groups, such as pregnancy[7] and patients at increased risk of bleeding, e.g. patients who are very over or underweight and patients with renal dysfunction[6]. When Anti-factor Xa monitoring is required, local haematology departments should be consulted to advise on monitoring requirements, and the most suitable target range for anti-factor Xa activity due to variations in laboratory techniques[9]. For this reason, it is expected that LMWH prescribing for this patient group will usually be retained by secondary care.
Weight	Patients should be weighed on initiation and then periodically throughout treatment as appropriate. Use of LMWHs for prophylaxis or treatment in patients who are very over or underweight can pose a clinical challenge and may justify the off-label use of LMWHs, or adjustments in dosing regimens[10]. There is a lack of evidence relating to the appropriate dosing of low molecular weight heparin, for prevention of thrombosis in patients at extremes of body weight, particularly relating to clinically relevant outcomes. [10] However, based on an evaluation of the available evidence, the HAT Committee, UKCPA would suggest that: Low molecular weight heparin doses should be adjusted according to body weight and a table of suggested doses is provided for enoxaparin, dalteparin and tinzaparin in Q&A 326.2 [10] This decision should only be made following specialist advice and careful consideration of risks introduced by changing standard practice. Monitoring anti-factor Xa is key to the safe use of LMWHs in patients who receive an altered dosage regimen.[10] N.B. The SPCs for enoxaparin and tinzaparin do not make a recommendation on dose-capping in overweight patients but the SPC for dalteparin states that VTE treatment doses should be no higher than 18 000 units regardless of body weight.

5. REFERENCES

1. Electronic Medicines Compendium. eMC: *Summary of product Characteristics, Dalteparin sodium.* https://www.medicines.org.uk/emc/medicine/26891 (accessed 29 November 2017).
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