Guideline for COVID-19 Patients: Thromboprophylaxis and Management of Suspected Pulmonary Embolism and Deep Vein Thrombosis

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**Guideline for COVID-19 Patients:**
**Thromboprophylaxis and Management of Suspected PE and DVT**

**ALL patients should receive VTE prophylaxis with enoxaparin, dosed according to actual body weight (unless contraindicated):**

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Dose of Enoxaparin (eGFR&gt;30mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50kg</td>
<td>20mg od</td>
</tr>
<tr>
<td>50–99kg</td>
<td>40mg od</td>
</tr>
<tr>
<td>100–150kg</td>
<td>40mg bd</td>
</tr>
<tr>
<td>&gt;150kg</td>
<td>60mg bd</td>
</tr>
</tbody>
</table>

- **Worsening clinical situation (e.g. increasing O₂ requirements)**
- **Clinical suspicion of a pulmonary thrombi**
- **Otherwise unexplained increase in D-dimers**

**INITIATE THERAPEUTIC ANTICOAGULATION:**
Enoxaparin 1mg/kg BD

**New thrombosis on imaging?**

- **NO**
  - **Consider other causes for clinical deterioration**
  - **Prophylactic enoxaparin** *(see section 5.1 of full guidance)*

- **YES**
  - **Very high clinical suspicion of a pulmonary thrombi but imaging impractical**
  - **Unexplained extracorporeal circuit thrombosis**

**THERAPEUTIC ANTICOAGULATION:**
Enoxaparin 1mg/kg BD

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1. **Overview** (What is this guideline about?)

This guideline sets out the initial management of suspected PE in Covid-19 patients, including recommendations for imaging, practical dosing and monitoring requirements of prophylactic and treatment anticoagulation for patients admitted with proven or suspected Covid-19.

If you have any concerns about the content of this document please contact the author or advise the Document Control Administrator.

2. **Scope** (Where will this document be used?)

For use in patients with proven or strongly suspected COVID-19 only, admitted to North Manchester General Hospital.

These guidelines exclude:
- Critical care unit patients
- Patients already receiving treatment dose/therapeutic oral anticoagulation
- Maternity patients – refer to ‘Venous Thromboembolism And Obstetrics SOP’

3. **Background** (Why is this document important?)

Evidence is emerging that supports a pro-thrombotic tendency in Covid-19 patients, but the optimal management strategy is unclear. Observational studies have reported a high risk of deep vein thrombosis (DVT). Local data has suggested an increased prevalence of pulmonary embolism (PE) compared to that seen in admissions due to other respiratory tract infections, such as community acquired pneumonia.

In addition, Covid-19 infection is associated with raised d-dimer levels, symptoms of breathlessness and hypoxia, which occur independently of venous thromboembolism (VTE) formation. This complicates utilising the current national guidance on the management of PE, which are heavily dependent on these factors in the diagnostic algorithm. It is imperative that patients receive optimal VTE prophylaxis, and those suspected of PE are managed effectively.

4. **What is new in this version?**

New document.

5. **Guideline**

5.1 **VTE Thromboprophylaxis**

5.1.1 Given the increased risk of VTE, all admissions with suspected Covid-19 should receive thromboprophylaxis (unless contraindicated). All patients should be weighed and the dose of enoxaparin adjusted according to actual body weight:
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### 5.1.2 Patients Receiving Non-Invasive Ventilation

Patients receiving non-invasive ventilation (eg: CPAP, BiPAP) outside of critical care areas for the management of Covid-19 should be prescribed intermediate-dose thromboprophylaxis as per table below:

<table>
<thead>
<tr>
<th>Actual Body Weight</th>
<th>Intermediate Dose of Enoxaparin (eGFR&gt;30mL/min)</th>
<th>Intermediate Dose of Enoxaparin (eGFR&lt;30mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50kg</td>
<td>20mg bd</td>
<td>20mg od</td>
</tr>
<tr>
<td>50–99kg</td>
<td>40mg bd</td>
<td>40mg od</td>
</tr>
<tr>
<td>100–150kg</td>
<td>60mg bd</td>
<td>60mg od</td>
</tr>
<tr>
<td>&gt;150kg</td>
<td>80mg bd</td>
<td>80mg od</td>
</tr>
</tbody>
</table>

Consideration should be given to antifactor Xa monitoring as per section 5.6.

### 5.1.3 On Discharge

All Covid-19 patients on prophylactic LMWH should be assessed at discharge for extended VTE thromboprophylaxis. If the patient is considered at high risk of VTE (eg: past history of VTE, cancer, significantly reduced mobility, critical care admission) and the risk of VTE is felt to outweigh the risk of bleeding, continuing standard-dose prophylactic LMWH (as per table in 5.1.1 above) for 4 weeks post-discharge should be considered. Where patients are unable to self-inject, a DOAC (eg: apixaban 2.5mg bd) could be considered.

### 5.2 DVT – Selecting Patients for Investigation

All patients presenting with suspected Covid-19 infection should be regularly evaluated for DVT and investigated as per standard national guidelines. Other than changes related to infection prevention, it is not anticipated for any differences in investigation compared to patients without Covid-19.

In those confirmed with DVT where there is a clinical suspicion of PE, additional investigation should only be undertaken where it will change clinical management.

### 5.3 PE – Selecting Patients for Investigation of Superimposed PE

PE should be considered in all admissions with suspected Covid-19 infection, as well as in inpatients that have increasing oxygen requirements. The algorithm on page 3 serves as a suggested decision-making tool. It stratifies patients based on risk of clinical deterioration and presence of clinical features suggestive of superimposed PE:
• Chest pain
• Oxygen requirements disproportionate to Covid-19 related changes on chest x-ray
• Haemoptysis
• Unexplained tachycardia or hypotension
• Suspected or confirmed DVT
• Syncope or pre-syncope

5.4 PE – Situations for Empirical Treatment of PE Without Imaging

In certain situations, CTPA will be deferred in favour of empirical treatment dose anticoagulation. This may occur when the patient is not stable enough for transfer to the radiology department for scanning, or is unable to hold their breath for 10 seconds as is required for the imaging protocol. A bleeding risk score (e.g: VTE-BLEED) may be useful in identifying patients at low risk of bleeding in whom anticoagulation without imaging may be safe and patients at higher risk of bleeding in whom imaging is more essential. These decisions should be made by the clinical team.

All patients given empirical treatment require the same duration and follow-up as patients diagnosed with PE, as per NICE guidelines.

5.5 Therapeutic Anticoagulation

5.5.1 Treatment-dose LMWH
If treatment dose LMWH is indicated, enoxaparin should be dosed as per table below using actual body weight and adjusted for renal function and risk factors:

<table>
<thead>
<tr>
<th>Renal Function</th>
<th>eGFR&lt;15mL/min</th>
<th>eGFR&lt;30mL/min</th>
<th>eGFR&gt;30mL/min</th>
<th>eGFR&gt;30mL/min + risk factors*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose of Enoxaparin</td>
<td>Discuss with haematology</td>
<td>1mg/kg od</td>
<td>1.5mg/kg od</td>
<td>1mg/kg bd</td>
</tr>
</tbody>
</table>

*Risk factors:
• Obesity
• Symptomatic PE
• Cancer
• Recurrent VTE
• Proximal thrombosis

5.5.2 Switching from Treatment-Dose LMWH to Oral Anticoagulants
When possible, patients on treatment-dose LMWH should be switched to treatment doses of oral anticoagulation for discharge.

• Choice: Ideally this should be a DOAC to minimise monitoring requirements. Apixaban is the first-line DOAC at NMGH, but see GMMMG DOAC Prescriber Decision Aid for comparative information.
• Interactions: Check BNF and product literature. (See Liverpool Covid-19 Interactions for COVID trial/treatment interactions).
• Duration: Treatment should be continued for a minimum of 3 months for proven or strongly suspected PE. This should be clearly documented on the discharge letter.
5.5.3 Stepping Down
Patients can be stepped down to prophylactic dose LMWH (as per 5.1 above) if a satisfactory CTPA scan showed no evidence of PE.

5.7 Monitoring LMWH Anticoagulation

- Platelet count should be measured before the initiation of therapy of enoxaparin and then regularly thereafter (eg: every 5–7 days)
- Renal function/potassium levels (every 5–7 days)
- Anti-Xa levels should be considered in patients with impaired renal function or for patients at extremes of body weight, to ensure appropriate dosing:
  - Peak (post-dose) levels should be taken 3–4 hours after the administration of the third dose of enoxaparin with the aim of achieving the following levels:
    - Prophylactic-dose enoxaparin: 0.2 – 0.4 units/mL
    - Treatment-dose twice daily enoxaparin: 0.6 – 1.0 units/mL
    - Treatment-dose once daily enoxaparin 1.0 – 2.0 units/mL
  - Following a dose change, anti-Xa levels should be monitored again after three doses to ensure appropriate dosing.
  - Repeated anti-Xa levels are not routinely required, but may be requested where clinically indicated – eg: deteriorating renal function, increased bleeding risk
  - Trough levels (pre-dose) are useful in monitoring accumulation and may be measured in high bleeding risk patients and/or renal dysfunction. Trough levels >0.25 units/mL should be discussed with haematology.

In all cases, the next dose can be administered even if test results are not yet available.

6. Roles & responsibilities

6.1 This document provides guidance to all staff on thromboprophylaxis in patients with proven or strongly suspected COVID-19. Treatment decisions should still be made on an individual basis and will ultimately be the responsibility of the doctor under which that patient is being cared.

6.2 Ward/Unit Managers and Clinical leads are responsible for investigating accidents, incidents and near misses in relation to failure to follow these guidelines and for reporting up to their Divisional Governance Committees where appropriate.

6.3 The relevant Divisional Governance Committees are responsible for reviewing incident reports within their remit and for the development, implementation and monitoring of action plans to address concerns where appropriate to ensure that lessons are learnt.

7. Monitoring document effectiveness

- **Key standards:** appropriate thromboprophylaxis in patients with proven or strongly suspected COVID-19
- **Method(s):** direct observation of prescribing and administration practices. Review of incident reports.
- **Team responsible for monitoring:** pharmacy, medical and nursing staff.
- **Frequency of monitoring:** continually
8. Abbreviations and definitions

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>AKI</td>
<td>Acute kidney injury</td>
</tr>
<tr>
<td>BD</td>
<td>Twice daily (bis in die)</td>
</tr>
<tr>
<td>BNF</td>
<td>British National Formulary</td>
</tr>
<tr>
<td>DOAC</td>
<td>Direct oral anticoagulant</td>
</tr>
<tr>
<td>DVT</td>
<td>Deep vein thrombosis</td>
</tr>
<tr>
<td>CrCl</td>
<td>Creatinine clearance</td>
</tr>
<tr>
<td>CTPA</td>
<td>Computed tomography pulmonary angiogram</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular filtration rate</td>
</tr>
<tr>
<td>GMMMG</td>
<td>Greater Manchester Medicines Management Group</td>
</tr>
<tr>
<td>INR</td>
<td>International normalised ratio</td>
</tr>
<tr>
<td>kg</td>
<td>Kilograms</td>
</tr>
<tr>
<td>LMWH</td>
<td>Low molecular weight heparin</td>
</tr>
<tr>
<td>mg</td>
<td>Milligrams</td>
</tr>
<tr>
<td>mL</td>
<td>Millilitre</td>
</tr>
<tr>
<td>NCA</td>
<td>Northern Care Alliance</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>NMGH</td>
<td>North Manchester General Hospital</td>
</tr>
<tr>
<td>OD</td>
<td>Once daily (omne in die)</td>
</tr>
<tr>
<td>PE</td>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>VKA</td>
<td>Vitamin K antagonist</td>
</tr>
<tr>
<td>VTE</td>
<td>Venous thromboembolism</td>
</tr>
</tbody>
</table>

9. References

Acknowledgement of sources:
Adapted from Manchester Foundation Trust Anticoagulation guideline for Covid-19 patients - Thromboprophylaxis and management of suspected pulmonary embolism (PE) and deep vein thrombosis (DVT) Version: 1 (April 2020)

10. Appendices

Appendix 1: Algorithm for the management of patients (previously anticoagulated at home) discharged on anticoagulation during COVID-19
Appendix 1: Management of patients (previously anticoagulated at home) discharged on anticoagulation during COVID-19

Start Here:
Patient on a DOAC/LMWH prior to admission and being discharged with DOAC/LMWH: Continue with this treatment.
- Ensure to continue the DOAC the patient was taking pre admission. If on discharge CrCl <30mL/min or patient prescribed new medication known to interact with the DOAC, contact the ward pharmacist for advice.

Patient to be discharged with Vitamin K antagonist (VKA) (i.e. warfarin):
- Discuss with pharmacy team if patient is suitable for switching to DOAC (see indications below).
- If appropriate to switch to a DOAC, discontinue the VKA and start DOAC when the INR ≤2.5 (nimoroxaban and edoxaban), or when INR < 2.0 (apixaban and dabigatran).
- AF: if no contraindications, switch to DOAC as per GMMMG DOAC Prescriber Decision Aid (See guidance for contraindications).
- VTE: DOACs are usually 1st line for treatment of VTE – Patient may be on warfarin because DOAC contraindicated.
- Other LMWH are a possible option for all other warfarin indications as a temporary measure if patient unable to have INR monitored. (Any use of a DOAC for an off-label indication requires MMC approval).
- Discuss with haematology if appropriate for switch as needed.

WARFARIN FOR DISCHARGE
(UNSUITABLE FOR SWITCH TO DOAC/LMWH)

WARFARIN

Self isolating as per government advice:
- ≥70 years of age, frail, immuno-compromised, chronic conditions
- Social distancing

Stable INR (2 or more consecutive INRs in range):
- Complete anticoagulation clinic referral
- If clinically safe, consider extending INR test
- Consider the district nurse services to take domiciliary

Erratic INR:
- Complete anticoagulation clinic referral
- Contact anticoagulation clinic/specialist to advise on dose to take and when to next test INR and book appointment
- Consider the district nurse services to take domiciliary INR

LMWH

Temporarily switching to a LMWH:
- Counsel patient/family members on the new medicine including administration and disposal of syringes
- Supply enough to cover until next review
- Document in discharge letter VKA temporarily switched to LMWH

WARFARIN

Self isolating
- COVID-19 positive confirmed
- COVID-19 symptomatic
- COVID-19 contact

Stable INR (2 or more consecutive INRs in range):
- Complete anticoagulation clinic referral
- If clinically safe, consider delaying INR test for 2 weeks
- Do NOT attend clinic/community sites
- If under the district nurse services, continue to utilise to take domiciliary INR

Erratic INR:
- Complete anticoagulation clinic referral
- Contact anticoagulation clinic/specialist to advise on dose to take and when to next test INR and book appointment
- Advise patient NOT to attend clinic/community sites and refer to district nurse
- Consider temporary switch to LMWH
- Consider the district nurse services to take
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