NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Heparin Dose Adjustment in the presence of Renal Impairment

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

HEPARIN DOSE ADJUSTMENT
IN THE PRESENCE OF RENAL IMPAIRMENT IN ADULTS

Heparin and heparin-like anticoagulants (unfractionated heparin (UFH), low molecular weight heparins (LMWH) and the pentasaccharide, fondaparinux) vary considerably in their glycosaminoglycan composition, specifically their average chain size (UFH > LMWH > fondaparinux). Even within the LMWH group there can be subtle differences in average chain size (tinzaparin > dalteparin > enoxaparin). These differences have important effects both on the antithrombin-mediated target specificity and dependence on renal clearance – smaller heparins having a higher anti-factor Xa: anti-factor IIa ratio and a greater dependence on renal clearance. The latter is very relevant when prescribing these agents, either at prophylactic or therapeutic doses, for patients with substantially reduced kidney function (CrCl<30mL/min) as observational data demonstrate clinically important increase in bleeding complications of anticoagulation in this group of patients. For this reason, in-patients in the NHS GGC renal unit with chronic kidney disease and CrCl <30mL/min do not routinely receive pharmaceutical thromboprophylaxis when admitted for non-operative reasons unless there are other risk factors for thrombosis.

Within NHS GGC the heparin agent of choice may vary between treatment and prophylaxis and for different indications – please consult NHS GGC Formulary or Therapeutics Handbook for preferred agent of choice. Based on relevant SPC guidance and limited additional literature the following recommendations are offered.

Note that this guideline is for adult non-pregnant patients only.

PROPHYLACTIC HEPARIN DOSING

<table>
<tr><td colspan="3">For dose adjustments in adult patients with very low or very high body weight,
refer to GGC guideline on the Clinical Guideline Platform.</td></tr>
<tr><td rowspan="2"></td><td colspan="2">CrCl (ml/min)
GGC CrCl calculator available here</td></tr>
<tr><td>≥ 30 ml/min</td><td>< 30 ml/min</td></tr>
<tr><td>Enoxaparin</td><td>40mg once daily</td><td>20mg once daily* if CrCl 30-15 ml/min
AVOID if CrCl < 15 ml/min
Use an alternative LMWH</td></tr>
<tr><td>Dalteparin</td><td>5,000 units once daily</td><td>5,000 units once daily* if CrCl 30-15 ml/min
2,500 units once daily* if CrCl < 15 ml/min</td></tr>
<tr><td>Tinzaparin</td><td colspan="2">3,500 / 4,500 units once daily* as per indication
AVOID if CrCl < 20ml/min, use an alternative LMWH</td></tr>
<tr><td>Fondaparinux</td><td colspan="2">2.5 mg once daily if CrCl > 50 ml/min
1.5 mg once daily if CrCl 50-20 ml/min
AVOID if CrCl < 20 ml/min, use a suitable LMWH</td></tr>
</table>

**If CrCl < 30ml/min and prophylactic LMWH treatment has continued for ≥10 days, re-assess anti-Xa activity after 10th dose of LMWH, to ensure there has been no significant drug accumulation (target 4h peak level: 0.1 - 0.4 units/ml)*

THERAPEUTIC HEPARIN DOSING

<table>
<tr><td colspan="4">For dose adjustments in adult patients with very low or very high body weight,
refer to GGC guideline on the Clinical Guideline Platform.</td></tr>
<tr><td></td><td colspan="3">CrCl (ml/min)
GGC CrCl calculator available here</td></tr>
<tr><td></td><td>≥ 30 ml/min</td><td>30-10 ml/min</td><td>< 10 ml/min</td></tr>
<tr><td>Dalteparin
(weight-banded dosing)</td><td>200 units/kg once daily
[max 18,000 units]

Consider dalteparin 100units/Kg twice daily in patients with high bleeding risk</td><td>200 units/kg once daily*
[max 18,000 units]

Consider dalteparin 100units/Kg twice daily in patients with high bleeding risk</td><td rowspan="3">Due to lack of evidence suggest use of UFH#

See page 4 for recommendations for anticoagulation prescribing during haemodialysis

#In the Renal Unit enoxaparin 1mg/kg once daily is regarded as an acceptable alternative</td></tr>
<tr><td>Enoxaparin
(weight-banded dosing)</td><td>VTE: 1.5 mg/kg once daily
Consider enoxaparin 1mg/Kg twice daily in patients with high bleeding risk or patients perceived to be at high risk of recurrent VTE

ACS: 1 mg/kg twice daily</td><td>VTE: 1 mg/kg once daily*
AVOID if CrCl < 15 ml/min
Use an alternative LMWH

ACS: 1mg/kg once daily*
(remains treatment of choice if CrCl < 15 ml/min)</td></tr>
<tr><td>Tinzaparin</td><td>175 units/kg once daily</td><td>175 units/kg once daily*
AVOID if CrCl < 20 ml/min
Use an alternative LMWH</td></tr>
<tr><td>Fondaparinux</td><td colspan="3">SVT: 2.5 mg once daily if CrCl > 50 (1.5 mg if CrCl 20-50 ml/min)
ACS: 2.5mg once daily if CrCl ≥20ml/min
AVOID if CrCl <20 ml/min, use a suitable LMWH</td></tr>
<tr><td>Unfractionated heparin (UFH)
(intravenous Na Heparin)</td><td colspan="3">**Use 1000 units/ml preparation at all times**
Loading IV dose: 5,000 units, if appropriate
Maintenance IV infusion: start at 18 units/kg/h, check APTT ratio 6 hours after commencement of infusion, and 4 hours after any change in infusion rate, then daily (target APTT ration: 1.8-2.6)</td></tr>
</table>

VTE: venous thrombosis; SVT: superficial vein thrombosis; ACS: acute coronary syndrome; UFH: unfractionated heparin

**If CrCl < 30 ml/min consider assessing anti-Xa activity after 3rd dose (to confirm therapeutic levels have been achieved) and after 8-10th dose to ensure there has been no significant drug accumulation (target 4h peak level: 0.5 – 1.2 units/ml)*

N.B. If a patient with a CrCl < 20 ml/min on a therapeutic LMWH regimen, which cannot be omitted for 36-48h, is scheduled for an invasive procedure (including small procedures such as a biopsy or central line insertion) it is recommended that the patient is switched to an UFH regimen prior to the procedure as follows:

- IV UFH is started 20-24h after the last dose of therapeutic LMWH
- IV UFH is stopped 6h prior to the procedure
- IV UFH is restarted, assuming adequate haemostasis, 4-6h post procedure

There are different concentrations of UFH currently available – only the 1000 units/ml preparation should be used at all times to reduce the risk of dose errors and serious clinical incidents.

If you require further advice consult Therapeutics Handbook or contact haematology.

USE OF HEPARIN DURING HAEMODIALYSIS PROCEDURES

If not on regular anticoagulation for other indications, haemodialysis patients should be considered for anticoagulation for the prevention of clotting of the extracorporeal circuit.

Within NHS GGC the LMWH of choice for use during haemodialysis is subject to regular review. Please seek advice from renal team before prescribing.

Tinzaparin dose regimen:

Tinzaparin	2,500 units,	if dialysis ≤ 4h
Tinzaparin	3,500 units,	if dialysis > 4h, or circuit clotting on 2,500 units

Dalteparin dose regimen:

If dry weight ≤ 60Kg	2,500 units
If dry weight > 60Kg	5,000 units

Please note that dalteparin dose is ***not*** dependent on duration of dialysis.

When LMWH is used for haemodialysis anticoagulation, routine monitoring of anti-Xa activity is not required.

Authors: Dr Sokratis Stoumpos and Debbie Thomson on behalf of NHS GGC Thrombosis Committee (with input from Dr Catherine Bagot)
Approved by: Medicines Utilisation Sub-Committee, NHS GGC ADTC
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