Low Molecular Weight Heparin Prescribing and Administration (Adults)

The National Patient Safety Agency issued guidance on ways of reducing dosing errors when prescribing low molecular weight heparins (LMWH) in July 2010. The main issues highlighted include:

- Lack of consideration of patients’ accurate weight before dosing
- The dose of LMWH may still be miscalculated based on the known weight
- LMWH doses and frequencies are sometimes used outside guideline recommendations for the required clinical indication or other predisposing factors such as renal failure.
- Limited information is communicated during transfer of care – i.e. indication, dosage, intended duration of treatment and the patient’s weight.

This guideline is to provide information to support the safe and appropriate use of LMWHs across both secondary and primary care.

**Choice of LMWH**

The choice of low molecular weight heparin used at Wirral University Teaching Hospital (WUTH) depends on the indication of treatment and the patient’s renal function.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Renal function</th>
<th>Choice of LMWH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous Thromboembolism (VTE) prophylaxis*</td>
<td>Irrespective of renal function</td>
<td>Tinzaparin</td>
</tr>
<tr>
<td>Treatment of VTE</td>
<td>CrCl ≥ 20ml/min</td>
<td>Tinzaparin</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt;20ml/min</td>
<td>Enoxaparin</td>
</tr>
<tr>
<td>Acute coronary syndrome (ACS) alone (i.e. no other indications requiring full anticoagulation)</td>
<td>CrCl ≥ 20ml/min</td>
<td><strong>Fondaparinux</strong></td>
</tr>
<tr>
<td></td>
<td>CrCl &lt;20ml/min</td>
<td>Enoxaparin</td>
</tr>
<tr>
<td>ACS plus other indications requiring full anticoagulation (e.g. mechanical prosthetic valves, treatment of VTE or atrial fibrillation requiring high level anticoagulation)</td>
<td>Irrespective of renal function</td>
<td>Enoxaparin</td>
</tr>
</tbody>
</table>

*except orthopaedics directorate – orthopaedics VTE prophylaxis guidelines are being updated at the time of writing this joint LMWH guideline

**Fondaparinux is a synthetic pentasaccharide that inhibits factor Xa.
CrCl = Creatinine Clearance
Dosing considerations

Renal function

A patient’s renal function should be considered before prescribing a LMWH as this may affect the choice and the dose of LMWH. However, this should not delay initiation of treatment but every effort must be made to calculate subsequent dose based on this information. Renal function should be checked before starting treatment and then at appropriate intervals if continuing on LMWH (i.e. routinely every 3 months or sooner if the patient’s condition changes in a way that might affect renal function).

A patient’s estimated creatinine clearance can be calculated using Cockcroft and Gault’s equation.

**Cockcroft and Gault equation for creatinine clearance**

\[
\text{Creatinine clearance (mL/min)} = Y \times (140 \text{- age}) \times \text{weight} \\
\text{Serum creatinine umol/L}
\]

Where \( Y = 1.23 \) for males and 1.04 for females

For obese patients, adjusted body weight should be used

Adjusted body weight = ideal body weight + 0.4 \times (actual body weight – ideal body weight)

Ideal body weight (IBW) should be used to calculate the creatinine clearance unless patients are underweight.

IBW can be calculated using the following equation:

\[
\text{IBW Females} = [45.5kg + (2.3 \times \text{every inch over 5ft})] \text{ kg} \\
\text{IBW Males} = [50kg + (2.3 \times \text{every inch over 5ft})] \text{ kg}
\]

For underweight patients – use actual body weight.

An online creatinine clearance calculator is available at: http://bnf.org/bnf/extra/current/450019.htm

N.B: Renal function may be reported as estimated Glomerular Filtration Rate (eGFR) (in mL/min/1.73m²) which is not equivalent to the estimates of creatinine clearance described above (reported in mL/min). Since eGFR estimates have not yet been validated for drug dosing, dose adjustment for renal impairment continues to be based on estimates of creatinine clearance (e.g. calculated from the Cockcroft and Gault equation or from a 24-hour urine collection)

**Weight**

Treatment doses of LMWHs are calculated based on the patient’s weight. Therefore, where possible, an accurate weight (in kg) should be obtained using validated weighing equipment by personnel trained in using the weighing equipment. In exceptional circumstances, when a patient cannot be weighed, body weight information can be obtained from the patient or carer. However, if this information cannot be obtained, as a last resort, the weight may be estimated by the prescriber. The patient’s weight should be documented in the clinical notes (medical or nursing notes or GP clinical system) AND the hospital prescribing system (when in use) or the community patient medication administration chart (PMAC) at the start of the treatment. The patient’s weight should be added to the FP10 prescription. This is required by the community pharmacist when assessing the dose. It should then be rechecked at appropriate intervals, at least every 3 months or sooner if the patient’s clinical condition changes in a way that might affect their body weight.

Every effort should be made to ensure an accurate weight (in kg) is obtained prior to a LMWH being prescribed but this should not delay treatment. If it is not possible to weigh the patient, or an estimated weight is used to calculate the dose of LMWH, this should be made clear in the patient’s clinical notes and re-assessed at a later date if appropriate.


**Prevention of venous thromboembolism**

**Duration**

LMWH should continue to be administered for as long as the patient remains at risk of venous thromboembolism (VTE).

**Calculating the right dose**

**ALL** patients who are admitted to hospital MUST have their risk of developing a venous thromboembolism (VTE) assessed on admission, reassessed within 24 hours of admission and whenever the clinical situation changes².

PCIS will provide guidance on the choice of LMWH and dose depending on the patient’s renal function (and patient’s weight if their CrCl <20ml/min). For areas that do not use PCIS, please refer to Table 1 for dosing information. There are 2 different strengths of tinzaparin syringes available – 10,000units/ml and 20,000units/ml. Tinzaparin 10,000units/ml strength syringes are licensed for the prophylaxis of VTE.

**Table 1 – Doses of tinzaparin for prophylaxis against VTE**

<table>
<thead>
<tr>
<th>Indication</th>
<th>LMWH</th>
<th>Dose for patients with a creatinine clearance ≥ 20mL/min</th>
<th>Dose for patients with creatinine clearance &lt;20mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical thromboprophylaxis</td>
<td>Tinzaparin</td>
<td>4500 units sc once daily</td>
<td>If patient’s weight is:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• &gt;70kg: 3500 units sc once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• &lt;70kg: 2500 units sc once daily</td>
</tr>
<tr>
<td>Surgical thromboprophylaxis* - Moderate</td>
<td></td>
<td>3500 units sc once daily</td>
<td>If patient’s weight is:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• &gt;70kg: 3500 units sc once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• &lt;70kg: 2500 units sc once daily</td>
</tr>
<tr>
<td>Surgical thromboprophylaxis* - High risk</td>
<td></td>
<td>4500 units sc once daily</td>
<td></td>
</tr>
</tbody>
</table>

*For VTE prophylaxis in orthopaedic patients – please refer to Trauma and Orthopaedic Venothromboembolic (VTE) Prophylaxis Guidelines on the intranet.

http://nww.wirralhealth.nhs.uk/clinical_guidance/trauma_and_orthopaedics.html

**VTE prophylaxis in pregnancy**

For prophylaxis of VTE in pregnancy – please refer to Wirral Women and Children’s Guideline no 33: Venous Thromboembolism Prophylaxis and Treatment.

Treatment of VTE

Duration
For the initial treatment of VTE, a LMWH should be continued for at least 6 days AND until an oral anticoagulant (if used) is established — i.e. until the patient's INR is in the specified therapeutic range.

Short term therapy with LMWH
Although oral anticoagulation is preferred for the treatment of VTE, LMWHs should be considered for up to 6 weeks for the small subgroup of patients:

- With very low risk VTE (i.e. those who suffered a below knee DVT for which there were likely precipitating factors)

And

- For whom oral anticoagulation appears unjustified or inappropriate, such as those with:
  - Poor compliance, cognitive impairment, chaotic lifestyle* or recreational drug misuse*
  - Increased bleeding risk (e.g. due to falls, peptic ulcer disease)
  - Liver dysfunction (indicated by elevated INR >1.2)

NOTE: This will be a very small subgroup of patients
*For patients with chaotic lifestyle or recreational drug misuse, the risks in treating these patients with LMWH should be considered e.g. safe sharps disposal

Extended (>6weeks) or long term (indefinite) LMWH therapy
A LMWH may be considered for longer periods in patients who are at higher risk of VTE than the very low risk VTE group described above and for whom oral anticoagulant may be unsuitable (as outlined above). It may also be considered for patients with an active malignancy (within 6 months of malignancy diagnosis or treatment) or to prevent or treat a VTE in pregnant women.

NOTE: The use of LMWHs for longer than 6 weeks is not licensed

Calculating the right dose
At WUTH, PCIS provides guidance on the choice of LMWH and dose depending on the patient's indication, weight and renal function. For areas that do not use PCIS, refer to Table 2a/2b (overleaf) for dosing information.
1. If the patient’s creatinine clearance is ≥20mL/min

Tinzaparin 175units/kg, by SC injection once daily.

NOTE: There are different strengths of tinzaparin syringes - 10,000units/ml and 20,000units/ml. Tinzaparin 20,000units/mL strength syringes are graduated and licensed for the treatment DVT/PE. 2 ml multidose vials are also available. Select the most appropriate size syringe or multidose vial to give the required dose.

**Table 2a. Doses of tinzaparin for the initial treatment of DVT/PE if CrCl ≥20ml/min**

<table>
<thead>
<tr>
<th>Syringe size</th>
<th>Body weight</th>
<th>Daily dose (international units)</th>
<th>Injection volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5ml</td>
<td>40kg</td>
<td>7,000</td>
<td>0.35ml</td>
</tr>
<tr>
<td></td>
<td>45kg</td>
<td>8,000</td>
<td>0.40ml</td>
</tr>
<tr>
<td></td>
<td>50kg</td>
<td>9,000</td>
<td>0.45ml</td>
</tr>
<tr>
<td></td>
<td>55kg</td>
<td>10,000</td>
<td>0.50ml</td>
</tr>
<tr>
<td>0.7ml</td>
<td>60kg</td>
<td>11,000</td>
<td>0.55ml</td>
</tr>
<tr>
<td></td>
<td>65kg</td>
<td>11,000</td>
<td>0.55ml</td>
</tr>
<tr>
<td></td>
<td>70kg</td>
<td>12,000</td>
<td>0.60ml</td>
</tr>
<tr>
<td></td>
<td>75kg</td>
<td>13,000</td>
<td>0.65ml</td>
</tr>
<tr>
<td></td>
<td>80kg</td>
<td>14,000</td>
<td>0.70ml</td>
</tr>
<tr>
<td>0.9ml</td>
<td>85kg</td>
<td>15,000</td>
<td>0.75ml</td>
</tr>
<tr>
<td></td>
<td>90kg</td>
<td>16,000</td>
<td>0.80ml</td>
</tr>
<tr>
<td></td>
<td>95kg</td>
<td>17,000</td>
<td>0.85ml</td>
</tr>
<tr>
<td></td>
<td>100kg</td>
<td>18,000</td>
<td>0.90ml</td>
</tr>
<tr>
<td></td>
<td>105kg</td>
<td>18,000</td>
<td>0.90ml</td>
</tr>
<tr>
<td>Multidose vial</td>
<td>110kg</td>
<td>19,000</td>
<td>0.95ml</td>
</tr>
<tr>
<td></td>
<td>115kg</td>
<td>20,000</td>
<td>1ml</td>
</tr>
<tr>
<td></td>
<td>120kg</td>
<td>21,000</td>
<td>1.05ml</td>
</tr>
<tr>
<td></td>
<td>125kg</td>
<td>22,000</td>
<td>1.10ml</td>
</tr>
<tr>
<td></td>
<td>130kg</td>
<td>23,000</td>
<td>1.15ml</td>
</tr>
<tr>
<td></td>
<td>&gt;130kg</td>
<td>Use an unfractionated heparin infusion – see unfractionated heparin infusion guidelines on intranet</td>
<td></td>
</tr>
</tbody>
</table>

Doses have been rounded to the nearest 5kg and 0.05ml
2. If the patient’s creatinine clearance is <20mL/min

**Enoxaparin** 1mg/kg, by SC injection, **once daily**.
There are different size graduated syringes. Select the most appropriate size to give the required dose.

**Table 2b. Doses of enoxaparin for the initial treatment of DVT/PE if CrCl <20ml/min**

<table>
<thead>
<tr>
<th>Syringe size</th>
<th>Body weight</th>
<th>Daily dose</th>
<th>Injection volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>40mg</td>
<td>40kg</td>
<td>40mg</td>
<td>0.4ml</td>
</tr>
<tr>
<td>60mg</td>
<td>50kg</td>
<td>50mg</td>
<td>0.5ml</td>
</tr>
<tr>
<td></td>
<td>60kg</td>
<td>60mg</td>
<td>0.6ml</td>
</tr>
<tr>
<td>80mg</td>
<td>70kg</td>
<td>70mg</td>
<td>0.7ml</td>
</tr>
<tr>
<td></td>
<td>80kg</td>
<td>80mg</td>
<td>0.8ml</td>
</tr>
<tr>
<td>100mg</td>
<td>90kg</td>
<td>90mg</td>
<td>0.9ml</td>
</tr>
<tr>
<td></td>
<td>100kg</td>
<td>100mg</td>
<td>1ml</td>
</tr>
<tr>
<td>Combination of above syringes</td>
<td>110kg</td>
<td>110mg</td>
<td>1.1ml</td>
</tr>
<tr>
<td></td>
<td>120kg</td>
<td>120mg</td>
<td>1.2ml</td>
</tr>
<tr>
<td></td>
<td>130kg</td>
<td>130mg</td>
<td>1.3ml</td>
</tr>
<tr>
<td></td>
<td>140kg</td>
<td>140mg</td>
<td>1.4ml</td>
</tr>
<tr>
<td></td>
<td>150kg</td>
<td>150mg</td>
<td>1.5ml</td>
</tr>
</tbody>
</table>

Weight rounded to nearest 10kg and 0.1ml

**VTE treatment in pregnancy**
For prophylaxis and treatment of VTE in pregnancy – please refer to Wirral Women and Children’s Guideline no 33: Venous Thromboembolism Prophylaxis and Treatment.

Contraindications/Cautions to LMWH

Do not prescribe or administer LMWHs to patients who have:

- Known hypersensitivity to active ingredients
- Current or previous history of heparin-induced thrombocytopenia.
- Hypersensitivity to benzyl alcohol (only if using enoxaparin or tinzaparin multidose vials)
- Generalised or local haemorrhagic tendency, including:
  - uncontrolled severe hypertension (i.e. BP >220/120mmHg as per British Hypertension Society definition). The decision on whether to use LMWH should be considered on the balance of risk versus benefit.
  - severe liver insufficiency
  - active peptic ulcer
  - acute or subacute septic endocarditis
  - intracranial haemorrhage, or injuries
  - operations on the central nervous system, eyes and ears, and in women with abortus imminens

Patients should not have an epidural inserted or removed or spinal inserted until at least 10 hours have elapsed since the last dose of prophylactic LMWH. Prophylactic LMWH should not be given within 2 hours of epidural insertion or catheter removal. If insertion was difficult or bloody then prophylactic LMWH should not be given within 4 hours of insertion or removal.

Treatment doses of LMWH must not be given to patients who have an epidural catheter in situ. Remove the epidural catheter and only start the treatment dose of LMWH 4 hours after the catheter has been removed. If the patient has had a spinal anaesthetic, do not start treatment doses of LMWH until 4 hours after the spinal was performed. (see Acute Pain Guidelines).

Prophylactic LMWH therapy is not required if patients are already receiving therapeutic anticoagulation.

Monitoring

For patients receiving a LMWH for longer than 5 days, the following should be monitored:

- **Platelets** — this is due to the risk of antibody-mediated heparin-induced thrombocytopenia. Monitor platelets approximately 7 to 10 days after initiation and then 3 monthly whilst LMWH treatment continues. Treatment should be stopped immediately in those who develop thrombocytopenia. Signs of heparin-induced thrombocytopenia include a 50% reduction of platelet count, thrombosis or skin allergy.

- **Potassium** — LMWHs can cause hyperkalaemia due to suppression of aldosterone secretion. Patients at higher risk of this include those with diabetes mellitus, chronic renal failure, pre-existing metabolic acidosis, raised plasma potassium or those taking potassium-sparing drugs. Monitor potassium approximately 7 to 10 days after initiation and then 3 monthly thereafter whilst LMWH treatment continues (or sooner if clinically indicated).
Administration of LMWHs

In hospital
Nursing staff should ensure that an accurate weight in kg is documented in the medical or nursing notes or hospital prescribing system to enable an appropriate LMWH dose to be calculated. Where possible, the nursing staff should ensure that the dose of LMWH has been verified by a pharmacist (indicated by a “v” on the current drugs list) before it is given. If the weight, renal function or pharmacist verification is not available immediately, this should not delay the initiation of treatment but efforts should be made to ensure these are obtained as soon as possible.

For discharge
If the patient is required to self administer a LMWH, appropriate training must be given prior to discharge. The patient needs to be deemed competent by the nurse before discharge. If the patient is unable to self-administer, a referral must be sent to the district nurse to continue administration at home after discharge. In this circumstance, a PMAC must also be filled in clearly by the prescriber before discharge and clinically checked by pharmacist.

Clinical requirements for discharge

It is the responsibility of the ward prescriber AND consultant to ensure the indication, dose, duration of treatment, patient’s weight and renal function is documented on the discharge letter.

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 ‘IDDA’ 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 Indication (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)
• Dose – appropriate for the patient’s renal function and weight
• Duration
• Appropriately trained person to Administer the LMWH in the community if the patient is unable to self-administer.
Prescribing LMWHs in the community

Patients prescribed LMWHs in the community should have their weight and renal function checked every 3 months (or sooner if clinically indicated) and documented in their medical notes. Prescribers must check the patient’s weight and renal function before prescribing.

Prescribers should use the dose calculation tables 2a (see page 5) and 2b (see page 6) when calculating doses of tinzaparin and enoxaparin, respectively.

If a patient medication administration chart (PMAC) is required for community nurse administration, this must include the patient’s weight and renal function and be completed in full by the prescriber.

All prescriptions in the community should include the patient’s weight. A prompt will be added to Scriptswitch to facilitate this.

Patients receiving a LMWH in the community for >3 months will usually be under the supervision of a haematologist. The patient’s weight, renal function and anti factor Xa level should be checked approximately 3 monthly to ensure the dose of LMWH is still appropriate. The haematologist will advise on any potential dose change. The weight and renal function should be reported in the hospital correspondence from the Consultant Haematologist to the GP.

Requirements of community pharmacy

Community pharmacists should check the following before dispensing a LMWH:

- Indication – whether prophylaxis or treatment
- Duration of treatment
- Weight of patient
- Renal function
- Strength of syringe required
- Volume of syringe required
- Dose in international units and in millilitres
- Route and frequency of administration

Requirements of community nurses

Community nurses should check the following before administering a dose of LMWH:

- Indication – whether prophylaxis or treatment
- Duration of treatment
- Weight of patient
- Renal function
- Strength of syringe required
- Volume of syringe required
- Dose in international units and in millilitres
- Route and frequency of administration
References


4. Summary of Product Characteristics. Innohep. Leo Pharma. and http://www.medicines.org.uk/EMC/medicine/5176/SPC/Innohep+20%2c000+IU+ml+and+Innohep+syringe+20%2c000+IU+ml/#CONTRAINDICATIONS (20,000units/ml strength) and http://www.medicines.org.uk/EMC/medicine/2623/SPC/Innohep+10%2c000+IU+ml+and+Innohep+Syringe+10%2c000+IU+ml/ (10,000units/ml) <accessed 06/01/11>


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