Bedfordshire Clinical Commissioning Group
Luton Clinical Commissioning Group

BEDFORDSHIRE AND LUTON JOINT PRESCRIBING COMMITTEE

Bulletin 242: **Low Molecular Weight Heparins (LMWHs), Fondaparinux and Novel Oral Anticoagulants – Prescribing Guidance and Responsibilities**

Aims

To support the prescribing and monitoring of treatment and prophylactic doses of LMWHs, Fondaparinux and NOACs across the primary/secondary care interface for venous thromboembolism (VTE).

To 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 LMWH, Fondaparinux and NOACs for primary care prescribers.
- Identify who is responsible for the initiation and continued supply (where relevant) of these agents thereby minimising confusion.
- Ensure that these agents are used safely and appropriately across Bedfordshire and Luton CCGs.

Low Molecular Weight Heparins (LMWHs) and Fondaparinux – Prescribing Guidance

This guidance is applicable to all health care professionals who may be involved in the prescribing, dispensing or administration of LMWH for patients in primary care.

Prescribing Advice	For treatment doses, essential information such as dose, weight, renal function, indication and duration of treatment must be communicated at transfers of care (e.g. discharge letters/information to community nursing services) and used to ensure that future doses are safe. Consult the summary of product characteristics (http://www.medicines.org.uk/emc) for full (and up to date) prescribing advice.
Choice of LMWH	Bedford and the Luton and Dunstable Hospital Hospitals use Tinzaparin for prophylaxis and treatment. The most cost-effective treatment choice for initiation in primary care is Enoxaparin (Arovi®).
Patient Weight	Ensure you are using an accurate patient weight. This 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. For pregnancy the weight 'at booking' should be used. (Significant changes in

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	weight during pregnancy may warrant a dose recalculation which would be specialist led). Do not estimate weight. It is often inaccurate and can lead to incorrect dosing. 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. A dose reduction and monitoring of factor Xa may be required or alternatively use unfractionated heparin (hospital infusion only). See individual product literature found in Summary of Product Characteristics for details. Dosing should be based on up-to-date licensing and obtained from the current BNF (http://www.evidence.nhs.uk/formulary/bnf/current) or Summary of Product Characteristics (http://www.medicines.org.uk/emc/)
Dosing and duration	Ensure the prescription dosing is correct according to the indication (Tables 2-4). Consult the summary of product characteristics (http://www.medicines.org.uk/emc) for full prescribing advice. Where a Specialist has chosen LMWH over warfarin, the reason should be communicated to the GP. Specialists from the Luton and Dunstable Hospital have advised that in some situations, the total daily dose would be split e.g. overweight patients, pregnant women, increased bleeding risk, in renal impairment. GPs would be advised of this on an individual patient basis by the Specialist team. Duration including a prescription STOP date must be specified and documented on the prescription and in the consultation medical notes within the GP practice.
Monitoring (Treatment doses)	Reference: BNF (Version 78 Sept 19- March 20): <u>Heparin-induced thrombocytopenia</u> Platelet counts should be measured just before treatment with unfractionated or low molecular weight heparin, and regular monitoring of platelet counts may be required if given for longer than 4 days. See the British Society for Haematology's Guidelines on the diagnosis and management of heparin-induced thrombocytopenia: second edition. Br J Haematol 2012; 159: 528–540. <u>Hyperkalaemia</u> Plasma-potassium concentration should be measured in patients at risk of hyperkalaemia before starting the heparin and monitored regularly thereafter, particularly if treatment is to be continued for longer than 7 days. <u>Factor Xa</u> The BNF states that routine monitoring of anti-Factor Xa activity is not usually required during treatment with LMWHs, but may be necessary in patients at risk of bleeding (e.g. in renal impairment and those who are underweight or overweight). However, t**he need to monitor Factor Xa will be assessed by the hospital Specialist. If monitoring is required, this will be secondary care led as the required tests are not always available within the primary care setting.**

Contra-Indications [12]	Circumstances when the use of LMWHs may be contraindicated 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; concurrent use of antiplatelets and other interacting medicines; or, lumbar puncture/epidural/spinal anaesthesia within the previous four hours, or expected within the next 12 hours;inherited bleeding disorder, thrombocytopenia and platelets less than 30. NB: GPs should be advised to look out for any contra-indications that may develop while the patient is receiving treatment.

Table 1. LMWH indications and Clinician Responsibilities – (Based on current Information at time of writing)

NB: In general, the information contained in the table applies to both Luton & Dunstable NHS Trust (L&D) patients and Bedford Hospital NHS Trust (BHT) patients. Where prescribing practice differs between the L&D and BHT, the specific details relating to each hospital are specified in the table below. Please note for some of the indications, there is still a degree of uncertainty with regards prescribing responsibility.

Speciality	Indication	Duration	Initiated by	Prescribing continued by	Monitored by
Oncology/Haematology	**Prophylaxis** of cancer-related VTE	Determined by the Hospital Specialist	Hospital	Hospital	Hospital
		Determined by palliative Care Specialist	Hospice	GP	GP
Oncology/Haematology *Further information on NOAC use for VTE in cancer patients	**Treatment** of cancer-related VTE	Determined by the Hospital Specialist **L&D Hospital** Specialists have indicated that this would be for a minimum of 6 months)	Hospital	Hospital where the patient is on active cancer treatment. GP where oncology patient is being managed in primary Care.	Hospital where the patient is on active cancer treatment. GP where oncology patient is being managed in primary Care.

Speciality	**Indication**	**Duration**	**Initiated by**	**<u>Prescribing continued by</u>**	**Monitored by**
Obstetrics & Gynaecology	Identified as a high risk pregnancy – VTE prophylaxis	Until the onset of labour and advice sought from hospital specialist to continue after birth	GP to initiate – on hospital advice but only for **bridging** until the patient is seen by the obstetrician	Hospital	Hospital
	Identified as an intermediate risk pregnancy –VTE prophylaxis	Until the onset of labour and advice sought from hospital specialist to continue after birth	Hospital	**L&D Patients** Hospital **Bedford Hospital Patients** GP under shared care	**L&D Patients** Hospital **Bedford Hospital Patients** GP under shared care
	Treatment of DVT/PE	Determined by the Hospital Specialist	Hospital	GP	**L&D Patients** GP with input from the Haematology/Oncology clinic **Bedford Hospital Patients** GP
Cardiology	ACS	Maximum of 8 days or until hospital discharge	Hospital	Hospital	Hospital

Speciality	Indication	Duration	Initiated by	Prescribing continued by	Monitored by
Haematology	Heparin Induced thrombocytopenia	Determined by the Consultant Haematologist	Avoid LMWH for this indication and use Fondaparinux for this group of patients.		
Anticoagulation **(Inpatient)**	When INR is sub therapeutic AND Interim treatment is required (bridging) within first month of diagnosis of a DVT[1] or PE OR Where a recurrent DVT or PE is suspected OR AF (fast AF/high stroke risk) as bridge to warfarin	Until warfarin initiated and/or target INR is in range OR Until a diagnosis of DVT is excluded	Hospital	Hospital	Hospital
	Bridging peri surgically on interrupting warfarin	Peri surgically	Hospital	Hospital	Hospital

Speciality	Indication	Duration	Initiated by	Prescribing continued by	Monitored by
Bariatric surgery	VTE prophylaxis	1 dose pre-operatively Up to 2 weeks post-operatively (depending on the surgical procedure)	L&D Hospital	L&D Hospital	L&D Hospital

Table 2. Fondaparinux indications and Clinician 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
Haematology	Heparin-induced thrombocytopenia	Determined by the hospital haematologist	Hospital	Hospital	Hospital

Table 3: Thromboprophylaxis in pregnancy (Unlicensed indication)

Dosages of LMWHs are based on weight, not on BMI. For thromboprophylaxis, the booking weight is used to guide dosing. It is also important to avoid 'dose capping' as there are no data to guide appropriate doses of LMWH for pregnant women who are obese or puerperal. The dosages below are only suggestions provided from the RCOG and doses for obese women are not evidence based.

Weight in kg (at booking) – Use accurate pre-pregnancy weight (if available) or current weight at presentation	**Tinzaparin dose (75u/kg/day)[7]**
< 50	3,500 units daily
50–90	4,500 units daily
91-130	7,000 units daily*
131-170	9,000 units daily*
>170	75 units/kg/day*
High prophylactic dose for women weighing 50 – 90 kg	4,500 units 12 hourly

Weight in kg (at booking) – Use accurate pre-pregnancy weight (if available) or current weight at presentation	**Enoxaparin dose[7]**
< 50	20mg daily
50–90	40mg daily
91-130	60mg daily*
131-170	80mg daily*
>170	0.6mg/kg/day*
High prophylactic dose for women weighing 50 – 90 kg	40mg 12 hourly

Table 4: The Luton & Dunstable NHS Trust Tinzaparin Dose Banding in Bariatric patients

Weight range	Dose
50-100kg	4500units OD
100-150kg	7000units OD
151-190kg	9000units OD
191-250kg	12000units OD
251-300kg	14000units OD

All doses are based on 50units/kg of Tinzaparin and are rounded to use the nearest whole syringe.

Table 5: Novel Oral Anticoagulants (NOACs) as an alternative to low molecular weight heparins (LMWH)

NOACs are licensed for the prevention and treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) in adults. NOACs may be considered as a therapeutic option in these clinical indications.
Note that Edoxaban and Dabigatran require at least 5 days of initial treatment with parental anticoagulation prior to the switch to oral anticoagulation. Use with caution in patients with renal impairment.

	Apixaban	**Dabigatran**	**Edoxaban**	**Rivaroxaban**
Initial treatment dose	10mg TWICE daily for 7 days	Parenteral anticoagulation for ≥ 5 days	Parenteral anticoagulation for ≥ 5 days	15mg TWICE daily for 21 days
Maintenance treatment dose	5mg TWICE daily*	150mg TWICE daily*	60mg ONCE daily*	20mg ONCE daily*
Long term secondary prevention dose	2.5mg TWICE daily*	150mg TWICE daily*	60mg ONCE daily*	20mg ONCE daily*

Prevention of VTE post elective hip and knee replacement surgery

Edoxaban, Rivaroxaban and Dabigatran are licensed for the prevention of VTE in adult patients post elective hip and knee replacement surgery.

NOAC	**Dose**
Rivaroxaban **(Used at BHT)**	10 mg once daily*
Apixaban	2.5 mg twice daily*
Dabigatran **(Used at the L&D)**	220 mg once daily*

* Dose reduction may apply – refer to SPC for further information

Adapted from: Specialist Pharmacy Services, UKMI – Comparative table of low molecular weight heparins

Should NOACs be prescribed for VTE treatment & prophylaxis in oncology patients?

Comments from LDH Macmillan Pharmacist:

- Tinzaparin is still being prescribed first line for our oncology/haematology patients.
- NOACs have only been used for a few patients due to individual circumstances (e.g. needle-phobic, initiated by another hospital).
- The L&D hospital do not have a guideline locally for using NOAC's in cancer patients yet.
- Generally see treatment dose tinzaparin being prescribed.

Comments from BHT Oncology Pharmacist:

- Oncology patients who are not undergoing treatment will be seen via the normal VTE treatment pathway (i.e. GP referral in) and would not be given Tinzaparin, probably a NOAC.

Advantages:

- Patients initiated on oral agents are at significantly lower risk to discontinue therapy relative to LMWH.
- Cost effective treatment option compared to LMWHs.
- Improved compliance compared to LMWHs particularly in needle phobic patients.
- Were more effective than LMWHs to prevent recurrent VTE.

Disadvantages:

- NOACs are not recommended if expected malabsorption in stomach or small bowel.
- There is limited data for the use of NOACs in patients with cancer-associated thrombosis. It is not recommended in any national guidelines.
- Were associated with a significantly increased risk of major bleeding as well as a trend toward more clinically relevant non major bleeding.

Transfer of Care

An internal transfer of care document was approved by the Bedfordshire and Luton Joint Prescribing committee (JPC) in April 16. For further information, please contact Jacqueline Clayton or Sandra McGroarty at the BCCG Medicine Management Team.

References:-

1. Joint Formulary Committee. British National Formulary (online) London: BMJ Group and Pharmaceutical Press; accessed Jan 2020 https://bnf.nice.org.uk/drug/
2. Bedfordshire and Luton Joint Prescribing Committee, Shared Care Guideline for Low Molecular Weight Heparin (LMWH) Use In Obstetric Venous Thromboembolism Prophylaxis – Intermediate Risk Patients Treated At Bedford Hospital Only, approved Feb 14. http://www.gpref.bedfordshire.nhs.uk/referrals/bedfordshire-and-luton-joint-prescribing-committee- (jpc).aspx

3. NHS England Patient Safety Alert (January 2015): Harm from using Low Molecular Weight Heparins when contraindicated. http://www.england.nhs.uk/2015/01/19/psa-heparins/ viewed Jan 2020
4. Chemist and Druggist, January 2020
5. Comparative table of low molecular weight heparins https://www.sps.nhs.uk/articles/comparative-table-of-low-molecular-weight-heparins/ Viewed January 2020
6. Direct oral anticoagulant (DOAC) versus low-molecular-weight heparin (LMWH) for treatment of cancer associated thrombosis (CAT): A systematic review and meta-analysis. https://www.ncbi.nlm.nih.gov/pubmed/29506866 viewed January 2020