NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Heparin Dose Adjustment in Adult Patients with Very High or Low Body Weight

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:

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HEPARIN DOSE ADJUSTMENT IN ADULT PATIENTS WITH VERY HIGH OR LOW BODY WEIGHT

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

Occasionally patients with very high or very low body weight will require prophylactic or therapeutic heparin treatment. Unfortunately most clinical studies on which licences are based included very few patients at these extremes of weight. Furthermore, dosing advice from manufacturers of different low molecular weight heparins (LMWHs) in patients with high body weight differs. However LMWH clearance seems to be faster in patients with high body mass index (BMI).

Several different approaches have been suggested for LMWH dose modifications in patients at very high body weight. The NHS GGC Thrombosis Committee has reviewed the published literature and favours a conservative approach to increased dosing of LMWH at high body weight. Based on relevant guidance from manufacturers and limited additional literature the following recommendations are offered.

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 Summary Product Characteristics (SPC) guidance and limited additional literature the following recommendations are offered.

THERAPEUTIC HEPARIN DOSING (see separate guidelines for dosing in pregnancy)

	Total body weight less than 34 kg	Total body weight more than 120 kg
Dalteparin	**200 units/kg once daily** (consider using 5,000 unit pre-filled syringe*)	18,000 units once daily (monitor anti-Xa activity as advised below)
Enoxaparin	**VTE:** 1.5 mg/kg once daily **ACS:** 1 mg/kg twice daily	120 mg twice daily
Tinzaparin	175 units/kg once daily	Switch to dalteparin
Unfractionated heparin *(intravenous Na Heparin)*	***If patient weighs less than 50 kg*** IV loading dose: 80 units/kg Maintenance IV infusion: start at 18 units/kg/h	***If patient weighs more than 100 kg*** IV loading dose: 10,000 units Maintenance IV infusion: start at 1,800 units/h
	Check APTT ratio 6 hours after commencement of infusion, and 4 hours after any change in infusion rate, then daily	

VTE: venous thromboembolism; ACS: acute coronary syndrome

**Dalteparin 5,000 units pre-filled syringes are only licensed for thromboprophylaxis - use for treatment of VTE is off-label*

Renal impairment

If patient has CrCl 10-30 ml/min monitor anti-Xa activity and adjust dose accordingly (see below for details). Consider using dalteparin 100 units/kg twice a day (up to a maximum initial total daily dose of 18,000 units) in patients with high bleeding risk. If considering prescribing an alternative LMWH, please consult SPC for full prescribing information. If CrCl < 10 ml/min, liaise with renal team for advice.

GGC CrCl calculator is available in the Clinical Info section of Staffnet (direct link here).

Monitoring anti-Xa activity

Target 4h peak level: 0.5-1.2 units/ml (contact haematology for advice if anti-Xa activity is out with target range)
Anti-Xa activity should be assessed after 3rd dose of LMWH, to ascertain therapeutic levels achieved, if:

- **Renal impairment (CrCl < 30 ml/min)** – also re-assess anti-Xa activity after 10th dose of LMWH, to ensure there has been no significant drug accumulation
- **Extremes of body weight –** extremely low weight (< 35 kg) or extremely heavy (>120 kg) patients
- **Concerns of lack of therapeutic efficacy** – such as recurrent thrombosis during treatment
- **Increased risk of bleeding** – such as
  - □ active bleeding
  - □ platelets < $75x10^9$/L
  - □ liver failure
  - □ uncontrolled hypertension (BP≥230/120 mmHg)
  - □ untreated inherited bleeding disorder
  - □ acute bacterial endocarditis
  - □ patients due imminent surgery or spinal intervention (or patients who had surgery within past 48 hours) – consider using UFH in patients at high risk of bleeding

PROPHYLACTIC HEPARIN DOSING (see separate guidelines for dosing in pregnancy)

	Total body weight less than 50 kg	Total body weight more than 120 kg
Enoxaparin	**20 mg once daily**	Refer to chart for bariatric patients below
Dalteparin	2,500 units once daily	
Tinzaparin	2,500 units once daily	

Monitoring anti-Xa activity

Target 4h peak level: 0.1-0.4 units/ml (contact haematology for advice if anti-Xa activity is out with target range)

Anti-Xa activity should be assessed after 3rd dose of LMWH if:

- **Renal impairment (CrCl < 30 ml/min)** (LMWH dose may need reduced; also re-assess anti-Xa activity after 10th dose of LMWH, to ensure there has been no significant drug accumulation). GGC CrCl calculator is available in the Clinical Info section of Staffnet (direct link here).
- **Extremely low body weight** (< 35 kg)
- **Risk of bleeding is significantly increased** (as above)

BARIATRIC PATIENTS

While the following 'multi-modal approach' is designed specifically for extreme body weight patients undergoing bariatric surgery, we recommend its application for high body weight patients (>120 kg) deemed to require pharmacological thromboprophylaxis in medical wards or undergoing other types of surgery.

Most evidence for this guideline was taken from bariatric surgery, and extended to non-bariatric surgery and medical patients. Since there is currently a lack of good evidence, these guidelines have a pragmatic approach and are only intended for patients with normal renal function.

This guidance should be used in conjunction with the relevant specialty-specific thromboprophylaxis policy. Each patient has to be assessed individually for VTE and bleeding risks by the responsible medical team.

General advice

1. Encourage weight loss
2. Stop smoking preoperatively
3. If appropriate, stop HRT and oestrogen containing contraception 4 weeks prior surgery (ensuring adequate alternative contraception)
5. Aim for good hydration peri-operatively
6. Early mobilisation (first 12 hours post op), enhanced recovery
7. Epidural and spinal anaesthetic techniques should not be carried out within 12 hours of a prophylactic dose of LMWH. Likewise epidural catheters should not be removed within 12 hours of a prophylactic dose of LMWH. Wait at least 4 hours after any of these procedures before giving the next dose of enoxaparin. **In the case of patients receiving 40 mg enoxaparin twice daily due to high body weight this means that a dose will have to be omitted when the catheter is removed and its administration delayed for at least 4 hours after the catheter removal.**

Pharmacological prophylaxis

Every patient should receive pharmacological prophylaxis unless contraindicated. Start 6 hours post surgery or when haemostasis is secured.

Enoxaparin is the LMWH of choice for thromboprophylaxis within NHS GGC.

Body weight 120-150 kg	**Body weight 120-150 kg**	**Body weight more than 150 kg**
without additional VTE risk factors *or* with high risk of bleeding	with additional VTE risk factors such as: • previous VTE • known thrombophilia • major restriction to mobility	
Enoxaparin 40 mg once daily *or* Dalteparin 5,000 units once daily	**Enoxaparin 40 mg twice daily*** *or* Dalteparin 5,000 units twice daily*	**Enoxaparin 40 mg twice daily*** *or* Dalteparin 5,000 units twice daily*

**Monitoring of anti-Xa activity is recommended for all patients receiving thromboprophylaxis with twice daily LMWH and any patient with a high risk of bleeding. Target 4h peak level: 0.1-0.4 units/ml (usually after 3rd dose of LMWH) (contact haematology for advice if anti-Xa activity is out with target range)*

Contraindications for pharmacological prophylaxis

- Concurrent use of therapeutic anticoagulant (eg warfarin, DOAC)

Cautions for pharmacological prophylaxis

- Spinal intervention (see above – LMWH timing is crucial)
- Any high bleeding risk factors (see above)
- CrCl < 30 ml/min - for patients >120Kg, recommendation is to prescribe 40mg enoxaparin or 5,000 units dalteparin once daily with subsequent assessment of anti-Xa activity. GGC CrCl calculator is available in the Clinical Info section of Staffnet (direct link here).

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Approved by: Medicines Utilisation Sub-Committee, NHS GGC ADTC

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