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 online 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 on haemodialysis or 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. Those deemed high thrombosis risk receive 20mg once daily (as per the prophylactic table below) including on dialysis days.

Within NHS GGC the heparin agent of choice may vary between treatment and prophylaxis and for different indications – please consult Therapeutics Handbook or relevant local guidelines 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

For dose adjustments in adult patients with very low or very high body weight, refer to GGC guideline on the Clinical Guideline Platform.			
	CrCl (ml/min) GGC CrCl calculator available via Therapeutics Handbook app		
	≥ 30 ml/min	**15-29 ml/min**	**< 15 ml/min**
Enoxaparin	40mg once daily	20mg once daily	20mg once daily (off-label)*
Dalteparin	5,000 units once daily	5,000 units once daily	2,500 units once daily

*Reflects national practice by renal teams, expert opinion and historical experience. In most patients with severe renal impairment, prophylactic dose of enoxaparin does not appear to be associated with an increased bleeding risk and can be used without the need for anti-Xa monitoring.

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 rowspan="2"></td><td colspan="3">CrCl (ml/min)
GGC CrCl calculator available via the Therapeutics Handbook app</td></tr>
<tr><td>≥ 30 ml/min</td><td>15-29 ml/min</td><td>< 15 ml/min</td></tr>
<tr><td>Dalteparin
(weight-banded dosing)</td><td>200 units/kg once daily
[max 18,000 units]

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

Consider 100units/kg twice daily in patients with high bleeding risk</td><td rowspan="3">There is a limited evidence base for treatment LMWH in severe renal impairment and a significantly increased bleeding risk.

Use UFH where suitable

(note includes a complex prescribing and administration regime that may not be suitable in all clinical areas)

If UFH unsuitable use enoxaparin 1mg/kg OD (off-label, max 120mg)

(note associated with a significant increased bleeding risk, ensure anti-Xa monitoring in place)

See page 4 for recommendations for anticoagulation prescribing during haemodialysis</td></tr>
<tr><td>Enoxaparin
(weight-banded dosing)</td><td>VTE: 1.5 mg/kg once daily
Consider 1mg/kg twice daily in patients perceived to be at high risk of recurrent VTE

ACS: 1 mg/kg twice daily</td><td>VTE: 1 mg/kg once daily

ACS: 1mg/kg once daily (remains treatment of choice if CrCl < 15 ml/min)</td></tr>
<tr><td>Fondaparinux</td><td colspan="2">SVT: 2.5 mg once daily if CrCl > 50ml/min
1.5 mg once daily if CrCl 20-50 ml/min

ACS: 2.5mg once daily if CrCl ≥ 20ml/min
AVOID if CrCl < 20 ml/min</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

Monitoring: 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 per anticoagulants in the peri-operative period guideline. For further advice contact haematology.

USE OF HEPARIN DURING HAEMODIALYSIS PROCEDURES

If not on regular anticoagulation for other indications, patients should be considered for anticoagulation during haemodialysis 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.

<table>
<tr><td colspan="2">Patient requiring anticoagulation for chronic dialysis</td></tr>
<tr><td colspan="2">Exceptions: acute HD, trauma, post-op, clotting disorder</td></tr>
<tr><td colspan="2">Already on warfarin or DOAC?</td></tr>
<tr><td colspan="2">If yes, discuss with renal doctor</td></tr>
<tr><td colspan="2">If not on oral anticoagulation, Check dry weight</td></tr>
<tr><td><60 kg</td><td>≥60 kg</td></tr>
<tr><td>Enoxaparin 20 mg</td><td>Enoxaparin 40 mg</td></tr>
<tr><td colspan="2">Dose adjustments</td></tr>
<tr><td>If circuit clotting:
Increase next Enoxaparin dose by 20 mg (max single dose 60 mg)</td><td>If prolonged bleeding:
Reduce next Enoxaparin dose by 20 mg and consider protamine</td></tr>
<tr><td colspan="2">If the dose of Enoxaparin needs to be increased to ≥60 mg a peak or patient weighs >100 kg anti-XA level should be taken on the 4th dose of Enoxaparin to check for over or under coagulation</td></tr>
</table>

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Approved by: Medicines Utilisation subcommittee of ADTC
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