DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Guidance on prescribing of Low Molecular Weight Heparin (Enoxaparin and Tinzaparin)

Introduction

Low molecular weight heparin (LMWH) provides effective, rapid anticoagulation and is used in the acute management of venous thromboembolic disease (VTE), often in conjunction with warfarin until INR target is reached. Those who are not suitable for oral anticoagulation may require extended LMWH treatment. The LMWH of choice is enoxaparin (**prescribe by brand**, preferred cost effective brand Inhixa) at UHDBFT and tinzaparin at CRHFT. Note they are not always used within their licensed indications and there is no LMWH licensed for use in pregnancy.

Short courses (up to 6 weeks) of LMWH are provided by the acute hospital trusts for the following indications:

- Post-operative VTE prophylaxis (eg. post hip/knee replacement)
- Pre-operative use as warfarin replacement
- Post-operative use in conjunction with warfarin whilst waiting for the INR to come into range
- *VTE prophylaxis in post-natal patients (if course length is up to 6 weeks, also see below)

Longer courses for the following indications may be continued by GP with little monitoring requirement:

- Treatment/*Secondary prophylaxis of DVT and PE in patients with cancer, intravenous drug abuse, or intolerance/poor control/failure of oral anticoagulation
- *Treatment of thromboembolic disease in pregnancy
- *VTE prophylaxis throughout pregnancy and up to 12 weeks post-partum.
- Concurrent LMWH during warfarin treatment when patient unexpectedly failed to reach target INR during loading (DVT/PE within last four weeks) OR INR persistently below target range AND patient at high risk of VTE e.g. mechanical heart valve. ***small amount only at request of a specialist or INR clinic***

*unlicensed indications

JAPC consensus and agreement for the management of sub-therapeutic INR

1. It is not uncommon for INRs to fall below the target value in patients taking long-term warfarin. There is though a lack of national guidance on what to do in this situation.
    - In a patient with a single INR value below therapeutic value, the clinician should check medication compliance with the patient, and investigate any interacting medicines (prescribed, brought over the counter or herbal). Include questions on lifestyle or dietary changes to see if these are the cause. Decide on a patient by patient basis whether to increase the dose and/or address causes and then retest the INR accordingly within the next 3-5 days.
    - In patients with serial INRs (on 3 or more occasions) below therapeutic range where there is no improvement in control following interventions, seek advice from specialists (e.g. in patients with artificial valves).
2. The use of LMWH is only advocated when the warfarin INR falls outside the therapeutic range, **within the first four weeks of acute VTE**, as recommended by the fourth edition of the British Committee for Standards in Haematology until the patient is within therapeutic range for warfarin. All other patients are deemed low risk. Patients taking warfarin for AF do not require LMWH cover for sub-therapeutic INRs.
3. LMWH is commonly prescribed in patients where rapid thrombolysis is necessary and often used in conjunction with warfarin until target INR is reached. The provider trusts will supply a suitable quantity of LMWH to meet the patients need. However in **exceptional circumstances** primary care clinicians may be requested to supply small quantities of LMWH where patients fail to reach their target INR at the request of a specialist or INR clinic.

The following proformas are examples of the type of information which should be shared with patients GP when requesting continued prescribing of LMWHs

Enoxaparin prescribing proforma- prescribe by brand (preferred cost effective brand Inhixa)

Patient detail _____ **Weight**_____**kg** **eGFR**_____**ml/min/1.73m²** ☐ **Baseline bloods completed**		
Indication (please select from below)	**Dose** _____ **IU** **Dose** _____**mg** **Once Twice daily**	**Duration** _____ **Stop date** _____
☐ Treatment/Secondary prophylaxis of DVT and PE in patients with e.g. active cancer or intolerance/poor control of oral anticoagulation	150 IU per kg (1.5mg per kg) once daily in uncomplicated patients with low risk of VTE recurrence. 100 IU per Kg (1mg per kg) twice daily in all other patients such as those with obesity, with symptomatic PE, cancer, recurrent VTE or proximal (vena iliaca) thrombosis.	3 months to long term
☐ Treatment of thromboembolic disease in pregnancy	100 IU per kg (1mg per kg) twice daily initially, adjusted according to the antiXa assay	Until 6-12 weeks postpartum
☐ VTE prophylaxis in pregnancy	2000 IU-8000 IU (20-80mg) daily depending on weight if >170kg 0.6mg/kg/day divided over 2 doses	Throughout pregnancy
☐ Concurrent LMWH during warfarin loading when patient unexpectedly failed to reach target INR of _____ (DVT/PE within last four weeks) ***small amount only at request of a specialist or INR clinic*** **Clinical details and monitoring arrangements must be clearly communicated to GP**		
Reduce dose if eGFR less than 30 mL/minute/1.73 m^2—specialist advice, consult product literature for details No dose adjustment in moderate or mild renal impairment although careful clinical monitoring is advised. No dose adjustment required for obese patients No routine monitoring required (except post-cardiopulmonary bypass patients) unless clinical condition changes or is likely to change (platelet count, U&Es)		
☐ **4 weeks enoxaparin supplied** ☐ **Arrangement made for administration (self or district nurse)**		

Tinzaparin prescribing proforma

Patient detail _____ **Weight**_____**kg** **CrCl**_____**ml/min** ☐ **Baseline bloods completed**		
Indication (please select from below)	**Dose** _____**IU** **Once Twice daily**	**Duration** _____ **Stop date** _____
☐ Treatment/Secondary prophylaxis of DVT and PE in patients with e.g. active cancer or intolerance/poor control of oral anticoagulation	175 IU per kg once daily (doses rounded to the nearest 0.05ml)	3 months to long term
☐ Treatment of thromboembolic disease in pregnancy	175 IU per kg once daily	Until 6-12 weeks postpartum
☐ VTE prophylaxis in pregnancy	3500-4500 IU once or twice daily 75 IU/kg for patients weighing more than 170kg	Throughout pregnancy
☐ Concurrent LMWH during warfarin loading when patient unexpectedly failed to reach target INR of _____ (DVT/PE within last four weeks) ***small amount only at request of a specialist or INR clinic*** **Clinical details and monitoring arrangements must be clearly communicated to GP**		
Manufacturer advises caution if creatinine clearance less than 30 mL/minute/ Treatment dose for patients >165kg - seek specialist advice No routine monitoring required (except post-cardiopulmonary bypass patients) unless clinical condition changes or is likely to change (platelet count, U&Es)		
☐ **4 weeks tinzaparin supplied** ☐ **Arrangement made for administration (self or district nurse)**		

Monitoring
BSH guideline 2012 recommends that routine platelet monitoring is not required for LMWH except for cardiopulmonary bypass patients. Responsibility remains with secondary care if monitoring is considered appropriate in the first 14 days of LMWH. No routine monitoring required thereafter.

Heparin Induced Thrombocytopenia (HIT)
If the platelet count falls by 30% or more and/or the patient develops new thrombosis or skin allergy or any of the other rarer manifestations of HIT between days 4 and 14 of heparin administration, HIT should be considered and a clinical assessment made (refer to specialist).

Other information
- Sharps bins will initially be provided by hospital and continued provision will be through the GP.
- Enoxaparin/ Tinzaparin can be stored at room temperature. Avoid excessive direct sunlight exposure.

Contacts
Hospital Contacts:
Chesterfield Royal Hospital

Medicines helpline 01246512153 for discharge queriesRoyal Derby Hospital

Anticoagulation clinic – 01332 789419

DVT clinic – 01332 783207

Antenatal clinic – 01332 785165

Out of hours contacts and procedures:
Pharmacy, UHDBFT, ask for on-call pharmacist via switchboard – 01332 340131

Contact the A&E department for any complications such as bleeding

Pregnancy triage – 01332 786894

References
SPC Innohep Accessed https://www.medicines.org.uk/emc/medicine/29742 21/10/2020
SPC Clexane Accessed https://www.medicines.org.uk/emc/medicine/10054 2/10/2020
NICE CG144 Venous thromboembolic disease: diagnosis, management and thrombophilia testing https://www.nice.org.uk/guidance/CG144/chapter/Recommendations#treatment-2
MHRA Rapid response Report http://www.nrls.npsa.nhs.uk/alerts/?entryid45=75208
British Society for Haematology's Guidelines on the diagnosis and management of heparin-induced thrombocytopenia: second edition. *Br J Haematol* 2012; **159**: 528–540
Royal College of Obstetrics and Gynaecology (RCOG) Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium guideline.
https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg37a/ 17/11/2020

Document produced by
Derbyshire Medicines Management Guidelines Group adapted from JAPC shared care guidance for Low Molecular Weight Heparin (Enoxaparin and Tinzaparin)

Document update	Date

Appendix 1. Enoxaparin/ Tinzaparin dosage chart- TREATMENT DOSES

Enoxaparin

150 IU per kg (1.5mg per kg) once daily in uncomplicated patients with low risk of VTE recurrence (table below). 100 IU per Kg (1mg per kg) twice daily in all other patients such as those with obesity, with symptomatic PE, cancer, recurrent VTE or proximal (vena iliaca) thrombosis. E.g. 60kg dose 6000 IU (60mg) twice daily.

Dose: 1.5mg/kg (150IU/kg) SC once daily for treatment of DVT/ PE					
Patient Weight (Kg)	**Dose in IU SC once daily**	**Dose in mg SC once daily**	**Injection volume (ml)**	**Preparation (syringe)**	
40	6000 IU	60 mg	0.60	6000 IU (60mg) / 0.6ml	10,000 IU (100mg)/ml syringe
45 50	6800 IU 7500 IU	68 mg 75 mg	0.7 0.75	8000 IU (80mg) / 0.8ml 8000 IU (80mg) / 0.8ml	
55 60 65	8300 IU 9000 IU 9800 IU	83 mg 90 mg 98 mg	0.85 0.90 1	10,000 IU (100mg) / 1ml 10,000 IU (100mg) / 1ml 10,000 IU (100mg) / 1ml	
70 75 80	10,500 IU 11,250 IU 12,000 IU	105 mg 112.5 mg 120 mg	0.70 0.75 0.80	12,000 IU (120mg) / 0.8ml 12,000 IU (120mg) / 0.8ml 12,000 IU (120mg) / 0.8ml	15,000 IU (150mg)/ml syringe
85 90 95 100	12,750 IU 13,500 IU 14,250 IU 15,000 IU	127.5 mg 135 mg 142.5 mg 150 mg	0.85 0.90 0.95 1.00	15,000 IU (150mg) / 1ml 15,000 IU (150mg) / 1ml 15,000 IU (150mg) / 1ml 15,000 IU (150mg) / 1ml	

Tinzaparin

Tinzaparin **20,000IU/mL** strength syringes are graduated and licensed for the treatment of DVT/PE.

Dose: 175 IU/kg SC once daily (rounded to the nearest 0.05ml) for treatment of DVT/ PE			
Weight (Kg*)	**International units (IU)**	**Injection volume (ml)**	**Preparation (20,000 iunits/ml)**
32-37	6,000	0.30	**0.5ml prefilled syringe**
38-42	7,000	0.35	
43-48	8,000	0.40	
49-54	9,000	0.45	
55-59	10,000	0.50	
60-65	11,000	0.55	**0.7ml prefilled syringe**
66-71	12,000	0.60	
72-77	13,000	0.65	
78-82	14,000	0.70	
83-88	15,000	0.75	**0.9ml prefilled syringe**
89-94	16,000	0.80	
95-99	17,000	0.85	
100-105	18,000	0.90	
106 - 111	19,000	0.95	**2ml multi-dose vial or combination of two prefilled syringes (depending on ability)**
112 - 117	20,000	1.00	
118 - 122	21,000	1.05	
123 - 128	22,000	1.10	
129 - 134	23,000	1.15	
135 - 139	24,000	1.20	
140 - 145	25,000	1.25	
146 - 151	26,000	1.30	
152 - 157	27,000	1.35	
158 - 162	28,000	1.40	
163 - 168	29,000	1.45	