

**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 – June 2018**

PATIENT'S NAME:

PATIENT'S ADDRESS:

HOSPITAL NAME AND NUMBER / NHS NUMBER:

CONSULTANT'S NAME:

GP's NAME:

**What are key elements of the process to ensure good shared care arrangements are in place?**

- It is imperative that the GP is contacted to discuss shared care arrangements **before** treatment is commenced to ensure that they are willing to jointly manage the patient's therapy.
- It is reasonable to expect the hospital clinician to prescribe if the patient will have to regularly attend hospital for specialist monitoring.
- In addition, CCG policies on clinical effectiveness should be adhered to.
- The general practitioner should have sufficient information on the drug to either allow them to monitor the patient's response to therapy and adjust dosages as required or know in what circumstances they should refer the patient back to the hospital clinician.
- Where the hospital clinician retains responsibility for monitoring drug therapy or making dosage adjustments, the general practitioner must be informed of any dose changes as soon as possible to avoid an incorrect dose being administered. Similarly if the GP changes the patient's medication then the hospital clinician involved in the shared care agreement should be informed of any changes that the GP undertakes.
- If a GP is unhappy to participate in a shared care agreement, the CCG should be asked for assistance in facilitating suitable prescribing arrangements for the patient.
- Informing the patient's usual community pharmacist of the medication will help ensure that supplies are available.
- **N.B.** – The Healthcare Professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

<b>Hospital Specialist Responsibilities:</b>	<b>GP Responsibilities:</b>	<b>Midwife Responsibilities</b>
Initial risk assessment of patient. Provide RCOG patient information leaflet regarding risk assessment	Inform hospital specialist of accurate pre-pregnancy weight (if available) or current weight at presentation.	Identification of intermediate/high risk patients at antenatal booking appointment – refer to Hospital Specialist.

and prophylaxis for VTE in pregnancy.		
Initiation of prescribing (28 days) in accordance with shared care guideline. Supply sharps container. (Patients should be asked to return the container to the hospital Obstetric clinic {not Pharmacy} for disposal when full {for replacement} or when no longer needed).	Take over prescribing in accordance with shared care guideline after 28 days. Ensure that patient has ongoing supplies of replacement sharps containers as necessary.	Monitoring patient during routine ante-natal and postnatal appointments.
Ensure that patient is trained in self-administration of subcutaneous low molecular weight heparin.	Seek advice, if necessary, from Specialist if starting a potentially interacting therapy.	Monitor the patient for any side-effects to the LMWH therapy and inform the GP if any occur. Report any serious side-effects to the MHRA.
Undertake agreed baseline monitoring including:- <ul style="list-style-type: none"> <li>weighing patient prior to initiation of LMWH if necessary (Pre-pregnancy weight {if available} or weight at presentation to be provided by GP)</li> <li>FBC</li> </ul>	Monitor the patient for any side-effects to the LMWH therapy and inform the Specialist if any occur. Report any serious side-effects to the MHRA.	Monitor patient during routine ante-natal appointments.
Ask GP to participate in shared care and provide Shared Care Guideline to GP. The shared care guideline will provide details of the patient risk assessment, patient weight, dosage, details of any blood tests undertaken (with dates) expected duration of the LMWH therapy.	Refer back to Specialist service – e.g. additional risk factors developing which would result in patient in need of management by specialist service, adverse drug reaction, suspected deterioration in renal or hepatic function.	
Undertake monitoring of potassium levels, if this becomes necessary.		
Monitor the patient for any side-effects to the LMWH therapy and inform the GP if any occur. Report any serious side-effects to the MHRA.		
Decide when to stop therapy		

**Patient's Responsibilities:**

Discuss potential benefits and side-effects of treatment with the Specialist and GP or Midwife and share any concerns that they have in relation to their treatment.

To report any side-effects to the Specialist and GP or Midwife.

To attend regular antenatal and postnatal appointments at the hospital and GP/Community midwife as agreed.

To inform Specialist/GP/Midwife/Pharmacist of all medicines (including OTC preparations) that the patient is currently taking.

To participate in the monitoring of therapy (including having blood tests carried out at agreed intervals).

**BACK-UP ADVICE AND SUPPORT – CONTACT DETAILS:**

**Bedford Hospital: Pharmacy Medicines Information Department – 01234 792175**

**References:**

1. Electronic British National Formulary, October 2012, accessed 08/11/12, 23/3/13, Jan 2014, May 2018. (<https://bnf.nice.org.uk/>)
2. Summary of Product Characteristics for Clexane® (Enoxaparin), 28/4/17. <https://www.medicines.org.uk/emc/product/4499/smpc>, accessed May 2018.
3. Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism, NICE Guideline 89, March 18 National Institute for Health and Care Excellence. <https://www.nice.org.uk/guidance/ng89>
4. Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium, Green-top Guideline No 37a, Royal College of Obstetricians & Gynaecologists (RCOG), April 2015. <https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf>
5. Summary of Product Characteristics for Innohep Syringe 10,000 IU/ml (Tinzaparin), and Tinzaparin Sodium Syringe 10,000 IU/ml, 7/3/17, accessed May 2018 <https://www.medicines.org.uk/emc/product/2022> ; <https://www.medicines.org.uk/emc/product/3633>
6. Prevention and treatment of Venous Thromboembolism in pregnancy and the puerperium, Clinical Guideline, Bedford Hospital, August 2017.
7. British Society for Haematology's Guidelines on the diagnosis and management of heparin-induced thrombocytopenia; second edition. Br J Haematol 2012; 159: 528-540. (<https://onlinelibrary.wiley.com/doi/epdf/10.1111/bjh.12059>).

## **Introduction/Overview**

Low molecular weight heparins (LMWHs) include the following preparations: Dalteparin (Fragmin®), Enoxaparin (Clexane®, Enoxaparin Becat®, Inhixa®), and Tinzaparin (Innohep®). They are used to prevent and treat venous thromboembolism and to treat acute coronary syndromes. **Use in pregnancy is an unlicensed indication**, but is recommended by both NICE and the Royal College of Obstetricians and Gynaecologists (RCOG).

## **Bedford Hospital uses both Enoxaparin and Tinzaparin for venous thromboembolism (VTE) prophylaxis in pregnancy. Prescribing information on both products is included in the shared care guideline (Appendices 1 and 2).**

The BNF advises that heparins are used for the management of venous thromboembolism in pregnancy because they do not cross the placenta. LMWHs are increasingly preferred to unfractionated heparin for thromboprophylaxis because they have a lower risk of osteoporosis and of heparin-induced thrombocytopenia. Treatment should be stopped at the onset of labour and will be reassessed postnatally.

## **Risk Assessment/Scope of Shared Care Protocol**

As the absolute risk of VTE in pregnancy is low, some form of risk stratification is required to decide which women warrant pharmacological thromboprophylaxis. The threshold for recommending postpartum thromboprophylaxis is lower because the risk/day is higher and the duration of risk is shorter.

The JPC (September 12) agreed to support the production of shared care guidelines in principle for intermediate risk patients. Specialists would be asked to clarify the patients who would fall into the 'intermediate risk' category.

'High risk' patients require specialist management by experts in haemostasis and pregnancy and therefore should be under the care of the hospital Obstetric Haematology team (or equivalent) for the duration of their pregnancy.

## **VTE prophylaxis for this group of patients is therefore excluded from this shared care guideline.**

Postpartum patients are not included in the shared care arrangements at the LMWH treatment (either 7 days or 6 weeks) should be provided by the hospital under current contractual arrangements.

## **Criteria for Patient Selection:**

### **Bedford Hospital**

Patient will be assessed at booking, 28 and 36 weeks and repeated if admitted. The criteria for patient selection is outlined in appendix 3. **(N.B.** Not all patients assessed as immediate risk receive this treatment).

Patients assessed as 'high' risk of VTE will be under the care of a consultant obstetrician and are therefore not suitable for shared care. This would include patients with poor renal function (creatinine clearance  $\leq 30$ ml/min).

### **Baseline Monitoring Requirements (at booking)**

Record patient's weight in Kg where necessary (accurate pre-pregnancy weight or weight at presentation to be provided by the GP).

Check platelet count as part of routine full blood count (FBC).

### **Ongoing Monitoring**<sup>1,,4,7</sup>

The BNF states that the standard prophylactic regimen does not require anticoagulant monitoring. The BNF also states that regular monitoring of platelet counts **may** be required if given for longer than 4 days and refers to the British Society for Haematology's Guidelines on the diagnosis and management of heparin-induced thrombocytopenia. These guidelines state that medical patients and obstetric patients receiving heparin do not need routine platelet monitoring. The RCOG Guidelines state that it is only necessary to monitor the platelet count if the woman has had prior exposure to unfractionated heparin.

### **Stopping Criteria**

All women on LMWH should be advised to omit the daily injection and seek advice from their midwife or doctor if there is any bleeding or if labour begins.

### **Referral back to Specialist Criteria**

Refer back to Specialist service – e.g. additional risk factors developing which would result in patient in need of management by specialist service. E.g. bleeding (especially PV), adverse drug reaction, impaired renal or hepatic function.

Seek advice, if necessary, from Specialist if starting a potentially interacting therapy.

**Appendix 1**

**Enoxaparin Fact Sheet** <sup>1,2</sup> – (N.B. Please consult current BNF and Summary of Product Characteristics for full prescribing information)

<https://bnf.nice.org.uk/>

<https://www.medicines.org.uk/emc>

**Description of product and available preparations**

Available as solution for injection of, enoxaparin sodium as pre-filled syringes as follows:-

20 mg in 0.2 ml; 40 mg in 0.4 ml; 60mg in 0.6 ml; 80 mg in 0.8 ml; 100 mg in 1.0 ml; 120mg in 0.8 ml; 150mg in 1.0 ml.

(The use of the multidose vial is not included in the shared care as it contains the preservative benzylalcohol which should not be given to pregnant women, premature babies or neonates).

**NB.** A number of product brands are available.

**Indication (unlicensed)**

For the prophylaxis of venous thromboembolism in pregnancy.

**Dosage and administration**

Enoxaparin should be administered when the patient is lying down by deep subcutaneous injection. The administration should be alternated between the left and right anterolateral or posterolateral abdominal wall. The whole length of the needle should be introduced vertically into the skin fold held between the thumb and index finger. The skin fold should not be released until the injection is complete. Once the plunger is fully pressed down the safety device is activated automatically and this protects the used needle.

Patients should be advised to follow instructions provided in the patient information leaflet included in the pack of this medicine.

Dosages of LMWH are based on weight, not BMI. For thromboprophylaxis, the booking weight is used to guide dosing. There is no data to guide appropriate doses of LMWH for obese pregnant or puerperal women. The dosages below are only suggestions provided from the RCOG and doses for women who are obese are not evidence based.<sup>4</sup>

Weight in kg (at booking) – Use accurate pre-pregnancy weight (if available) or current weight at presentation	Enoxaparin dose <sup>4</sup>
< 50	20mg daily
50–90	40mg daily
91-130	60mg daily*
131-170	80mg daily*
>170	0.6mg/kg/day*
High prophylactic (intermediate) dose for women weighing 50 – 90 kg	40mg 12 hourly

\*may be given in two divided doses

### **Dosage adjustment – renal impairment:-**

**Severe renal impairment** (creatinine clearance or eGFR < 30 ml/min) – **excluded from shared care**

**Moderate** (creatinine clearance 30-50 ml/min) **or mild** (creatinine clearance 50-80 ml/min) **renal impairment** – No dosage adjustments recommended but careful clinical monitoring is advised.

### **Contraindications (Source – Summary of Product Characteristics/eBNF)**

Acute bacterial endocarditis; after major trauma; epidural anaesthesia with treatment doses; haemophilia and other haemorrhagic disorders; peptic ulcer; recent cerebral haemorrhage; recent surgery to eye; recent surgery to nervous system; severe hypertension; spinal anaesthesia with treatment doses; thrombocytopenia (including history of heparin-induced thrombocytopenia); Hypersensitivity to enoxaparin sodium, heparin or its derivatives, including other low molecular weight heparins (LMWH) or to any of the excipients; Active clinically significant bleeding and conditions with a high risk of haemorrhage; Spinal or epidural anaesthesia or loco-regional anaesthesia when enoxaparin sodium is used for treatment in the previous 24 hours.

### **Contraindications (Source – Advice from Secondary Care Specialists)**

LMWH should be avoided, discontinued or postponed in women who are at risk of bleeding after careful consideration of the balance of risks of bleeding and clotting. Risk factors for bleeding are:

- Women with active antenatal or postpartum bleeding
- Women considered at increased risk of major haemorrhage
- Women with bleeding disorders, such as von Willebrand's disease, haemophilia or acquired coagulopathy
- Women with thrombocytopenia (platelet count less than  $75 \times 10^9$ )
- Acute stroke in the last 4 weeks (ischaemic or haemorrhagic)
- Severe renal disease (GFR less than 30ml/minute/1.73m<sup>2</sup>)
- Severe liver disease (prothrombin time above normal range or known varices)
- Uncontrolled hypertension (blood pressure greater than 200mmHg systolic or greater than 120mmHg diastolic)

### **Precautions**

- LMWHs should not be used interchangeably.
- Use with extreme caution in patients with a history (>100 days) of heparin-induced thrombocytopenia without circulating antibodies.
- Low body weight (Increased risk of bleeding).
- Elderly
- Pregnant women with mechanical prosthetic heart valves - The use of enoxaparin sodium for thromboprophylaxis in pregnant women with mechanical prosthetic heart valves has not been adequately studied. In a clinical study of pregnant women with mechanical prosthetic heart valves given enoxaparin sodium (100 IU/kg (1 mg/kg ) twice daily) to reduce the risk of thromboembolism, 2 of 8 women developed clots resulting in blockage of the valve and leading to maternal and foetal death. There have been isolated post-marketing reports of valve thrombosis in pregnant women with mechanical prosthetic heart valves while receiving enoxaparin sodium for

thromboprophylaxis. Pregnant women with mechanical prosthetic heart valves may be at higher risk for thromboembolism.

- Hepatic impairment – use with caution due to an increased potential for bleeding.
- Hyperkalaemia - Heparins can suppress adrenal secretion of aldosterone leading to hyperkalaemia, particularly in patients such as those with diabetes mellitus, chronic renal failure, pre-existing metabolic acidosis, taking medicinal products known to increase potassium. 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.
- Enoxaparin injection, as with any other anticoagulant, should be used with caution in conditions with increased potential for bleeding.
- There have been cases of neuraxial haematomas reported with the concurrent use of enoxaparin sodium and spinal/epidural anaesthesia or spinal procedures resulting in long term or permanent paralysis. These events are rare with enoxaparin sodium dosage regimens 4,000 IU (40mg) once daily or lower. The risk of these events is higher with the use of post-operative indwelling epidural catheters, with the concomitant use of additional drugs affecting haemostasis such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), with traumatic or repeated epidural or spinal puncture, or in patients with a history of spinal surgery or spinal deformity.

### **Side-effects**

#### **Rare**

Alopecia (on prolonged use); anaphylaxis; angioedema; hyperkalaemia; hypersensitivity reactions; injection-site reactions; osteoporosis (risk lower with low molecular weight heparins); priapism; rebound hyperlipidaemia (following unfractionated heparin withdrawal); skin necrosis; urticaria

#### **Frequency not known**

Haemorrhage; thrombocytopenia

### **Side-effects, further information**

#### **Haemorrhage**

If haemorrhage occurs it is usually sufficient to withdraw unfractionated or low molecular weight heparin, but if rapid reversal of the effects of the heparin is required, protamine sulfate is a specific antidote (but only partially reverses the effects of low molecular weight heparins).

#### **Heparin-induced thrombocytopenia**

Clinically important heparin-induced thrombocytopenia is immune-mediated and does not usually develop until after 5–10 days; it can be complicated by thrombosis.

Signs of heparin-induced thrombocytopenia include a 30% reduction of platelet count, thrombosis, or skin allergy. If heparin-induced thrombocytopenia is strongly suspected or confirmed, the heparin should be stopped and an alternative anticoagulant, such as danaparoid, should be given. Ensure platelet counts return to normal range in those who require warfarin.

### **Drug Interactions**

#### **Concomitant use not recommended:**

- *Medicinal products affecting haemostasis*

It is recommended that some agents which affect haemostasis should be discontinued prior to enoxaparin sodium therapy unless strictly indicated. If the combination is indicated, enoxaparin sodium should be used with careful clinical and laboratory monitoring when appropriate. These agents include medicinal products such as:

- Systemic salicylates, acetylsalicylic acid at anti-inflammatory doses, and NSAIDs including ketorolac,
- Other thrombolytics (e.g. alteplase, reteplase, streptokinase, tenecteplase, urokinase) and anticoagulants.

**Concomitant use with caution:**

The following medicinal products may be administered with caution concomitantly with enoxaparin sodium:

*Other medicinal products affecting haemostasis such as:*

- Platelet aggregation inhibitors including acetylsalicylic acid used at antiaggregant dose (cardioprotection), clopidogrel, ticlopidine, and glycoprotein IIb/IIIa antagonists indicated in acute coronary syndrome due to the risk of bleeding,
- Dextran 40,
- Systemic glucocorticoids.

• *Medicinal products increasing potassium levels:*

Medicinal products that increase serum potassium levels may be administered concurrently with enoxaparin sodium under careful clinical and laboratory monitoring.

**See also – detailed drug interaction information in the BNF -**

**<https://bnf.nice.org.uk/interaction/enoxaparin.html>**

### **Breast Feeding**

RCOG recommends that LMWHs are safe when breastfeeding. This is classified as a category A recommendation, i.e. at least one meta-analysis, systemic reviews or randomised controlled trial rated as 1++, and directly applicable to the target population; or A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results.<sup>4</sup>

### **Prescribing and dispensing information**

Enoxaparin sodium is a biological medicine. Biological medicines must be prescribed and dispensed by brand name.

### **Special Precautions for disposal and other handling**

Disposal in sharps container.

**Appendix 2**

**Tinzaparin Fact Sheet <sup>1,5</sup> – (N.B. Please consult current BNF and Summary of Product Characteristics for full prescribing information)**

<https://bnf.nice.org.uk/>

<https://www.medicines.org.uk/emc>

**Description of product and available preparations**

Available as a solution for injection of tinzaparin sodium 10,000 anti-Factor Xa IU/ml as follows:-A prefilled unit dose syringe with needle safety device containing: 2,500 anti-Factor Xa IU in 0.25 ml; 3,500 anti-Factor Xa IU in 0.35 ml; 4,500 anti-Factor Xa IU in 0.45 ml (N.B. The use of Innohep® multi-dose vial formulations are not included in the shared care guideline as they contain the preservative benzyl alcohol which should not be given to pregnant women, premature babies or neonates)

**Indication (unlicensed)**

For the prophylaxis of venous thromboembolism in pregnancy.

**Dosage and administration**

Administration is by subcutaneous injection when given as prophylaxis of thromboembolic events in adults. This can be done in abdominal skin, the outer side of the thigh, lower back, upper leg or upper arm. Do not inject in the area around the navel, near scars or in wounds.

For abdominal injections, the patient should be in a supine position, alternating the injections between the left and right side. The air-bubble within the syringe should not be removed. During the injection, the skin should be held in a fold.

Dosages of LMWH are based on weight, not BMI. For thromboprophylaxis, the booking weight is used to guide dosing. There no data to guide appropriate doses of LMWH for regnant obese or puerperal women. The dosages below are only suggestions provided from the RCOG and doses for women who are obese are not evidence based. <sup>4</sup>

Weight in kg (at booking) – Use accurate pre-pregnancy weight (if available) or current weight at presentation	Tinzaparin dose (75u/kg/day) <sup>4</sup>
< 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 (intermediate) dose for women weighing 50 – 90 kg	4,500 units 12 hourly

\*may be given in two divided doses

**Dosage adjustment – renal impairment:-**

Risk of bleeding may be increased; monitoring of anti-Factor Xa may be required if eGFR less than 30 mL/minute/1.73 m<sup>2</sup>; dose reduction may be required if eGFR less than

20 mL/minute/1.73 m<sup>2</sup>; unfractionated heparin may be preferable. **Patients with this degree of renal impairment are excluded from shared care.**

### **Contraindications (Source – Summary of Product Characteristics/eBNF)**

Acute bacterial endocarditis; after major trauma; epidural anaesthesia with treatment doses; haemophilia and other haemorrhagic disorders; peptic ulcer; recent cerebral haemorrhage; recent surgery to eye; recent surgery to nervous system; severe hypertension; spinal anaesthesia with treatment doses; thrombocytopenia (including history of heparin-induced thrombocytopenia)

Hypersensitivity to the active substance or to any of the excipients; Active major haemorrhage or conditions predisposing to major haemorrhage. Major haemorrhage is defined as fulfilling any one of these three criteria: a) occurs in a critical area or organ (e.g. intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, intra-uterine or intramuscular with compartment syndrome), b) causes a fall in haemoglobin level of 20 g/L (1.24 mmol/L) or more, or c) leads to transfusion of 2 or more units of whole blood or red blood cells;

### **Contraindications (Source – Advice from Secondary Care Specialists)**

LMWH should be avoided, discontinued or postponed in women who are at risk of bleeding after careful consideration of the balance of risks of bleeding and clotting. Risk factors for bleeding are:

- Women with active antenatal or postpartum bleeding
- Women considered at increased risk of major haemorrhage
- Women with bleeding disorders, such as von Willebrand's disease, haemophilia or acquired coagulopathy
- Women with thrombocytopenia (platelet count less than  $75 \times 10^9$ )
- Acute stroke in the last 4 weeks (ischaemic or haemorrhagic)
- Severe renal disease (GFR less than 30ml/minute/1.73m<sup>2</sup>)
- Severe liver disease (prothrombin time above normal range or known varices)
- Uncontrolled hypertension (blood pressure greater than 200mmHg systolic or greater than 120mmHg diastolic)

### **Precautions**

- LMWHs should not be used interchangeably.
- Elderly
- Caution is advised when administering tinzaparin sodium to patients at risk of haemorrhage.
- Tinzaparin sodium must be discontinued in patients who develop immune-mediated heparin-induced thrombocytopenia (type II).
- Hyperkalaemia - Heparin products can suppress adrenal secretion of aldosterone, leading to hyperkalaemia. Risk factors include diabetes mellitus, chronic renal failure, pre-existing metabolic acidosis, raised plasma potassium at pre-treatment, concomitant therapy with drugs that may elevate plasma potassium, and long-term use of tinzaparin sodium. In patients at risk, potassium levels should be measured before starting tinzaparin sodium and monitored regularly thereafter.
- Pregnant women with prosthetic heart valves - Therapeutic failures and maternal death have been reported in pregnant women with prosthetic heart valves on full anti-coagulant doses of tinzaparin sodium and other low molecular weight heparins. In the

absence of clear dosing, efficacy and safety information in this circumstance, tinzaparin sodium is not recommended for use in pregnant women with prosthetic heart valves.

- Caution is advised when performing neuraxial anaesthesia or lumbar puncture in patients receiving prophylactic doses of tinzaparin sodium due to the risk of spinal haematomas resulting in prolonged or permanent paralysis. Epidural anaesthesia in pregnant women should always be delayed until at least 24 hours after administration of the last treatment dose of tinzaparin sodium. Prophylactic doses may be used as long as a minimum delay of 12 hours is allowed between the last administration of tinzaparin sodium and the needle or catheter placement.

### **Side-effects**

**Uncommon** - headache

### **Rare**

Alopecia (on prolonged use); anaphylaxis; angioedema; hyperkalaemia; hypersensitivity reactions; injection-site reactions; osteoporosis (risk lower with low molecular weight heparins); priapism; rebound hyperlipidaemia (following unfractionated heparin withdrawal); skin necrosis; urticarial

### **Frequency not known**

Haemorrhage; thrombocytopenia

### **Side-effects, further information**

#### **Haemorrhage**

If haemorrhage occurs it is usually sufficient to withdraw unfractionated or low molecular weight heparin, but if rapid reversal of the effects of the heparin is required, protamine sulfate is a specific antidote (but only partially reverses the effects of low molecular weight heparins).

#### **Heparin-induced thrombocytopenia**

Clinically important heparin-induced thrombocytopenia is immune-mediated and does not usually develop until after 5–10 days; it can be complicated by thrombosis.

Signs of heparin-induced thrombocytopenia include a 30% reduction of platelet count, thrombosis, or skin allergy. If heparin-induced thrombocytopenia is strongly suspected or confirmed, the heparin should be stopped and an alternative anticoagulant, such as danaparoid, should be given. Ensure platelet counts return to normal range in those who require warfarin.

### **Drug Interactions**

The anticoagulant effect of tinzaparin sodium may be enhanced by other drugs affecting the coagulation system, such as those inhibiting platelet function (e.g. acetylsalicylic acid and other non-steroidal anti-inflammatory drugs), thrombolytic agents, vitamin K antagonists, activated protein C, direct factor Xa and IIa inhibitors. Such combinations should be avoided or carefully monitored.

**See also – detailed drug interaction information in the BNF -**

**<https://bnf.nice.org.uk/interaction/tinzaparin.html>**

### **Breast Feeding**

RCOG recommends that LMWHs are safe when breastfeeding. This is classified as a category A recommendation, i.e. at least one meta-analysis, systemic reviews or randomised controlled trial rated as 1++, and directly applicable to the target population; or A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results.<sup>4</sup>

### **Prescribing and dispensing information**<sup>1</sup>

Tinzaparin sodium is a biological medicine. Biological medicines must be prescribed and dispensed by brand name.

### **Special Precautions for disposal and other handling**

Disposal in sharps container.

Dear Dr

**Venous Thromboembolism Prophylaxis in Pregnancy – Enoxaparin/Tinzaparin\***

Your patient..... (NHS No..... DoB.....) has been prescribed **Clexane® (Enoxaparin) / Innohep® (Tinzaparin)\*** at a dose of .....**once/twice** daily for venous thromboembolism prophylaxis during pregnancy and was given a 28 day supply of treatment on .....

Patient's weight (kg) at booking - .....  
Results of any blood tests (FBC/Renal function) with dates.....

Risk Assessment attached

Please find attached a copy of the Bedfordshire and Luton Joint Prescribing Committee Shared Care Guideline for 'low molecular weight heparin use in obstetric venous thromboembolism prophylaxis – intermediate risk patients only'.

You are being asked to share care with **Bedford hospital** and in particular to provide ongoing enoxaparin / tinzaparin\* prescriptions for the patient until labour starts.

The patient will be seen at the hospital antenatal clinic.....

If you are aware of any reason your patient should not be on heparins please inform me urgently.

Thank you for your assistance.

Yours sincerely

\* Delete as appropriate. **Please prescribe the LMWH by brand name.**

.....  
...  
...

**Venous Thromboembolism Prophylaxis in Pregnancy – Clexane® (Enoxaparin)/ Innohep® (Tinzaparin)\***

I can confirm that I am/am not\* willing to participate in shared care arrangements for the provision of Venous thromboembolism prophylaxis in pregnancy for:

**Patient's name** .....

NHS No.....

DoB.....

**GP name** (please print).....

**GP signature**.....**Date**.....

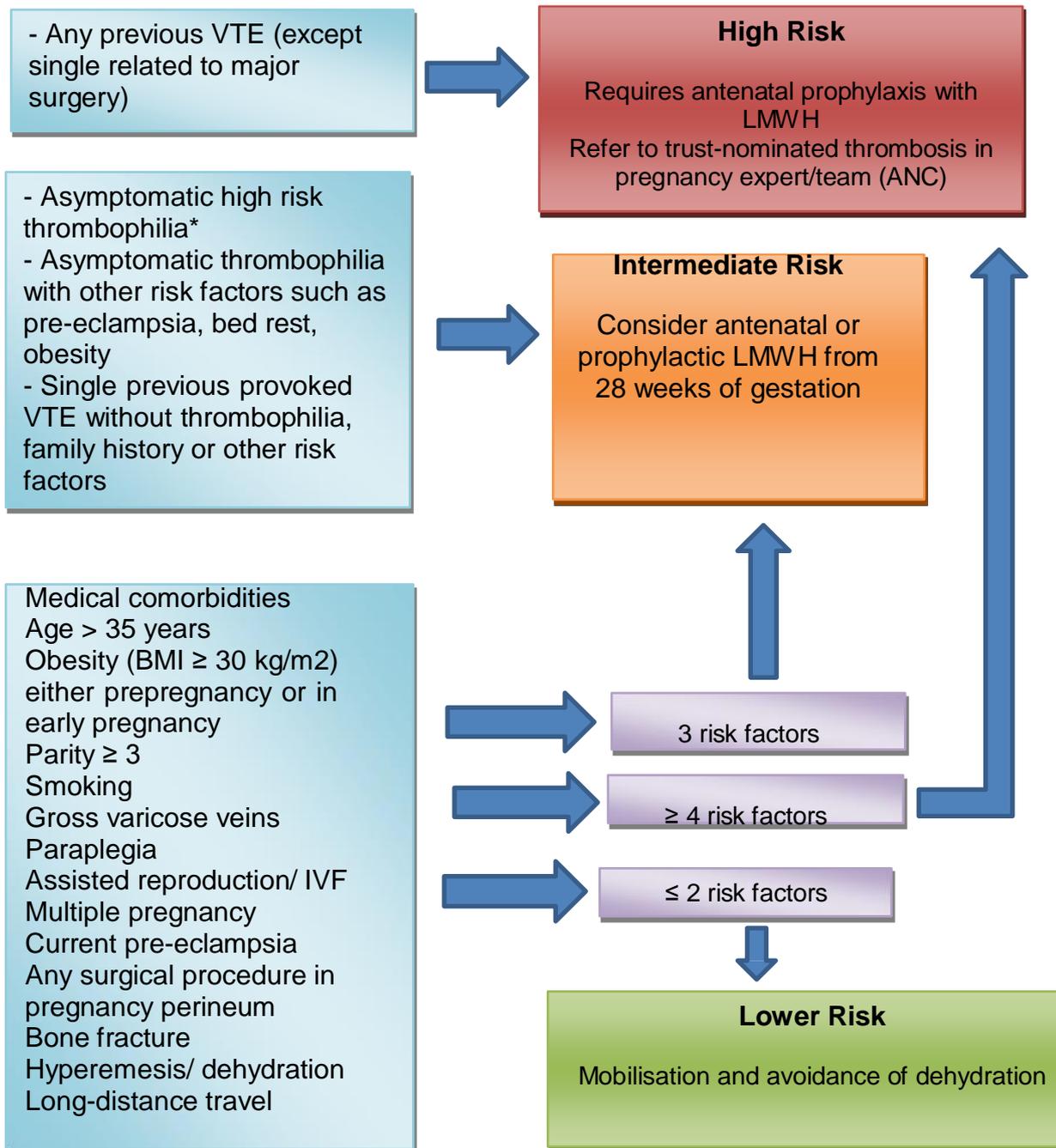
Please return to.....

\*Delete as appropriate. **Please prescribe the LMWH by brand name.**

## VTE ASSESSMENT AND MANAGEMENT

### Antenatal assessment and management

(To be assessed at booking, 28 and 36 weeks and repeated if admitted)



#### Key

BMI = body mass index (based on booking weight), gross varicose veins = symptomatic, above the knee or associated with phlebitis/oedema/skin changes, immobility = ≥ 3 days, LMWH = low-molecular-weight heparin, V = intra-venous, long distance travel = > 4 hours, VTE = venous thromboembolism