Guidance for Primary Care - Low Molecular Weight Heparins (LMWH) and Fondaparinux

Aim

Support primary care prescribers in the governance and safety of initiating and/or continuing the prescribing of these agents.

Objectives

- Define the place in therapy of LMWHs and fondaparinux for primary care prescribers.
- Identify who is responsible for the initiation and continued supply (where relevant) of these agents thereby minimising confusion.
- Ensure that LMWHs are used safely and appropriately across Cambridgeshire and Peterborough Integrated Care System.

Guidance for General Practice

Prescribing Advice

Essential information, such as dose, weight, renal function, indication and duration of treatment, is communicated at transfers of care (e.g., by discharge letters) and used to ensure that future doses are safe.

A Patient Safety Alert from NHS England identified that contraindications to LMWH must be considered by healthcare professionals when prescribing, dispensing or administering this group of drugs. The alert adds that there can be various circumstances when the use of LMWHs may be contraindicated. These can include but are not limited to:

- active bleeding.
- acquired bleeding disorder (such as acute liver failure).
- concurrent use of anticoagulants known to increase risk of bleeding (e.g., warfarin, dabigatran).
- concurrent use of anti-platelets and other interacting medicines (e.g., clopidogrel, aspirin, clarithromycin).
- lumbar puncture/epidural/spinal anaesthesia within the previous four hours or expected within the next 12 hours.

A full list of contraindications for each LMWH can be found in their respective Summary of Product Characteristics.

Choice

Compared to other LMWHs, dalteparin represents better value for money. This is also the LMWH of choice used by the majority of secondary care hospitals within C&P ICS. Full prescribing information can be found in the Summary of Product Characteristics.

The place in therapy of fondaparinux is outlined in Table 2: Fondaparinux indications and responsibilities.

Patient Weight

The dose of LMWH should be calculated based on patient weight.

Do not estimate weight as it is often inaccurate and can lead to incorrect dosing.

An accurate patient weight should be obtained and recorded at first contact with primary or secondary care and throughout treatment. Reasons for not obtaining weight should be clearly documented. The exception to this is in pregnancy where a pre-pregnancy weight should be used.

The range of weighing equipment available should prevent the need for estimation in all but the most exceptional circumstances. Your weighing device should meet the requirements for clinical weighing scales.

Renal Function

The risk of bleeding may be increased when the patient has existing renal impairment. The dose should be appropriately adjusted in patients with renal impairment in accordance with the most up-to-date information in the BNF, Summary of Product Characteristics or on Consultant Haematologist advice.

Dosing and duration

Ensure the prescription dosing is correct according to the indication (see Table 3: Licensed Indications, dosage and costs for LMWH initiated by primary care prescribers).

A duration including a prescription STOP date or 'life-long' (where clinically appropriate) must be specified and documented on the prescription, and in the consultation medical notes within the GP practice.

Monitoring

Risk assessment and clinical monitoring are important predictors of the risk of potential bleeding. Reassess risk/benefit of thromboprophylaxis at regular intervals.

Full Blood Count (including platelets) and Urea & Electrolytes: Monitor on initiation of treatment with LMWH and at regular intervals thereafter, clinically appropriate;

- Thrombocytopenia, if it occurs, usually appears between the 5th and 21st day after starting therapy.
- Hyperkalaemia risk increases with duration of therapy.

In addition, in renal impairment contact Haematology for advice with regard to monitoring. Anti-Xa activity monitoring might be considered in those patients treated with LMWH who also have either an increased risk of bleeding such as those with renal impairment, elderly and extremes of weight.

References

1. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press; August 2014. Accessed 14.08.14 via electronic medicines compendium.
2. Summary of Product Characteristics. Fragmin 10,000 IU/0.4ml solution for injection, Pfizer Limited. Date last updated 16.10.13. Accessed 14.08.14 via electronic medicines compendium.
3. Summary of Product Characteristics. Fragmin 12,500 IU/0.5ml solution for injection, Pfizer Limited. Date last updated 16.10.13. Accessed 14.08.14 via electronic medicines compendium.
4. Summary of Product Characteristics. Fragmin 15,000 IU/0.6ml solution for injection, Pfizer Limited. Date last updated 16.10.13. Accessed 14.08.14 via electronic medicines compendium.
5. Summary of Product Characteristics. Fragmin 18,000 IU/0.72ml solution for injection, Pfizer Limited. Date last updated 16.10.13. Accessed 14.08.14 via electronic medicines compendium.
6. Summary of Product Characteristics. Fragmin 5,000 IU, Pfizer Limited. Date last updated 16.10.13. Accessed 14.08.14 via electronic medicines compendium.
7. NHS England. Patient Safety Alert Stage One: Warning. Harm from using low molecular weight heparins when contraindicated; 19th January 2015. Accessed 25.02.15 via the Central Alerting System.
8. Summary of Product Characteristics. Fragmin 7,500 IU/0.3ml solution for injection, Pfizer Limited. Date last updated 05.16. Accessed 26.03.20 via electronic medicines compendium.

Document Ratification Details

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Table 1: LMWH indications and responsibilities

Specialty	Indication	Duration	Initiated by	Prescribing continued by	Monitored by
Anticoagulation (in general practice)	When international normalised ratio (INR) is sub-therapeutic, ***and*** interim treatment is required (bridging) within first month of diagnosis of Venous thromboembolism (VTE). ***or*** Where VTE is suspected in general practice.	Until warfarin initiated, ***and/or*** target INR is in range. ***or*** Until a diagnosis of VTE is excluded.	GP	GP	GP
Anticoagulation (in hospital)	When INR is sub-therapeutic, ***and*** interim treatment is required (bridging) within first month of diagnosis of a VTE. ***or*** Where VTE is suspected.	Until warfarin initiated, ***and/or*** target INR is in range. ***or*** Until a diagnosis of DVT is excluded.	Hospital (up to 7 days is supplied).	Hospital	Hospital until discharge, then GP.
Obstetrics & Gynaecology	High risk pregnancy confirmed in **general practice** (VTE Prophylaxis).	Until the onset of labour and advice sought from hospital specialist to continue after birth.	GP	GP	GP
Obstetrics & Gynaecology	High risk pregnancy confirmed at **hospital** appointment (VTE Prophylaxis).	Until the onset of labour and advice sought from hospital specialist to continue after birth.	Hospital	GP	GP

Specialty	Indication	Duration	Initiated by	Prescribing continued by	Monitored by
Obstetrics & Gynaecology	Treatment of DVT / PE	Until warfarin initiated, ***and/or*** target INR is in range. ***or*** Until a diagnosis of DVT is excluded.	Hospital (up to 7 days is supplied)	Hospital	Hospital until discharge, then GP.
Oncology/ Haematology	Treatment of cancer-related VTE	Until warfarin initiated, ***and/or*** target INR is in range. ***or*** Until a diagnosis of DVT is excluded.	Hospital (up to 7 days is supplied).	Hospital	Hospital until discharge, then GP.
Oncology/ Haematology	Extended prophylaxis of cancer-related VTE	Determined by the hospital specialist, usually 6 months.	Hospital	GP	Hospital until discharge, then GP.
Orthopaedics	Prophylaxis of DVT post-surgery	28 days	Hospital	Hospital	Hospital until discharge, then GP.
Investigations	Interim treatment required (bridging) for patients taking oral anticoagulant, e.g., endoscopy, gastroscopy, biopsies, right heart catheter insertion.	Clear communication from hospital specialist specifying the number of days, patient weight, and dose.	GP	GP	GP

N.B. Some patients may require long-term LMWH because warfarin is clinically inappropriate. In these circumstances, LMWH would be initiated by the hospital and then continued by GP.

Table 2: Fondaparinux indications and responsibilities

Specialty	Indication	Duration	Initiated by	Prescribing continued by	Monitored by
Cardiology	Acute Coronary Syndrome	Maximum of 8 days or until hospital discharge	Hospital	Hospital	Hospital (until discharge)
Haematology	Heparin-induced thrombocytopenia	Determined by the hospital haematologist	Hospital	Hospital	Hospital

Table 3: Licensed Indications, dosage and costs for LMWH initiated by primary care prescribers

Indication: Treatment of VTE
LWMH: Dalteparin

Bodyweight (Kg)	Dose (Creatinine clearance ≥30 ml/min)	Frequency & Route	Cost per dose (BNF)
Less than 46	7,500 units	Once daily (single dose) subcutaneously	£4.23
46 to 56	10,000 units	Once daily (single dose) subcutaneously	£5.65
57 to 68	12,500 units	Once daily (single dose) subcutaneously	£7.06
69 to 82	15,000 units	Once daily (single dose) subcutaneously	£8.47
83 or more	18,000 units	Once daily (single dose) subcutaneously	£10.16

Note: 18,000 units is the maximum licensed dose. For patients weighing over 100kg seek specialist advice.

Indication: Extended prophylaxis of cancer-related VTE.
LWMH: Dalteparin - 1st month.
See 'Treatment of VTE' dosing table, above.

Indication: Extended prophylaxis of cancer-related VTE.
LWMH: Dalteparin - 2nd month onwards.

Bodyweight (Kg)	Dose (Creatinine clearance ≥30 ml/min)	Frequency & Route	Cost per dose (BNF)
Less than 56	7,500 units	Once daily (single dose) subcutaneously	£4.23
57 to 68	10,000 units	Once daily (single dose) subcutaneously	£5.65
69 to 82	12,500 units	Once daily (single dose) subcutaneously	£7.06
83 to 98	15,000 units	Once daily (single dose) subcutaneously	£8.47
99 or more	18,000 units	Once daily (single dose) subcutaneously	£10.16

Note: 18,000 units is the maximum licensed dose. For patients weighing over 100kg seek specialist advice.

Indication: Medical thromboprophylaxis.
LWMH: Dalteparin.

Bodyweight (Kg)	Dose (Creatinine clearance ≥30 ml/min)	Frequency & Route	Cost per dose (BNF)
N/A	5,000 units	Once daily (single dose) subcutaneously	£2.82