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Guideline for the Management of Obstetric Thromboprophylaxis

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1 INTRODUCTION / BACKGROUND

Thrombosis and thrombo-embolism remain the leading direct cause of maternal mortality in pregnancy, childbirth and the puerperium accounting for 1.39 deaths per100, 000 maternities in the UK[1].

Terms:

Low Molecular Weight Heparin	LMWH
Unfractionated Heparin	UFH
Direct oral anticoagulants (DOACs)	DOACs
Venous thromboembolism	VTE
Anti-embolism stockings	AES
Intermittent compression devices	ICDs

2 SCOPE OF GUIDELINE

This guideline applies to all clinical staff.

The purpose of this guideline is to ensure the correct thromboprophylaxis is used during and after pregnancy, as guided by national recommendations: RCOG Green-top Guideline: Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium[2] and NICE guidance: Venous thromboembolism: reducing the risk for patients in hospital[3].

3 DUTIES & RESPONSIBILITIES

Designated Lead for Risk
The Clinical director is responsible for implementing this guideline; this role has been delegated to the Designated Lead for Risk. It is the responsibility of the Clinical Directors, or their delegates, to ensure that all relevant staff under their management (including bank agency, contracted, locum and volunteers) are aware of and meet their individual responsibilities under this Guideline, including monitoring compliance by subordinate staff.

Clinical Staff
All clinical staff have a duty to be familiar with this guideline and to use it to guide their practice.

Local Policy Officer
The Local Policy Officer has a duty to ensure this guideline is compliant with the Trust Guideline on Policies. The Local Policy Officer must ensure this guideline is reviewed within the designated time period or as changes in national guidance arise. The guideline should comply with the current base of evidence and best practice guidance and be current and in date.

4 SUBJECT MATTER OF GUIDELINE

General considerations:

All women should undergo a documented assessment of risk factors for VTE at booking.

Risk assessment should be repeated if the woman is admitted to hospital for any reason or develops other intercurrent problems.

Risk assessment should be repeated again intrapartum or immediately postpartum.

All women will be provided with written information about VTE risk assessment and prevention via Badgernet (Mat Notes). Verbal information will also be provided by clinicians.

These guidelines apply to all pregnant women, and to women who have delivered or had a miscarriage or termination of pregnancy within the last 6 weeks.

4.1 Antenatal Booking Risk Assessment

- All women should have a VTE risk assessment undertaken and during the booking appointment (see appendix A). The VTE risk assessment should be undertaken as part of the SMART Booking Antenatal Assessment on Badgernet.
- **If a woman scores 4** or more on this risk assessment (high risk), she should be considered for LMWH as soon as possible (and she is likely to continue LMWH upto 6 weeks postnantally)
  If a woman scores 3 (intermediate risk of VTE), she should be considered for LMWH from 28 weeks of pregnancy (and she is likely to continue LMWH upto 6 weeks postnantally).
  The community midwife undertaking the risk assessment should contact the Antenatal Clinic to arrange a consultant appointment **as soon as possible for high risk women** and **between 22-24weeks for intermediate risk women**, using the Antenatal Referral Pathway SOP.
- All women who score intermediate or high risk for VTE should be under consultant led care.

Specific considerations for prophylaxis:

Risk stratification of women who have had a single previous VTE:		
Single VTE was:	related to major surgery from which they have recovered and no other risk factors	LMWH from 28 weeks and for 6 weeks postpartum
	associated with antithrombin	Higher dose LMWH (either 50%, 75% or full treatment dose) (see Appendix B) antenatally

	deficiency or APS* *see section below	and for 6 weeks postpartum or until returned to oral anticoagulant therapy after delivery.
	• unprovoked/idiopathic • related to estrogen (estrogen-containing contraception/pregnancy) • related to a transient risk factor other than major surgery • who have other risk factors	Thromboprophylaxis with LMWH throughout the antenatal period.

4.1a Heritable and Acquired Thrombophilia associated VTE:

Heritable thrombophilia:

Antithrombin III deficiency: the woman should be offered thromboprophylaxis with higher dose LMWH (either 50%, 75% or full treatment dose) (see Appendix B) antenatally and for 6 weeks postpartum or until returned to oral anticoagulant therapy after delivery.

Management should be undertaken in collaboration with a haematologist with expertise in thrombosis in pregnancy and consideration given to antenatal anti-Xa monitoring and the potential for antithrombin replacement at initiation of labour or prior to caesarean section

If anti-Xa levels are measured, a test that does not use exogenous antithrombin should be used and 4-hour peak levels of 0.5–1.0 iu/ml aimed for.

Other heritable thrombophilic defects are lower risk and can be managed with standard doses of thromboprophylaxis.

Acquired thrombophilia

Women with VTE associated with the **antiphospholipid syndrome (APS)** (who will often be on long- term oral anticoagulation) should be offered thromboprophylaxis with higher dose LMWH (either 50%, 75% or full treatment dose) (see Appendix B) antenatally and for 6 weeks postpartum or until returned to oral anticoagulant therapy after delivery.

Pregnant women with APS and prior VTE or arterial thromboses should be managed in collaboration with a haematologist and/or rheumatologist with expertise in this area and the woman should be referred to a Consultant Hematologist and Consultant Rheumatologist during her pregnancy.

4.1b Previous recurrent VTE

Advice regarding doses of LMWH in pregnancy should be sought from Consultant Hematologist with expertise in haemostasis and pregnancy.Some women with previous recurrent VTE require higher doses of LMWH.

Women on long-term warfarin or other oral anticoagulants should be counselled about the risks of these agents to the fetus and advised to stop their oral anticoagulant therapy and change to LMWH as soon as pregnancy is confirmed, ideally within 2 weeks of the missed period and before the sixth week of pregnancy.

Women not on warfarin or other oral anticoagulants should be advised to start LMWH as soon as they have a positive pregnancy test.

4.1c Testing for thrombophilia in pregnant women with prior VTE:

Prior to testing for thrombophilia, women should be counselled regarding the implications for themselves and family members of a positive or negative result. Women with a family history of VTE and either antithrombin deficiency or where the specific thrombophilia has not been detected should be tested for antithrombin deficiency.

4.1d Asymptomatic Heritable and Acquired thrombophilia

Women should be stratified according to level of risk associated with their thrombophilia and the presence or absence of a family history or other risk factors. See Appendix A for risk assessment associated with heritable thrombophilia.

Antiphospholipid antibodies

Persistent antiphospholipid antibodies (lupus anticoagulant and/or anticardiolipin and/or β_2-glycoprotein 1 antibodies) in women without previous VTE should be considered as a risk factor for thrombosis (see Appendix A) such that if she has other risk factors she may be considered for antenatal or postnatal thromboprophylaxis as above.

Women with positive antiphospholipid serology and recurrent pregnancy loss will usually be managed with prophylactic LMWH throughout pregnancy.

4.2 Risk Assessment on Antenatal Admission

The process is outlined in appendix C.

On admission to hospital for any indication, women should have a VTE risk assessment (appendix A). All women admitted in the antenatal period should be offered thromboprophylaxis with LMWH, once a risk assessment is undertaken to determine whether there are any contraindications to LMWH (Appendix C). This should be documented on Badgernet.

If prophylactic LMWH is to be used, it should be commenced within 14 hours of risk assessment.

Particular care should be taken to carry out risk assessments on pregnant women who are admitted on gynaecology wards (e.g. for hyperemesis or ovarian hyperstimulation syndrome) or other medical wards.

4.3 Interruption of Thromboprophylaxis

Women receiving antenatal thromboprophylaxis should be advised to stop taking it in the following situations described below:

Vaginal Bleeding

If women experience vaginal bleeding, they should be advised to stop taking thromboprophylaxis immediately and to contact the maternity unit. They should subsequently be advised to attend the maternity department, where they should be assessed and further doses, if required, prescribed by medical staff

Induction of Labour
Thromboprophylaxis should be discontinued on admission for induction of labour. Women should be advised to omit the dose of LMWH on the day of admission for induction of labour and wear anti embolic devices (TED Stockings®) instead.

Labour
Women should be advised to stop taking low weight molecular heparin if they experience contractions and believe that they are going into labour.

Regional Anaesthesia
Regional anaesthesia should be avoided until at least 12 hours a prophylactic dose of low molecular weight heparin.
For women on doses of low molecular weight heparin higher than standard prophylactic doses (either intermediate or full treatment dose) regional anaesthesia should be avoided for 24 hours after the last dose.

Low molecular weight heparin should not be given for 4 hours after administration of spinal anaesthesia or after removal of the epidural catheter
The epidural catheter should not be removed within 12 hours of the most recent injection of low weight molecular heparin.

Elective Caesarean Section (and other elective surgical procedures)
Women receiving antenatal low weight molecular heparin should be advised to have a dose the day prior to delivery, and on the day of delivery, omit the morning dose.

Women who have had to stop their prophylactic LMWH for an elective surgery, should have their surgery scheduled for a morning list as much as possible practically.
The first thromboprophylactic dose should be administered 4 hours following delivery if regional anaesthesia is used (provided haemostasis is secure).
The first thromboprophylactic dose can be administered 4-8 hours after delivery if a general anaesthetic was given (provided haemostasis is secure).

Vaginal delivery

Women who have had to stop their prophylactic LMWH because of labour, should restart the thromboprophylactic dose 4 – 8 hours after delivery

Women at risk of worsening complications with LMWH
Women at high risk of haemorrhage with risk factors including major antepartum haemorrhage, coagulopathy, progressive wound haematoma, suspected intra-abdominal bleeding and postpartum haemorrhage may be managed with anti-embolism stockings (AES) or intermittent compression devices (ICDs 'Flowtrons'). Unfractionated heparin (UFH) may also be considered.
Pharmacological thromboprophylaxis should be started or reinstituted as soon as the immediate risk of haemorrhage is reduced.

4.4 Risk Assessment following Delivery

A postnatal thromboprophylaxis risk assessment, should be undertaken following delivery, at 24 hours of admission, at 72 hours of admission and at any readmission. This should be documented on Badgernet using the VTE/Thromboprophylaxis form and selecting Type as Postnatal.

Women should be prescribed thromboprophylaxis as indicated in the risk assessment (Appendix D).

Thromboprophylaxis should be continued for 6 weeks in high-risk women and for 10 days in intermediate-risk women.

In general mechanical prophylaxis is only used for patients who cannot receive pharmacological prophylaxis (see below). The exception to this is women hospitalised post caesarean section or other surgery, and felt to be particularly high risk for VTE (> 4 risk factors antenatally, > 2 risk factors post natally, or with significantly reduced mobility for 3 or more days). These women should be considered for combined prophylaxis with LMWH and intermittent compression devices in the absence of contraindications.

4.5 Management of women with contraindications to Low Molecular Weight Heparin

Where women are hospitalised and have contraindications to low molecular weight heparin, anti-embolism stockings (AES) should be fitted. Where women require and receive thromboprophylaxis, AES are not required (but see section 8 for exception).

Use and monitoring of AES should be as per the main Trust VTE Policy.

4.6 Choice and dosage of drugs for Thromboprophylaxis:

LMWHs are the agents of choice for antenatal and postnatal thromboprophylaxis and thromboprophylaxis should be prescribed as per Appendix D.

Doses of LMWH are based on weight. For thromboprophylaxis the booking or most recent weight
can be used to guide dosing. Doses of LMWH should be reduced in women with renal impairment.

Dalteparin is the LMWH that is stocked at RSCH.

Other forms of low molecular weight are not stocked by the hospital. Should women who have been prescribed other forms of low molecular weight heparin, such as clexane®, should be advised to either bring in their own stock of medication or should be advised to start receiving fragmin® instead.

It is only necessary to monitor the platelet count if the woman has had prior exposure to unfractionated heparin (UFH).

Monitoring of anti-Xa levels is not required when LMWH is used for thromboprophylaxis.

LMWH is safe in breastfeeding.

Unfractionated heparin(UFH)

In women at very high risk of thrombosis **UFH** may be used peripartum in preference to LMWH where there is an increased risk of haemorrhage or where regional anaesthetic techniques may be required.
If UFH is used after caesarean section (or other surgery), the platelet count should be monitored every 2–3 days from days 4–14 or until heparin is stopped.

The benefits of UFH are that it has a shorter half-life than LMWH and there is more complete reversal of its activity by protamine sulfate.

So, for example, if no LMWH has been given for 24 hours but the woman has not yet delivered and there is concern about delaying further doses of anticoagulants, a prophylactic dose of 5000 iu subcutaneously of UFH could be used and repeated every 12 hours until LMWH can be resumed after delivery.

The required interval between a prophylactic dose of UFH and regional analgesia or anaesthesia is less (4 hours) than with LMWH (12 hours) and there is less concern regarding neuraxial haematomas with UFH.Any exposure to UFH is associated with an increased risk of heparin induced thrombocytopenia (HIT).

Low-dose aspirin

Aspirin is not recommended for thromboprophylaxis in obstetric patients.

Warfarin

Warfarin in pregnancy is associated an increased risk of congenital abnormalities including a characteristic warfarin embryopathy (hypoplasia of nasal bridge, congenital heart defects, ventriculomegaly, agenesis of the corpus callosum, stippled epiphyses) in approximately 5% of fetuses exposed between 6 and 12 weeks of gestation. This incidence is dose-dependent with a higher incidence in women taking greater than 5 mg/ day. Other reported complications associated with warfarin therapy during pregnancy include an increase in the risk of spontaneous miscarriage, stillbirth,neurological problems in the baby and fetal and maternal haemorrhage.

Warfarin use in pregnancy is restricted to the few situations where heparin is considered unsuitable, e.g. some women with mechanical heart valves.

Women receiving long-term anticoagulation with warfarin can be converted from LMWH to warfarin postpartum usually 5–7 days after delivery, to minimise the risk of haemorrhage during the overlap of LMWH and warfarin.

Warfarin is safe in breastfeeding.

Other drugs for thromboprophylaxis:

Danaparoid and Fondaparinux should be in conjunction with a consultant haematologist with
expertise in haemostasis and pregnancy.

Dextran should be avoided antenatally and intrapartum because of the risk of anaphylactoid reaction.

Oral thrombin and Xa inhibitors - Direct oral anticoagulants (DOACs) should be avoided in pregnant women. Use of DOACs is not currently recommended in women who are breastfeeding.

5 TRAINING

All midwifery staff will receive training on thromboprophylaxis on the annual Maternity Update day and Preceptorship/Orientation Day. Refer to Training policy for further information. The regime is included in LFG Junior Doctors' Training Handbook as part of the trust medical Induction program.

6 IMPLEMENTATION

The implementation of this guideline will be monitored as below.

7 REVIEW, RATIFICATION AND ARCHIVING

The guideline will be reviewed every 3 years or earlier if national guideline or guidance changes are required to be considered. The review will then be subject to review and re-ratification.

The Central Policy Officer or Local Policy Officer is responsible for ensuring that archive copies of superseded working documents are retained in accordance with the Records Management: NHS Code of Practice, 2009. (Refer to Policy Development and Management: including policies, procedures, protocols, guidelines, pathways and other procedural documents)

8 MONITORING

Minimum requirement	Monitoring Process	Monitoring/ implementing Job title(s)	frequency of the monitoring	Name of responsible committee	Monitoring/ implementing committee (s)
that is to be monitored	e.g. review of incidents/ audit/ performance management	of individual(s) responsible for the monitoring and for developing action plan	(Minimum)	(that is responsible for review of the results and of the action plan)	of individual(s)/ committee responsible for monitoring implementation of the action plan
Title					
Compliance with Antenatal Booking VTE Risk Assessment	Audit/data obtained through Badgernet	Audit Midwife	Annual	Maternity Quality & Safety	Maternity Quality & Safety
Compliance with Antenatal Inpatient VTE Risk Assessment	Audit/data obtained through Badgernet	Audit Midwife	Annual	Maternity Quality & Safety	Maternity Quality & Safety
Compliance with Postnatal/after delivery VTE Risk Assessment	Audit/data obtained through Badgernet	Audit Midwife	Annual	Maternity Quality & Safety	Maternity Quality & Safety

9 DISSEMINATION AND PUBLICATION

- Circulated to all Matrons and Consultants and junior doctors via email.
- Included in LFG Junior Doctors' Training Handbook as part of Induction program.
- Circulated to the Local Policy officer for publishing the document on the Department policy library on the shared drive.
- Circulated to the Central Policy officer for publishing the document on the Trust's Central Library (intranet).

10 EQUALITY IMPACT ANALYSIS

The author of this guideline has undertaken an Equality Impact Analysis and has concluded there is no impact identified. The Equality Analysis Initial Screening has been archived and is available via the Central Policy Officer.

11 ASSOCIATED DOCUMENTS

NHSLA (2011) Maternity Clinical Risk Management Standards

12 REFERENCES

1. Knight M et al, on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014-16. Oxford: National Perinatal
2. Epidemiology Unit, University of Oxford 2018
3. Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium; RCOG Green-top Guidleine No. 37a April 2015
4. NICE guidance: Venous thromboembolism: reducing the risk for patients in hospitalClinical guideline [CG92] Published date: 27 January 2010 Last updated: 01 June 2015

13 APPENDICES

Appendix A: Venous Thromboembolism Risk Assessment at Booking

Risk Factors	Score
Previous VTE (except a single event related to a major surgery)	4
Previous VTE provoked by major surgery	3
High Risk Thrombophilia (no VTE)* • Antithrombin deficiency** • protein C or S deficiency • compound heterozygote or homozygous Factor V Leiden • antiphospholipid syndrome** *Thrombophilia and previous h/o VTE – see Appendix B ** will need to be on anticoagulation throughout pregnancy and requires high dose LMWH, see Appendix B	3
Low-risk thrombophilia (no VTE) * • heterozygous for Factor V Leiden • prothrombin G20210A mutation (MTHFR gene mutation is not an indication by itself for thromboprophylaxis)	1
Medical Comorbidities e.g. cancer, heart failure, active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease, nephrotic syndrome, Type 1 Diabetes with nephropathy, sickle cell disease, current intravenous drug user	Score 3 for each factor
Family history of unprovoked or oestrogen-related VTE in first- degree relative.	1
Age ≥35 years	1
Obesity ≥30	1
Obesity ≥ 40	2
Parity ≥ 3	1
Smoker	1
Gross Varicose Veins – above knee or associated with phlebitis, oedema or skin changes	1
Current pre-eclampsia	1
Multiple Pregnancy	1
Transient risk factors	
Assisted reproductive technology/ IVF (first trimester only)	1
Ovarian Hyperstimulation Syndrome (first trimester only)	4
Hyperemesis	3
Any surgical procedure in pregnancy e.g. appendicectomy	3
Current systemic infection	1
Immobility (> 3days), dehydration	1
Total score ☐ If ≥ 4 advise thromboprophylaxis from 1st trimester until delivery If 3 advise thromboprophylaxis from 28/40 until delivery Postnatal risk assessment to be completed after delivery	

Appendix B: Prophylactic Dosage of Dalteparin

Weight at booking or most recent weight	Dose of dalteparin (Fragmin)
< 50kg	2500 units daily
50 – 90kg	5000 units daily
91 – 130kg	7500 units daily
131 – 170kg	10,000 units daily
>170kg	75 units/kg/day units daily or 37.5units/kg/day units twice a day
Very High risk of thrombosis:	
• Antithrombin deficiency • Previous VTE on long-term oral anticoagulant therapy • Antiphospholipid syndrome with previous VTE	Antenatal **high-dose** LMWH* and at least 6 weeks' postnatal LMWH or until switched back to oral anticoagulant therapy
*High prophylactic dose for women weighing 50 - 90kg	5000 units 12hrly

Unfractionated Heparin:

In women at very high risk of thrombosis **UFH** may be used peripartum in preference to LMWH where there is an increased risk of haemorrhage or where regional anaesthetic techniques may be required.

For example, if no LMWH has been given for 24 hours but the woman has not yet delivered and there is concern about delaying further doses of anticoagulants, a prophylactic dose of 5000 iu subcutaneously of UFH could be used and repeated every 12 hours until LMWH can be resumed after delivery.

The required interval between a prophylactic dose of UFH and regional analgesia or anaesthesia is less (4 hours) than with LMWH (12 hours)

Contraindications to LMWH

- Known hypersensitivity to dalteparin or other low molecular weight heparins
- Active antenatal or postpartum bleeding
- Women at risk of major haemorrhage (e.g. placenta praevia)
- Known bleeding disorder (e.g. haemophilia, von Willebrand's disease, acquired coagulopathy
- Thrombocytopenia(platelets <75 x 10^9/l)
- Acute stroke in the last 4 weeks (ischemic or haemorrhagic)
- Severe renal disease (GFR<30ml/min/1.73m^2)
- Severe liver disease (Prothrombin time > normal range, known varices)
- Uncontrolled hypertension (blood pressure >200mmHg systolic or >120mmHg diastolic)

Renal disease

Lower doses of dalteparin and monitoring of plasma anti-Xa may be necessary if the

creatinine clearance is less than 30 ml/minute.
(equates to a serum creatinine of about 200 µmol/l for a 30-year-old woman weighing 70 kg). Seek specialist advice from the haematologist in this situation

Appendix C: Venous Thromboemebolism Risk Assessment Tool and Management Plan for Antenatal Admissions

All women who are admitted in the antenatal period should have a risk assessment performed for VTE (appendix A). Prophylactic LMWH should be offered to all women admitted in the antenatal period unless contraindicated.

1. Are there any **contraindications or cautions** to Low Molecular Weight Heparin (LMWH) use?
• In active or latent phase of labour • Induction of Labour • Known hypersensitivity to dalteparin or other low molecular weight heparins • Active antenatal or postpartum bleeding • Women at risk of major haemorrhage (e.g. placenta praevia) • Known bleeding disorder (e.g. haemophilia, von Willebrand's disease, acquired coagulopathy • Thrombocytopenia(platelets <75 x 10^9/l) • Acute stroke in the last 4 weeks (ischemic or haemorrhagic) • Severe renal disease (GFR<30ml/min/1.73m^2) • Severe liver disease (Prothrombin time > normal range, known varices) • Uncontrolled hypertension (blood pressure >200mmHg systolic or >120mmHg diastolic)

Findings	Action
No contraindications or cautions listed above	Prescribe thromboprophylaxis (see Appendix B for dosage of Dalteparin)
Patient has the following contraindications or cautions: • Known hypersensitivity to heparin/ LMWH • Active bleeding • Active or latent phase of labour • Induction of labour	- Do not prescribe thromboprophylaxis - Ensure patient is fitted TED stockings
Patient has the following contraindications or cautions: • Known bleeding disorder e.g. haemophilia, von Willebrand's disease or acquired coagulopathy • Thrombocytopenia (platelet count <75x10^9/l) • Women considered at increased risk of major haemorrhage (e.g. placenta praevia) • Active stroke in previous 4 weeks • Severe renal disease (glomerular filtrate rate<30ml/minute/1.73m^2) • Severe liver disease (prothrombin time above normal range or known varices) • Uncontrolled hypertension (BP >200mmHg systolic or >120mmHg diastolic)	- Request senior obstetric review of patient with regards to thromboprophylaxis - Ensure patient is fitted TED stockings

3. Discharge Assessment: to be completed by the obstetrician prior to discharge
Has the patient been diagnosed with pre- eclampsia or had any surgical procedure
If yes, Obstetrician to repeat 'VTE risk assessment at Booking' and prescribe appropriate thromboprophylaxis (Appendix A)

Appendix D: Venous Thromboemebolism Risk Assessment for Postnatal Women

A postnatal thromboprophylaxis risk assessment should be undertaken following delivery (1), at 24 hours of admission (2), at 72 hours of admission (3) and at any readmission (4)

Risk factors	1	2	3	4
Any Previous VTE				
Anyone requiring antenatal thromboprophylaxis				
High Risk Thrombophilia (Antithrombin III deficiency, protein C or S deficiency, compound heterozygote or homozygous Factor V Leiden, antiphospholipid syndrome)				
Low risk thrombophilia and family history of VTE				

→ HIGH RISK

6 weeks prophylactic Dalteparin and TEDs + / - ICDs if surgical

Caesarean Section in Labour				
BMI ≥ 40kg/m^2				
Readmission or Prolonged Admission (≥3 days)				
Any surgical procedure in the puerperium except immediate repair of the perineum				
Medical comorbidities e.g. cancer, heart failure, active SLE, IBD or inflammatory polyarthropathy, nephrotic syndrome, Type 1 Diabetes with nephropathy, sickle cell disease, current IV drug user				

→ INTERMEDIATE RISK

10 days prophylactic Dalteparin and TEDs + / - ICDs if surgical
If 3 or more additional risk factors, for 6 weeks prophylactic Dalteparin

↓

Age > 35 years				
BMI ≥ 30kg/m^2				
Parity ≥ 3				
Smoker				
Elective Caesarean Section				
Family history of VTE				
Low risk thrombophilia				
Gross varicose veins				
Current systemic infection				
Immobility e.g. paraplegia, SPD, long distance travel (>4 hours)				
Pre-eclampsia				
Multiple pregnancy				
Preterm delivery <37 weeks in this pregnancy				
Stillbirth in this pregnancy				
Mid-cavity rotational operative delivery				
Prolonged labour (>24 hours)				
Postpartum Haemorrhage >1L or blood transfusion				
Overall assessment:				

→ HIGH RISK

4 or more risk factors - 6 weeks prophylactic Dalteparin and TEDs + / - ICDs if surgical

→ INTERMEDIATE RISK

2 or more risk factors - 10 days prophylactic Dalteparin and TEDs + / - ICDs if surgical

→ LOW RISK

0 OR 1 risk factor – encourage mobilisation and avoid dehydration

Bleeding risk assessment:
-Known hypersensitivity to dalteparin or other low molecular weight heparins
-Active postpartum bleeding
-Known bleeding disorder (e.g. haemophilia, von Willebrand's disease, acquired coagulopathy
-Thrombocytopenia(platelets <75 x 10^9/l)
-Acute stroke in the last 4 weeks (ischemic or haemorrhagic)
-Severe renal disease (GFR<30ml/min/1.73m^2)

High Intermediate Low No risk factors other than pregnancy				

COVID 19 – anticoagulation and thromboprophylaxis

Version 2.2; 15.7.20. Review date: max 3 months.

Dr Matthew Rogers, Consultant Haematologist, Royal Surrey County Hospital. Developed in collaboration with ITU and GIM clinicians.

This information is for guidance only, and should not replace clinical judgment.

Due to the rapidly changing clinical situation and evidence base, it is likely that this action card will be updated frequently. Please check back regularly.

Venous thromboembolism (VTE) prophylaxis

Consistent VTE prophylaxis is particularly essential for COVID 19 patients – all patients hospitalised with COVID 19 would be counted "high risk" for VTE.

Contraindications to dalteparin prophylaxis have been revised for COVID 19 patients ONLY:

- Thrombocytopaenia. Dalteparin prophylaxis can be given down to a platelet count of **30,** provided there is no evidence of bleeding or concern that the patient is high risk for bleeding[1,5].
- Abnormal clotting tests should NOT be regarded as a contraindication to dalteparin prophylaxis, provided there is no evidence of bleeding or concern that the patient is high risk for bleeding.

Dosing of dalteparin for VTE prophylaxis in patients with COVID 19

This is a controversial area. Available guidelines support the use of standard doses of dalteparin prophylaxis (as in yellow drug charts)[1,2,8].

However, many clinicians caring for patients with COVID 19 feel that, given the high incidence of VTE in these patients, prophylactic doses of dalteparin should be increased for the sickest patients. Although trials are still ongoing, many UK trusts have adopted this practice pending results of trials.

Accepting this uncertainty, the following is a suggestion which accords with a recent international guideline[8] and guidance commissioned by NHS England[9]. This should not replace clinical judgment. A senior clinician (consultant / SpR) should be involved in the decision.

1. Standard prophylactic doses (as per yellow drug chart) as a minimum for all patients without contraindications or high risk for bleeding.

2. For critically ill patients, consider escalated prophylactic doses as below, provided platelets > 50 and not at high risk for bleeding.

Body weight	"Escalated" prophylactic dalteparin dose
Less than 46	2,500 twice daily
46-120	5,000 twice daily
121-150	7,500 twice daily
More than 150	10,000 twice daily

Cons / SpR decision. Critically ill patients could include:

i. Patients requiring intensive care
ii. Patients requiring CPAP

Escalated prophylactic doses of dalteparin for critically ill patients:

Patients on escalated doses whose clinical condition improves to the point of only requiring level 1 care should be considered for de-escalation back to standard prophylactic doses[9].

Dalteparin prophylaxis in renal impairment:

Doses of 5000 units daily or less can be used in all patients, regardless of renal function. Doses higher than 5000 units once daily should be used with caution in patients with Cr Cl < 20mls/min. If higher doses are felt to be required, anti Xa levels should be checked after 3 days (level taken 4 hours post dose – ensure full anticoagulant and timing details provided to lab). Results can be difficult to interpret, and haematology can be contacted for advice. As a guide: expected range for **standard** prophylaxis 0.2-0.4; expected range for **therapeutic** dose 0.5-1.

Mechanical prophylaxis

Intermittent pneumatic compression devices should be used **in addition** to dalteparin in completely immobilised patients, in the absence of contraindications.

If pharmacological prophylaxis contraindicated, ensure mechanical prophylaxis prescribed in the absence of contraindications.

Post-discharge prophylaxis[8]

All patients admitted COVID patients for whom it will be possible for dalteparin to be administered by the patient or a family member, consider discharge with **4 weeks of dalteparin at standard prophylactic doses (as in yellow drug chart)** – provided no contraindication or high bleeding risk.

If dalteparin administration will not be possible, for patients felt to be at high thrombotic risk (e.g. ongoing poor mobility, previous VTE) 4 weeks of prophylactic apixaban (2.5mg bd) can

be considered in the absence of bleeding risk. Check renal function and drug interactions carefully. This is unlicensed use, which should be discussed with the patient.

VTE prophylaxis for pregnant women (including up to 6 weeks post-partum)

All pregnant women who are COVID positive, who are admitted to hospital for any reason (including delivery), should receive dalteparin prophylaxis throughout their hospital stay unless contraindicated (but postpone first dose if birth expected within 12 hours of admission[7]).

Prophylactic dalteparin should continue for a minimum of 10 days post discharge, in the absence of contraindications[7]. Consideration should be given to extending this for up to 6 weeks post-partum for women with significant ongoing morbidity[7].

Standard prophylactic dalteparin doses in pregnancy differ slightly from those in the yellow drug charts. They can be found in the VTE quick reference guide available in the SPACE portal.

Critically ill women: any critically ill pregnant patient being considered for "escalated prophylaxis" should be the subject of careful MDT discussion involving medical and obstetric teams.

Pregnant Outpatients: COVID-19 infection should be considered as a transient risk factor and prompt a reassessment of VTE risk. Women self-isolating at home should be considered for dalteparin prophylaxis while unwell on a case-by-case basis. This should continue until recovery (generally 7-14 days).[7]

VTE Treatment

Dalteparin

Use dalteparin as initial first line treatment where suitable (may have anti-inflammatory action, with some suggestion of reduced mortality in COVID 19 patients treated with heparin[2]. Also fewer drug interactions than DOACs). Standard dosing is once daily. Consider splitting daily dose in half and giving bd if perceived high bleeding risk.

Doses below differ from current trust guidelines in order to provide more consistent anticoagulation in patients of high body weight, and with renal impairment.

These doses do NOT apply in pregnancy. For pregnant women, continue to use doses as per VTE quick reference guide on trust desktop.

Therapeutic dosing of Dalteparin - use **ACTUAL** body weight[3]

Standard dosing:

Body weight (kg)	Dose of dalteparin
Less than 46	7,500 units once daily
46-56	10,000 units once daily
57-68	12,500 units once daily
69-82	15,000 units once daily
83-98	18,000 units once daily
99-112	10,000 units twice daily
113-137	12,500 units twice daily
138-165	15,000 units twice daily
166 or more	18,000 units twice daily

(N.B. single doses should not exceed 18,000 units)

Therapeutic dosing in renal impairment (Creatinine clearance < 20 mls/min)[3]

Use doses below. Patients should have a peak anti Xa level checked after at least 3 days (citrate tube drawn 4 hours after dose. Ensure full anticoagulant and sample timing details provided to lab on request form). Discuss results with haematology: usual range about 1 unit/mL if given once daily (range 0.5-1.5), 0.5-1 if given twice daily. For patients on renal replacement therapy in ITU, unfractionated heparin is preferred.

Body weight (kg)	Dose of dalteparin
Under 46	5,000 units daily
46-56	6,500 units daily*
57-68	8,500 units daily*
69-82	10,000 units daily
83-98	12,500 units daily
99-112	15,000 units daily
113-137	18,000 units daily
138-165	10,000 units twice daily
166 or more	12,500 units twice daily

(* No pre-filled syringe available for this dose. Graduated syringes containing 10,000 units/mL are available)

Unfractionated Heparin

Unfractionated heparin (UFH) may be preferred if:

- Perceived high risk of bleeding
- Frequent need for procedures / lines (UFH can be stopped quickly)
- Severe renal impairment (e.g. renal replacement therapy)

UFH requires close monitoring, so in general should only be used in a high dependency setting.

Monitoring / dosing

The high levels of coagulation factors in some COVID 19 patients means that APTTR-based dosing may underestimate the anticoagulation intensity of UFH. Monitoring / dosing of UFH for COVID patients should therefore be via an anti Xa-based nomogram (see appendix).

It is crucial to provide accurate anticoagulant details to the lab when requesting Xa levels so the correctly calibrated test is run (specify “unfractionated heparin”).

Anticoagulant “failure”

This is a clinical diagnosis - evidence of new / progressive / worsening thrombosis despite anticoagulation.

Please discuss individual cases with haematology.

Always consider:

- Is anticoagulant dose correct for weight?
- Have all doses been administered?
- Check platelet count and consider heparin-induced thromboctyopaenia (HIT). See guidance on SPACE portal (section 2.18: The Management of Heparin Induced Thrombocytopaenia) and discuss with haematology. HIT should be considered of the platelet count falls by 30% or more, even if it is still in the normal range.

Patients on dalteparin: increase dose by 25-30%. Split dose in half and give bd. Anti Xa level measurement is NOT required if this dose increase is clinically effective.

Patients on unfractionated heparin: review monitoring records. Has anti Xa been consistently in range? If it has, consider switch to anticoagulant with a different mechanism of action e.g. argatroban in case low antithrombin levels (ITU only, unlicensed use. Dosing regime available on SPACE portal: section 2.18 The Management of Heparin Induced Thrombocytopaenia. Use regime for critically ill patients). Antithrombin levels can be measured, but results take several days.

References

1. Hunt B, Retter A, McClintock C. 2020. Practical guidance for the prevention of thrombosis and management of coagulopathy and disseminated intravascular coagulation of patients infected with COVID-19. Available at: https://thrombosisuk.org/covid-19-thrombosis.php. Accessed 16.4.2020
2. Bikdeli B *et al* 2020. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-up. J Am Coll Cardiol. Epublished DOI:10.1016/j.jacc.2020.04.031
3. Thachil, J. (2020), The versatile heparin in COVID‐19. J Thromb Haemost. Accepted Author Manuscript. doi:10.1111/jth.14821
4. Curry N, Collins, M. Treatment of venous thromboembolism (VTE) in adults with dalteparin (Fragmin®). Oxford University Hospitals Medicines Information Leaflet Volume 2 no 2, May 2019.
5. Oxford University Hospitals NHS Foundation Trust. Interim OUHFT thromboprophylaxis guidance for patients with suspected or proven COVID-19. Version 1, 22.4.2020
6. St George's Hospital: Management of thrombotic risk during the COVID-19 epidemic. Version 4, 18.4.2020
7. Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) Infection in Pregnancy. Information for Health Professionals Version 10.1: Published Friday 19 June 2020
8. Spyropoulos, A.C., et al. (2020), Scientific and Standardization Committee Communication: Clinical Guidance on the Diagnosis, Prevention and Treatment of Venous Thromboembolism in Hospitalized Patients with COVID‐19. J Thromb Haemost. Accepted Author Manuscript. doi:10.1111/jth.14929
9. Faculty of Intensive Care Medicine / Royal College of Physicians. Clinical guide for the prevention, detection and management of thromboembolic disease in patients with COVID-19. June 2020. Available at https://icmanaesthesiacovid-19.org/clinical-guide-prevention-detection-and-management-of-vte-in-patients-with-covid-19. Accessed 15.7.20

Sample nomogram for dosing unfractionated heparin by anti Xa levels.

Bolus: 80 units/kg (using total body weight), Maximum = 10,000 units

Initial infusion rate: 18 units/kg/hr (using total body weight), Maximum = 2000 units/hr

Check anti Xa level after 6 hours, and adjust as below.

Anti-factor Xa activity (IU/mL)	Response
0.00 to 0.09	Bolus 25 units/kg Increase infusion by 3 units/kg/hr Repeat assay in 6 hours
0.10 to 0.19	Increase infusion by 2 units/kg/hr Repeat assay in 6 hours
0.20 to 0.29	Increase infusion by 1 unit/kg/hr Repeat assay in 6 hours
0.30 to 0.7	NO CHANGE (within therapeutic range) Repeat assay in 6 hours Once therapeutic for two assays, may change to once daily assays
0.71 to 0.79	Decrease infusion by 1 unit/kg/hr Repeat assay in 6 hours
0.80 to 0.89	STOP INFUSION for 1 hour, then decrease by 2 units/kg/hr Repeat assay 6 hours after restarting the infusion
0.90 to 0.99	STOP INFUSION for 1 hour, then decrease by 3 units/kg/hr Repeat assay 6 hours after restarting the infusion
1.00 to 1.09	STOP INFUSION for 2 hours, then decrease by 4 units/kg/hr Repeat assay 6 hours after restarting the infusion
≥1.10	STOP INFUSION for 2 hours, then decrease by 5 units/kg/hr and notify clinician Repeat assay 6 hours after restarting the infusion

From Hull *et al*. Heparin and LMW heparin: Dosing and adverse effects. UptoDate, 2019. Accessed 17.4.2020