Dorset Medicines Advisory Group

SHARED CARE GUIDELINE FOR THE USE OF LOW MOLECULAR WEIGHT HEPARIN (LMWH) DRUGS SUCH AS DALTEPARIN (FRAGMIN®), ENOXAPARIN (CLEXANE®) OR TINZAPARIN (INNOHEP®) WITH ADULT PATIENTS

INDICATION

TREATMENT DOSES

Low molecular weight heparins (LMWHs) are indicated for the prevention of thromboembolic events in patients at increased risk e.g. post-operative, high risk pregnancies.

This shared care guideline covers the prescribing of LMWHs when used in the treatment of patients with a recently diagnosed thromboembolic disease.

Treatment with a LMWH for four weeks or less should be prescribed and monitored by the initiating physician (any indication), unless this responsibility is delegated e.g. to the anticoagulation team.

Treatment doses in the following indications have been identified to be suitable for initiation by a GP (green), or shared care (amber):

- Significantly sub-therapeutic INRs within one month of acute VTE,
- DVT in patients who are intravenous drug users
- Pregnant women with a high risk of VTE (initial doses only whilst referral to a specialist is processed)
- Treatment of superficial thrombophlebitis when treatment with warfarin is deemed inappropriate.
- Patients receiving warfarin who are at high risk for thromboembolic events and have sub-therapeutic INRs e.g. mechanical heart valves, atrial fibrillation and previous TIAs/strokes, patients who have suffered a thromboembolic event in the last 4 weeks.

This guideline does not cover:

- the use of low molecular weight heparins for the prevention of clotting in the extracorporeal circuit during haemodialysis in adults with chronic renal insufficiency.
- treatment of VTE in patients with cancer, see separate shared care guideline

Wherever possible patients should be trained and encouraged to self-administer LMWH.

If necessary seek advice from a Haematologist or the anticoagulation service. In cases of shared care all relevant information relating to the recommended dose (indication, renal function and weight) and duration of treatment should be clearly communicated between Primary and Secondary care.

PROPHYLACTIC DOSES

Prophylactic doses of LMWH should normally be prescribed by secondary care. Perioperative anticoagulation has been identified to be suitable for shared care.

Some patients require peri-operative bridging when warfarin is stopped for an operation or invasive procedure. If a LMWH is recommended, responsibility for advising the patient and informing the GP will be undertaken by the hospital team performing the procedure.

This aim is to ensure that patients are provided with consistent timely advice and treatment by professionals familiar with peri-operative anticoagulation. Patients will be attending a preoperative assessment clinic and those prescribed warfarin may be advised to switch to LMWH during the peri-operative period. The duration of alternative therapy is usually less than a week but advice will be dependent on the complexity of the surgery and underlying thromboembolic risk.

The GP and patient will be given written advice on when to stop the warfarin and what dose of LMWH to use and should ensure sufficient supplies are made available prior to surgery.

On discharge from hospital following surgery, patients will be issued with a supply of LMWH to cover the expected period until an INR in the target range is achieved or to cover a specified course length associated with the procedure e.g. 10-14 days for knee replacement surgery. Occasionally a patient may not reach therapeutic INR levels in time and so a small supply from the GP may be needed. Information on dosage will be included on the discharge summary and only a very short term supply would be necessary until this is achieved. Discharge information will also detail the durations of treatment and outline plans for restarting any routine anticoagulant or antiplatelet treatment(s).

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of LMWH can be shared between the specialist setting and the patient's GP (if different). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The clinician initiating treatment with a LMWH is also responsible for the provision of suitable sharps safety equipment to allow appropriate disposal of used syringes. Note prescribing of sharps containers on FP10 are limited to 1 litre containers.

REFERRAL AND INITIATION

Shared Care is only appropriate if it provides the optimum solution for the patient.

- Patients will only be referred to the GP once the GP has agreed in each individual case
- Patients should only be transferred to shared care once they are no longer routinely attending for treatment at the specialist service (no longer being seen on a monthly basis).
- Prescribing responsibility will only be transferred when the patient's condition is stable or predictable.
- The Consultant will communicate to the GP the reason for choice of LMWH over other anticoagulants, the specific indication for use and intended duration of treatment.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

Specialist Responsibilities	
1	Commence LMWH: • in the management of an acute VTE • for pregnant ladies at risk of a VTE or with recurrent miscarriages which is likely to be related to an underlying prothrombotic disorder (if not initiated in primary care, and maintain prescribing) • when patients on long term warfarin have sub therapeutic INRs • when patients deemed at higher risk for VTEs undertake surgery.
2	To ensure the patient is able to administer the drug as prescribed
3	To ensure there are no drug side effects or concerns regarding bleeding.
4	To ask the GP whether he or she is willing to participate in shared care. Requests to GPs should be made in writing and must include appropriate information to allow an informed decision to be made
5	To communicate promptly with the GP when treatment is changed, stopped or adjusted and to communicate changes in response to treatment or the condition itself.
6	Ensure that clear backup arrangements exist for GPs to obtain advice and support
7	To ensure the patient has sufficient supply of medication until such time as is appropriate for the GP to assume prescribing responsibility. This may include times to cover initial transfer of responsibility and/or after 3 month reviews
8	To ensure the patient / carer has given informed consent to their treatment.
9	To provide the patient / carer(s) with comprehensive advice and information about the expected side effects and their management, as well as a yellow anti-coagulant warning card and advise the patient to carry with them at all times
10	To arrange where suitable for the patient to be trained to self-administer the LMWH. The initiator should check that the patient is able and willing to comply with treatment. Advise the patient to report if they have any unexplained bruising.

11	To be available for advice if the patient's condition changes, ensuring that procedures are in place for the rapid re-referral of the patient by the GP.
12	To liaise with the GP on any suggested changes in prescribed therapy and to stop treatment where appropriate.
13	To review the patient in an outpatient appointment at least every 3 months (based on clinical need) and make suitable arrangements for long-term anticoagulation if patients are to continue treatment after 6 months of LMWH.

General Practitioner Responsibilities	
1	Reply to the request for shared care as soon as practicable
2	To kindly prescribe LMWH as outlined above as part of a shared care agreement with the hospital doctor. Where explicitly requested by the consultant to undertake platelet monitoring.
3	To refer back to the consultant if a change in the patient's clinical condition suggests that LMWH is no longer appropriate.
4	If comorbid conditions / medications instituted that may substantially affect renal function, to monitor biochemistry and refer back to consultant for advice if eGFR < 45ml/min/1.73m2 (dosing adjustments are indicated if CrCl < 30ml/min). Patients with renal impairment should have their dose determined and stabilised in secondary care, with factor Xa monitoring if appropriate, prior to shared care (re)commencing.
5	As part of the review process check to ensure that the patient is able to comply and is concordant with treatment.
6	Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
7	Report adverse events to the specialist and CSM. Advise the patient or carer to report any unexplained bruising.

Patient's role (or that of carer)	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Attend appropriate consultant and GP appointments
3	Be prepared to learn how to self-administer the injection.
4	Share any concerns in relation to treatment with LMWH.
5	Use written and other information on the medication.
6	Seek help urgently if it is suspected that LMWH is causing side effects, if they have any unexplained bruising, or if the patient is otherwise unwell.

SUPPORTING INFORMATION

Monitoring

As patient weight is used as the basis for calculating the required treatment dose, weight must be accurately recorded in kilograms (kg) in the clinical record. Patients should be weighed at the start of therapy and, where applicable, during treatment.

None required unless the baseline creatinine clearance was < 30 mls / minute or platelet count < 50 x 10^9/l where prescribing information should be checked with the summary of product characteristics for the individual preparation and where necessary a haematologist regarding the need to adjust dosing based on anti-Factor Xa activity.

Dosage and Administration

INFORMATION PROVIDED BELOW IS A SUMMARY OF DOSING REQUIREMENTS, A CLINICIAN PRESCRIBING DOSES SHOULD ENSURE THEY CONSULT THE SUMMARY OF PRODUCT CHARACTERISTICS FOR FULL DETAILS OF DOSES AND NECESSARY DOSE ADJUSTMENTS.

Dalteparin prophylactic treatment usually 5000 units by s/c injection. Therapeutic dose 200 iu/kg body weight once daily

Enoxaparin prophylactic treatment usually 40 mg by s/c injection. Therapeutic dose 1.5 mg/kg body weight once daily

Tinzaparin prophylactic treatment usually 4500 units s/c injection and therapeutic dose of 175 units/kg once daily

Contraindications

Contraindications included within the current Summary of Product Characteristic documents include:

- Hypersensitivity to either dalteparin sodium, enoxaparin, tinzaparin, heparin or derivatives
- Known bleeding disorders, e.g. haemophilia
- Thrombocytopenia, with platelet count < 50,000/mm^3 (note this figure is not universally quoted across the SPCs for the three LMWHs)
- History of heparin-induced thrombocytopenia (HIT)
- Peptic ulcer
- Recent cerebral haemorrhage
- Major / life threatening bleeding
- Severe hypertension – Systolic BP > 230 mmHg + Diastolic BP > 120mm Hg
- Severe liver disease with oesophageal varices
- Major trauma
- Recent eye, brain, spinal cord surgery
- Acute bacterial endocarditis

Cautions

All heparins can induce thrombocytopenia (low platelets) although this is significantly lower with LMWHs. In some patients this can be a benign phenomenon (Type 1 Heparin Induced Thrombocytopenia (HIT)). However, in rare patients HIT can be associated with a paradoxical increased risk of thrombosis (Type 2 HIT) which can have catastrophic consequences. Type 2 HIT is very rare and so routine screening for this is not required in any patients on prophylactic LMWH. There is a slightly increased risk (up to 1%) of Type 2 HIT in patients who have had cardiothoracic surgery with exposure to unfractionated heparin and in cancer patients when either of these groups of patients are managed with therapeutic LMWH. It is therefore recommended that these latter 2 patient groups should be screened for HIT with a baseline FBC performed and repeat on days 4 and between days 7 & 10 of therapeutic LMWH. HIT is most likely to occur between 5 and 21 days post initiation of the LMWH.

Any patient on LMWH (prophylactic or therapeutic) with a reduction in platelet count of >50% from baseline must be discussed with a consultant Haematologist. Note separate shared care guidance applicable to patients with cancer who require treatment for VTE are available.

Side effects include pain at injection sites, rarely allergic reactions, hyperkalaemia and heparin induced thrombocytopenia. Osteoporosis occurs only with prolonged use. Treatment for this should be considered where a patient presents with other risk factors and is likely to require longer term treatment with a LMWH.

Interactions

The possibility of the following interactions with LMWHs should be considered:
i) An enhancement of the anticoagulant effect by anticoagulant/antiplatelet agents e.g. aspirin/dipyridamole, GP IIb/IIIa receptor antagonists, Vitamin K antagonists, NSAIDs e.g. indometacin, cytostatics, dextran, thrombolytics, sulfinpyrazone, probenecid, and etacrynic acid.
ii) A reduction of the anticoagulant effect may occur with concomitant administration of antihistamines, cardiac glycosides, tetracycline and ascorbic acid.
Because NSAIDs and ASA analgesic/anti-inflammatory doses reduce production of vasodilatatory prostaglandins, and thereby renal blood flow and the renal excretion, particular care should be taken when administering LMWH concomitantly with NSAIDs or high dose ASA in patients with renal failure.

THIS LIST IS NOT EXHAUSTIVE. The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

Drug costs (Drug Tariff List price April 2016):

Dalteparin (Fragmin®) 5000unit syringe x10	£28.23
Enoxaparin (Clexane®) 40mg syringe x10	£30.27
Tinzaparin (Innohep®) 3500unit x10	£27.71

References

Summary of product characteristics for Dalteparin (Fragmin®) 5000unit syringes available at http://www.medicines.org.uk/emc/medicine/26896, accessed 22/4/16

Summary of product characteristics for Enoxaparin (Clexane®) syringes available at http://www.medicines.org.uk/emc/medicine/24345, accessed 22/4/16

Summary of product characteristics for Tinzaparin (Innohep®) 10,000 unit/ml syringes available at http://www.medicines.org.uk/emc/medicine/31578, accessed 22/4/16

Shared care guidelines for the prescribing of dalteparin, Salisbury NHS Foundation Trust available at: http://www.icid.salisbury.nhs.uk/MedicinesManagement/JointFormulary/Pages/SharedCareDalteparinPrescribing.aspx?UNLID=753021315201642511142O accessed 18/4/16

What is the evidence for the use of Low molecular weight heparins for the prophylaxis of travel related thrombosis? UKMi Medicines Q&A July 2014. Accessed 25/5/16 via NHS Evidence at: http://www.medicinesresources.nhs.uk/GetDocument.aspx?pageId=789669

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