66FM.3 COVID-19 VENOUS THROMBOEMBOLISM PREVENTION GUIDANCE FOR PATIENTS AGED 16 OR ABOVE ADMITTED ONTO WARDS (EXCEPT ICU)

Assess VTE risk in all patients on admission, at 24hrs, when clinical condition changes and on discharge

Check: **FBC, PT, APTT, fibrinogen, D-Dimer, eGFR**

Platelets <50 x 10^9/l and/or fibrinogen <2g/L, and/or prolonged PT

Yes → **Consider DIC** Escalate to Consultant / Haematologist. If not bleeding, do not correct empirically

No

Any Contraindications (CI) for Anticoagulation?

- Active bleeding
- Acute stroke – discuss with stroke physician
- eGFR <30 ml/min
- Hypertension (≥230/120)
- Epidural catheter *in situ* or neuraxial access performed in the last 4 hours or expected within the next 12 hours
- Platelet count <30x10^9/L (standard dose)
- Platelet count <50x10^9/L (therapeutic dose)

Yes → **Re-assess VTE and bleeding risk daily**
Dose reduction if eGFR <30 ml/min
If oral anticoagulation is contraindicated consider dalteparin therapeutic dose

No → Review pre-existing anticoagulation / antiplatelet treatment

If already on oral anticoagulation continue it or switch to dalteparin therapeutic dose if there are any drug interactions with oral anticoagulation or any other contraindications

Not on oral anticoagulation.
Is PE Suspected?

No

Yes → **If PE confirmed or high index of suspicion patient should be switched to a DOAC as per Trust Guideline 249 and continued for 3 months.**
Refer to anticoagulation clinic before d/c: buc-tr.anticoagulation@nhs.net
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If patient deteriorates, PE must be considered and therapeutic dalteparin started whilst awaiting imaging

Dalteparin therapeutic weight-based dose
Excludes pregnancy and puerperium
See maternity guideline

≤40 kg	Discuss w/ haematology
41-45 kg	7500 units SC OD
46-56 kg	10000 units SC OD
57-68 kg	12500 units SC OD
69-82 kg	15000 units SC OD
83-98 kg	18000 units SC OD
99-112 kg	10000 units SC BD*
113-137 kg	12500 units SC BD*
138-165 kg	15000 units SC BD*
166-179 kg	18000 units SC BD*
≥180 kg	Discuss w/ haematology

Dalteparin standard prophylactic weight-based dose
Unlicensed regime

Weight	Dose
≤49 kg	2500 units SC OD
50-99 kg	5000 units SC OD
100-149 kg	5000 units SC BD
≥150 kg	7500 units SC BD

Discharge Thromboprophylaxis: **All patients require discharge VTE risk assessment and should be considered for thromboprophylaxis as per table on page 2**

Discharge Thromboprophylaxis

All patients with confirmed COVID-19 should be considered for discharge pharmacological thromboprophylaxis depending on their VTE risk

Step 1: Pre-discharge assessment	Repeat VTE risk assessment and select all applicable VTE risk factors Repeat FBC, PT, APTT, Fibrinogen, eGFR Assess for contraindications to pharmacological thromboprophylaxis		
Step 2: Select the column that applies *Refer to the VTE risk assessment and clinical notes*	**Red**	**Orange**	**Green**
	Previous history of VTE	ALL other inpatient managed COVID-19 if any of the following apply: • Prolonged admission to ICU or • Any surgery within the last 12 weeks or • Active cancer / cancer treatment or • Likely to have reduced mobility compared to baseline or • Any other significant thrombosis risk factors other than those stated above (e.g. BMI >30, multiple co-morbidities, thrombophilia)	ALL other inpatient managed COVID-19 that DO NOT fit Red and Orange column's criteria
Step 3: Select thromboprophylaxis duration or follow local guidance*, whichever is the longest option	Minimum 30 days* *If VTE risk outweighs bleeding risk*	7* days *If VTE risk outweighs bleeding risk*	Do not usually require thromboprophylaxis for COVID-19 indication unless otherwise determined by local guidance*
* Check if thromboprophylaxis is required for any indication other than COVID-19. Local guidance on discharge thromboprophylaxis for surgical patients is available in Section 6 of the VTE Guideline 733FM			
Step 4: Select thromboprophylaxis agent and dose *Check inpatient dalteparin dose, discharge body weight and discharge eGFR*	**Thromboprophylaxis agent** (Choose either) **Dalteparin** SC at standard prophylactic weight-based dose or If patient unable to administer dalteparin and patient body weight ≤140 kg and CrCL >30 ml/min prescribe **rivaroxaban 10 mg** PO OD (rivaroxaban is unlicensed for this indication) **Patients who are receiving therapeutic anticoagulation for VTE should remain on anticoagulation for 3 months and be referred before discharge to the anticoagulation clinic.**		If applicable, follow local guidance* VTE guideline 733FM on type and duration of thromboprophylaxis for other indications than COVID-19 (e.g. surgery)
Step 5: Discharge	- Provide the patient information leaflet '*Blood Clots: Reducing the Risks*' - If applicable, prescribe and supply the full course of pharmacological thromboprophylaxis - If discharged on dalteparin, teach the patient how to self-administer dalteparin and observe their injection technique or refer to district nurse if unable to self-inject - If self-administering dalteparin, give the patient information leaflet '*Dalteparin pre-filled syringes. How to administer dalteparin at home, a patient guide*' - Give a yellow top sharps bin of an appropriate size for the number of injections provided		

Background

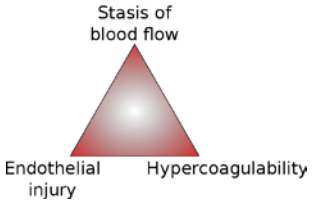
The recent publication of the NICE Ng186 COVID-19 rapid guideline 'Reducing the risk of venous thromboembolism in over 16s with COVID-19' led to the review of this guidance document, which will continue to be updated as new evidence emerges.

COVID-19 is associated with raised inflammatory markers and an unusual coagulopathy that is not typical of disseminated intravascular coagulation. The most marked abnormality is a raised D-Dimer, and high values are associated with a poor outcome and increased mortality. Thromboprophylaxis (the vast majority given at a prophylactic dose) has been associated with reduced mortality in those who are most unwell. Early published data suggests that the rate of VTE and arterial thrombosis is higher than one would usually expect despite standard thromboprophylaxis (VTE 27%, arterial thrombosis 4% in COVID patients on ICU). There is also a clinical impression across ICUs nationally of a prothrombotic state, for example recurrent clots within circuits on haemofiltration (OUHFT, 2020).

There is clinical concern of a significant inflammatory and pro-coagulant response with COVID-19 which may be associated with increased risk of thrombosis and mortality. **It is not known whether increasing the dose of thromboprophylaxis beyond STANDARD dose will result in reduced risk of thrombosis and improved survival, however it may increase bleeding risk. There are separate guidelines for patients in ICU.**

Whilst there are pathways in place to monitor rates of VTE in inpatients, there are no existing pathways to monitor rates of arterial events or bleeding rates out-with a clinical trial. Reported clinical experience shows that these patients are at increased risk of thromboembolic disease. In addition, they are immobile due to severity of illness leading to stasis of blood flow and exhibit a systemic inflammatory response which leads to hypercoagulability. There have been post-mortem findings of microvascular thrombosis within the injured lungs of COVID-19 patients, which may be consistent with endothelial injury. See Virchow's triad (see Fig.1).

Figure 1: Virchow's Triad: factors broadly contributing to thrombosis



Guidance for venous thromboembolism (VTE) risk assessment and thromboprophylaxis in suspected and confirmed COVID-19 patients aged 16 or above admitted onto wards. See separate guidance for patients admitted to ICU.

1. All patients admitted to hospital should have a **VTE risk assessment completed as soon as possible after admission and thromboprophylaxis prescribed and administered as soon as possible and within 14 hours of admission**. Do not delay anticoagulant doses, if they are not contraindicated. The VTE risk assessment should then be completed on the day after admission, when clinical condition changes, after a maximum of 7 days if not re-assessed by then and on discharge.

2. All patients at risk of VTE should be given verbal and written information about VTE prevention, including the patient information leaflet '*Blood Clots: Reducing the Risks*'.

3. **Pharmacological Thromboprophylaxis:** All admitted patients should have baseline full blood count (FBC), coagulation tests with Clauss fibrinogen and D-Dimer, and calculate creatinine clearance before prescribing pharmacological thromboprophylaxis.

4. If platelet count is <50 x 10^9/L and/or fibrinogen <2 g/L and/or prothrombin time prolonged, **then disseminated intravascular coagulation (DIC)** should be considered as a cause. Check the International Society on Thrombosis and Haemostasis (ISTH) score (see Table 3 below) if ISTH criteria for DIC are met, tranexamic acid should **NOT** be given. It is not recommended to empirically correct abnormal clotting parameters with replacement products in the absence of bleeding (Hunt, 2014). Do not withhold pharmacological prophylaxis on the basis of abnormal coagulation only.

5. If any clotting parameters are abnormal, this should be escalated to a senior ICU doctor or a haematologist for review of risk versus benefit for methods of thromboprophylaxis.

Table 3: ISTH score for DIC

Parameter	Score
Platelet Count	
>100 x10^9/L	0
50-100 x10^9/L	1
< 50 x10^9/L	2
D-dimer	
No increase	0
Moderate increase (1-10 times upper limit of normal)	2
Strong increase (>10 times upper limit of normal)	3
Fibrinogen	
>1.0 g/L	0
≤1.0 g/L	1
Prothrombin time prolongation	
< 3 seconds	0
3-6 seconds	1
>6 seconds	2
Overt Disseminated Intravascular Coagulation	**≥5**

6. Patients should have a drug history established and pre-existing anticoagulation or antiplatelet treatment should be documented clearly. Antiplatelet medication should be reviewed for continuation or discontinuation but not considered as VTE prophylaxis. A decision should be made regarding therapeutic anticoagulation. Conversion from oral anticoagulants to therapeutic dalteparin should be weight-adjusted as per the 'dalteparin therapeutic weight-based dose' table on the flowchart, unless there is a contraindication to dalteparin (e.g. heparin-induced thrombocytopenia, allergy, see Table 4). In the case of dalteparin allergy, consider the use of fondaparinux as an alternative, unless there is renal impairment.

7. As per usual practice, patients should not be prescribed pharmacological thromboprophylaxis if the bleeding risk outweighs the VTE risk. See **Table 4** for full list of cautions and contraindications to pharmacological thromboprophylaxis.

Table 4: Pharmacological Thromboprophylaxis Cautions and Contraindications
Active bleeding
Anticoagulants: therapeutic doses of UFH or LMWH, warfarin with INR >2, or direct oral anticoagulants
Inherited or acquired bleeding disorders (such as haemophilia or liver failure)
Acute stroke - discuss with stroke physician
Platelet count <30 x 10^9/L (standard prophylactic dose)
Platelet count <50 x 10^9/L (therapeutic dose)
Creatinine clearance <30 ml/min (refer to this guideline for dose adjustments)
Hypertension (≥230/120 mmHg)
Neurosurgery, spinal surgery or eye surgery or other procedure with high bleeding risk
Heparin allergy or history of heparin induced thrombocytopenia
Lumbar puncture, epidural catheter in situ or spinal anaesthesia performed within the last 4 hours or expected within next 12 hours

8. Where there is a relative contraindication this should be discussed at senior level and/or with a haematologist if necessary, before withholding pharmacological thromboprophylaxis. This decision should be reviewed on a daily basis with introduction of pharmacological thromboprophylaxis when appropriate without delay.

9. Coagulopathy without bleeding is not a contraindication to anticoagulation unless platelets fall below 30 x 10^9/L for standard prophylactic dose, or below 50 x 10^9/L for therapeutic doses. If the eGFR is <30 ml/min, Dalteparin doses should be reduced accordingly. While eGFR is acceptable to estimate renal function in most clinical situations, it is advisable to use creatinine clearance for certain patient groups as follows: elderly (>75 years), and patients at extremes of body weight (<18 kg/m^2 or >40 kg/m^2).

10. **Use in renal impairment:** Dalteparin is renally excreted. Care is required when administering it to patients with severe renal impairment (creatinine clearance less than 30 ml/min). For patients on standard prophylactic dose thromboprophylaxis, check trough heparin anti-Xa levels after 10 days. Expected trough levels 0.0-0.2 anti Xa units/ml. Levels can be discussed with Haematology if necessary.

11. **Use in patients on dialysis:** these patients can receive standard prophylactic weight-based dose thromboprophylaxis.

12. All patients should receive standard dose thromboprophylaxis as per table below, unless contraindicated or therapeutic anticoagulation is indicated.

Dalteparin standard prophylactic weight-based dose	
Unlicensed regime	
Weight	**Dose**
≤49 kg	2500 units SC OD
50-99 kg	5000 units SC OD
100-149 kg	5000 units SC BD
≥150 kg	7500 units SC BD

13. If there is an indication for therapeutic anticoagulation, then this should be reviewed for continuation. Assuming the patient is on oral anticoagulation, consider switching to therapeutic dose dalteparin if there are any drug interaction with oral anticoagulation or if there are any other contraindications for continued oral anticoagulation.

14. In any patient with clinical deterioration or increasing oxygen requirements with or without cardiovascular instability, PE should be considered as a cause. If PE is suspected, then therapeutic dose anticoagulation with dalteparin should be commenced immediately. Where PE is confirmed on imaging, patients should be switched to a DOAC as per Trust guideline 249. Patients should have imaging to confirm VTE when at all possible. If there is a high clinical index of suspicion of VTE, but cannot be confirmed with imaging, please document carefully and start therapeutic dose anticoagulation as per Trust guidelines. Patients with PE should continue anticoagulation for a total of 3 months and should be referred to the anticoagulation clinic.

Dalteparin therapeutic weight-based dose Excludes pregnancy and puerperium See maternity guideline	
≤40 kg	Discuss with Haematology
41-45 kg	7500 units SC OD
46-56 kg	10000 units SC OD
57-68 kg	12500 units SC OD
69-82 kg	15000 units SC OD
83-98 kg	18000 units SC OD
99-112kg	10000 units SC BD*
113-137kg	12500 units SC BD*
138-165 kg	15000 units SC BD*
166-179 kg	18000 units SC BD*
≥180 kg	Discuss with Haematology

If PE confirmed or high index of suspicion patient should be switched to a DOAC as per Trust Guidelines and continued for 3 months. Refer to anticoagulation clinic on d/c: buc-tr.anticoagulation@nhs.net

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15. **Discharge:** Repeat FBC, clotting, fibrinogen and creatinine clearance on day of discharge. Repeat VTE risk assessment and check for pharmacological thromboprophylaxis cautions and contraindications to assess the safety of extended thromboprophylaxis. Ensure patient takes home the patient information leaflet '*Blood Clots: Reducing the Risks*'.

16. **Extended pharmacological thromboprophylaxis:** On discharge, all patients should have a VTE risk assessment. Consideration must be given to the extended thromboprophylaxis that is recommended in the VTE guideline 733FM for that patient group (e.g. total knee replacement requires 14 days, Achilles tendon rupture requires 56 days). This must be considered when deciding about discharge thromboprophylaxis in patients with COVID-19 and other conditions **and the longest option should be prescribed. See Advice for COVID-19 patients below:**

17. **Patients with a previous history of VTE should receive a minimum of 30 days of standard weight-based dose thromboprophylaxis. This should be extended if required as per section 16.**

18. **The following groups of patients should be considered for discharge thromboprophylaxis for 7 days.**

- Prolonged admission to ICU or
- Any surgery within the last 12 weeks or
- Active cancer / cancer treatment or
- Likely to have reduced mobility compared to baseline or
- Any other significant thrombosis risk factors other than those stated above (e.g. BMI >30, multiple co-morbidities, thrombophilia)

19. If the patient does not fulfil the criteria set above in sections 17 and 18, they would not normally require thromboprophylaxis unless specified otherwise in local guidance for extended thromboprophylaxis in VTE guideline 733FM.

20. Prescribe standard prophylactic dalteparin subcutaneous injection at a weight-based dose. If patient is unable to administer dalteparin and weights ≤140 kg they can be prescribed rivaroxaban 10 mg oral tablet once daily. Rivaroxaban should be avoided in patients with a calculated CrCl less than 30 ml/min. It is not licensed for use as thromboprophylaxis after hospitalisation for medical illness. Rivaroxaban should not be administered with potent inhibitors and inducers of both CYP3A4 and P-gp.

21. All patients and/or carers should be fully counselled before discharge:

Patients discharged with dalteparin should be:

- Taught how to self-administer dalteparin (ideally, before the discharge day)
- Observed in their injection technique
- Given the patient information leaflet '*Dalteparin pre-filled syringes. How to administer dalteparin at home, a patient guide*'
- Given a yellow top sharps bin of an appropriate size for the number of injections provided

22. Patients who are receiving therapeutic anticoagulation for VTE should remain on anticoagulation for 3 months and be referred to the anticoagulation team by completing the e-referral on Evolve (if new to anticoagulation) or contacting the patient's Warfarin clinic, if it is BHT warfarin clinic, contact 01494 426270 / Bleep 3706 (WH) 01296 315510 / Bleep 776 (SMH) or email buc-tr.anticoagulation@nhs.net.

23. **Pregnancy and Puerperium:** The Royal College of Obstetricians and Gynaecologists (RCOG) have recently updated their guidelines to include VTE prophylaxis during COVID-19, to be used in conjunction with existing guidance about VTE prophylaxis in pregnancy (see RCOG Green-top guideline 37a for risk factors and risk stratification). Any pregnant inpatient, in the absence of contraindications, should have dalteparin prescribed according to Maternity Guideline 646FM. It is advised that any woman who is pregnant or postpartum (defined here as delivery within the preceding six weeks) and is hospitalised with COVID-19 should receive at least 10 days of dalteparin on discharge. There is no specific guidance about higher doses of dalteparin to be used in critically ill pregnant or recently delivered women, and the pregnancy-related changes in D-Dimer make it difficult to directly apply the table above. The decision about the use of dalteparin at higher doses than prophylaxis should therefore be made on a case-by-case basis by a multi-disciplinary team including obstetric, obstetric medicine, haematology and intensive care colleagues, taking into consideration factors including the gestation, obstetric concerns, anticipated delivery / delivery complications and severity of maternal illness (OUHFT, 2020).

24. **Children less than 16 years of age** should continue to be risk assessed on an individual basis using the VTE risk assessment for patients being nursed in paediatric areas.

References

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- Oxford University Hospitals Foundation Trust, 2020. 'Interim OUHFT thromboprophylaxis guidance for patients with suspected or proven COVID-19'.

Based on:
BHT 'Standard operating procedure for VTE monitoring and management in Intensive Care Unit in COVID-positive patients'

See also:

Guideline 249	*Assessment of Deep Vein Thrombosis (DVT) in the Ambulatory Setting and Anticoagulation Management of DVT and Pulmonary Embolism (PE) In Adults (Aged 16 and Over)* *(BHT users only)*
Guideline 646FM	*Venous Thromboembolism in Pregnancy*
Guideline 733FM	*Thromboprophylaxis in the Hospital Setting: Reducing the Risk of Hospital Acquired Deep Vein Thrombosis or Pulmonary Embolism*

Patient information leaflets:
Blood Clots – reducing the risks
Dalteparin pre-filled syringes. How to administer dalteparin at home, a patient guide

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