Guidance for management of Suspected Pulmonary Embolism (PE) in Adults

This guideline aims to assist the investigation and management of suspected and confirmed PE in adult patients, providing clear standards across ABMU Health Board.

Senior clinical advice is essential in the management of these patients.

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- Major risk factors for PE
- Basic tests

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- Latex Agglutination D-dimer testing

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- Initial management

**Step 4 - Radiological Investigations and Management of Proven PE**
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- Pulmonary Embolism Severity Index (PESI)
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- Adult warfarin dosing chart

**References**
Step 1 - Presentation and Initial Investigation

1.1 Common presenting symptoms of PE- patients could present with any of the following:
- Dyspnoea – breathlessness or difficulty breathing
- Chest pain (pleuritic) and haemoptysis
- Collapse in patient with poor cardiorespiratory reserve
- Circulatory collapse in a previously well patient suggestive of massive PE

1.2 Major risk factors for PE (relative risk x 5-20)

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Major abdominal/pelvic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive surgery</td>
<td>Hip/knee replacement</td>
</tr>
<tr>
<td></td>
<td>Postoperative intensive care</td>
</tr>
<tr>
<td>Obstetrics</td>
<td>Pregnancy</td>
</tr>
<tr>
<td></td>
<td>Caesarean section</td>
</tr>
<tr>
<td></td>
<td>Puerperium</td>
</tr>
<tr>
<td>Lower limb problems</td>
<td>Fracture</td>
</tr>
<tr>
<td></td>
<td>Varicose veins</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Abdominal/ pelvic</td>
</tr>
<tr>
<td></td>
<td>Advanced/ metastatic</td>
</tr>
<tr>
<td>Reduced mobility</td>
<td>Hospitalisation</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Institutional care</td>
</tr>
<tr>
<td>Family History (1st degree relative)</td>
<td>Previous proven DVT/ PE</td>
</tr>
</tbody>
</table>

1.3 Pulmonary Embolism Rule out Criteria (PERC)
Used in an emergency department setting to compliment clinical judgement rather than replace it, with positive criteria helping to form a clinical judgement that would justify a formal evaluation for PE. If all negative, probability of PE is very low.

<table>
<thead>
<tr>
<th>PERC</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;50 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse &gt; 100 bpm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SpO2 &lt; 95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral leg swelling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoptysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent trauma or operation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous DVT / PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormone usage</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.4 Basic Tests
In assessing patients for suspected PE, clinical judgement is required to determine which tests are appropriate for an individual patient. Markers of poor prognosis include: RV dysfunction/strain, ↑ BNP or ↑ troponin.

Tests on initial assessment include:
- CXR – most often normal, but may be following signs:
  - Linear / wedge-shaped shadows
  - Small pleural effusion
  - Localised subtle paucity of vasculature
- ECG – may be normal, but look for changes:
  - Tachycardia
  - S1 Q3 T3 pattern
  - T wave inversion antero-septal leads
  - Incomplete/complete RBBB pattern

and can include the following, if clinically indicated and after discussion with a senior clinician:
- Troponin I or T may be elevated in acute PE [of prognostic value in acute massive PE]
- BNP (if available) – elevation associated with poorer prognosis
- Blood gas on air – if hypoxic/ unwell
Step 2 – Initial Assessment

2.1 Dichotomised Wells Scoring – must involve senior clinician in assessment

<table>
<thead>
<tr>
<th>Dichotomised Well’s Score</th>
<th>Score</th>
<th>Patient’s Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical DVT</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Tachycardia &gt;100</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td>Immobility &gt; 3 days or Surgery &lt; 4 weeks</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td>Previous PE/DVT</td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Malignancy within 6 months</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis less likely (as assessed by senior clinician)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If score is \( \leq 4 \), proceed to D-dimer test to exclude PE.

There is **no** benefit from doing D-dimer in those patients with high probability of PE. Therefore if score is \( > 4 \), proceed straight to clinical differentiation of suspected PE (Step 3).

2.2 Latex Agglutination D-dimer Testing

If D-dimer test result is < 190μg/dl, PE can be excluded and an alternative diagnosis should be considered.

If D-dimer test result is \( \geq 190\mu g/dl \), review haemodynamic stability.
Step 3 – Clinical Differentiation and Initial Management

Investigation, management and outcomes of PE are dependent on clinical characteristics of each patient and assessment of haemodynamic stability at an early stage is essential. Defining subgroups of PE is helpful in tailoring management appropriately.

### 3.1 Suspected Massive PE

**Arterial hypotension and cardiogenic shock**

- Systolic BP < 90 mm Hg for at least 15 mins (or requiring inotropic support) or drop in known systolic BP of > 40 mm Hg
- Tachycardia, gallop rhythm, pulselessness or persistent profound bradycardia PR < 40 bpm
- Signs of cardiogenic shock: altered level of consciousness, tachypnoea, cool clammy extremities, temp < 36º, SpO2 sat < 90%

**Initial management of suspected massive PE**

Obtain senior clinical review
Start LMWH (App. 2) or IV bolus of UFH if considering thrombolysis.
If thrombolysis contraindicated (App. 2), consider surgical / cardiology assessment for embolectomy or other intervention.
If anticoagulation contraindicated or embolisation continues despite anticoagulation, consider use of IVC filter [see pg 5].

*In cardiac arrest situation, when PE is suspected- give 50mg alteplase as bolus stat*

### 3.2 Suspected Sub-Massive PE

**Without systemic hypotension but with RV dysfunction or myocardial necrosis**

- RV dysfunction – RV dilation +/or RV systolic dysfunction on echo +/or ↑ BNP +/or ↑troponin
- New ECG changes of complete or incomplete RBBB, anteroseptal ST segment or T wave changes
- Myocardial damage: ↑ BNP; ↑troponin

**Initial management of suspected sub-massive PE:**

Start LMWH (App. 2)
If anticoagulation contraindicated or embolisation continues despite anticoagulation, consider use of IVC filter [see pg 5].

### 3.3 Non-Massive PE

**Absence of clinical markers of adverse prognosis defining massive / sub-massive PE**

Some patients with lower risk PEs may still have significant rates of morbidity and mortality that are functions of old age and co morbidities. Therefore important to incorporate risk stratification into clinical decision-making (see Step 5).

**Initial management of suspected non-massive PE:**

Start LMWH (App. 2).
If anticoagulation contraindicated or embolisation continues despite anticoagulation, consider use of IVC filter [see pg 5].
**Step 4 – Radiological Investigations and Management of Proven PE**

All requests for CTPA, VQ/Q scans must be discussed and agreed by duty/on call Consultant Radiologist. All out-of-hours imaging requests to be agreed with on call Consultant Radiologist.

Pre-test probability (i.e. Dichotomised Wells score) to be completed on all requests.

Nuclear medicine (VQ or Q scans) imaging is available weekdays in-hours on all ABMU hospital sites. There is no out-of-hours availability of VQ or Q scans.

IVC filters are usually deployed as urgent elective procedures; they are rarely done out-of-hours.

See page 9 for imaging in pregnancy.

### 4.1 Suspected Massive PE

Urgent CTPA is the investigation of choice; if contraindicated, use Doppler leg USS. Echo can be done if available – may not be necessary if RV dilatation shown on CTPA.

**Management of proven massive PE**

Arrange admission to CCU / HDU / ITU.

If diagnosis of PE confirmed, continue LMWH or UFH if considering thrombolysis. If contraindication to anticoagulation / thrombolysis, consider surgical/cardiology assessment for embolectomy or other intervention.

Transfer to low dependency ward when stable. Warfarin loading protocol unless contraindicated; continue LMWH / UFH until INR in therapeutic range for 2 days. Perform echo if not already done.

Remain in hospital until condition stable and INR in therapeutic range for at least 2 days.

**Thrombolysis**

Currently no evidence that thrombolysis improves mortality in patients without shock, hypotension or cardiac arrest compared to LMWH. Risk of bleeding with thrombolysis and PE is around 10%.

See App.2 for contraindications to thrombolysis.

### 4.2 Suspected Sub-Massive and Non-Massive PE

CTPA is the investigation of choice, except in:

- young (≤45 years) patient with normal CXR - Q scan is investigation of choice
- contrast intolerance or documented contraindication to iodine or creatinine markedly elevated (unsafe to proceed) - Q scan appropriate if CXR normal; V/Q scan if CXR abnormal

**Management of proven Sub-Massive or Non-Massive PE:**

Currently no evidence that thrombolysis improves mortality in PE patients who are not shocked or hypotensive.

If diagnosis of PE is confirmed, proceed to risk stratification for management options. Will require Echo as outpatient if not performed prior to discharge.

**Note: Use of IVC filters**

IVC filters should only be considered in patients with:

1. Proven DVT +/- proven PE who cannot be anticoagulated, with the aim of preventing clot from embolising to the pulmonary circulation
2. Patients on anticoagulation who continue to embolise (proven on repeat imaging)

A proven PE does **not** need a filter if the veins are clear.

Individual detailed discussions with a vascular Consultant Radiologist on a case by case basis are required to assess factors such as burden of clot, caliber of IVC, venous access etc.
Step 5 – Risk Stratification

Selected patients at low risk of adverse outcome by stratification criteria can be considered for out-patient treatment of PE once diagnosis is confirmed. Patients with a confirmed PE must be:

- **Reviewed by a consultant** who agrees that patient is appropriate for outpatient management.
- Carefully selected for out-patient management according to very strict criteria and protocols.
- Regularly monitored and followed up by senior clinician.
- Informed of the potential risks of ambulatory management - written information for the patient and informed consent are essential.

5.1 Criteria for Suitability for Out Patient Treatment

Patients must have PESI ≤ 85, i.e. lie within Class 1 or 2: see Table 1 below and

Patients must have **no** additional high risk condition: see Table 2 below

### Table 1 - Pulmonary Embolism Severity Index (PESI)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
<th>Patient’s Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1 per year</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>HR 110 bpm</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Systolic BP &lt; 100 mm hg</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Resp rate ≥ 30 breaths/min</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Body temp &lt; 36 °C</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Disorientation, lethargy, stupor, coma</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Sa02 &lt; 90% on air</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low Risk Classes</th>
<th>Points</th>
<th>30 day all-cause mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1</td>
<td>&lt;66</td>
<td>0-1.6%</td>
</tr>
<tr>
<td>Class 2</td>
<td>66-85</td>
<td>1.7-3.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intermediate/High Risk</th>
<th>Points</th>
<th>30 day all-cause mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 3</td>
<td>86-105</td>
<td>3.2 - 7.1%</td>
</tr>
<tr>
<td>Class 4</td>
<td>106-125</td>
<td>4 - 11.4%</td>
</tr>
<tr>
<td>Class 5</td>
<td>&gt;125</td>
<td>10 - 24.5%</td>
</tr>
</tbody>
</table>

Patients must have **PESI ≤ 85** to be managed as an out patient.

### Table 2 - Additional High Risk Conditions / Groups

- Coexisting major DVT (high segment femoral and above) in addition to PE
- Severe renal dysfunction (eGFR < 30ml/ min/ 11.73m2)
- Pregnancy
- Bleeding risk: active bleeding, coagulopathy, ICH (ever), GI/GU bleed, trauma, surgery in last month, platelets <50, abnormal coagulation screen: (INR & APTR), FBC and/or Liver Function Test
- Allergy to warfarin/heparin or history of heparin induced thrombocytopenia
- Outpatient unfeasible in terms of: immobility, compliance unlikely, unable to obtain transport to and from hospital, unable to access telephone at home, unaware of adverse symptoms and how to obtain help
- Needing morphine for pain
- Weight >150Kg
- Already on anticoagulation
- Expected poor compliance

**NB** Patients must have **no** additional high risk condition to be managed as an out patient.
5.2 Out Patient Treatment
With LMWH and anticoagulation as in Appendix 2.

5.3 Review Arrangements for Out Patient Management
If the decision has been made that the patient is suitable for outpatient management, the following steps should be taken:

Senior clinician confirms suitability for out patient management
Patient informed of the relative benefits and risks of outpatient management
Patient signs informed consent sheet
Patient treated with LMWH (see App 2)
Patient discharged with hospital contact number and written information giving clear advice to return if symptomatic
Patient discharged home
Review in 24-48 hours on acute site by senior clinician to assess clinical condition and commence warfarin (unless CI)
Review every 1-3 days thereafter until INR in therapeutic range and clinically stable for > 2 days

Follow up arrangements as in Step 6.
**Step 6 – Follow Up Arrangements**

Patients with proven PE require follow-up as outpatients at 3 months. The risk of developing chronic thrombotic and/or embolic pulmonary hypertension is approximately 4% at 2 years.

Decisions regarding duration of anticoagulation (lifelong or not) in unselected patients should be made with reference to whether or not a first episode of venous thrombosis was provoked or not, other risk factors such as strong family history, and risk of anticoagulant therapy-related bleeding, regardless of whether a heritable thrombophilia is known.

### 6.1 Thrombophilia Testing

Thrombophilia testing is not appropriate during an acute episode of VTE, as results will be abnormal as a consequence of the thrombosis and do not impact on management (acute phase or longer term) in most cases.

The need for thrombophilia testing at follow up appointment should be discussed with Consultant Haematologist prior to testing (by phone or referral letter). Only those deemed clinically appropriate by a consultant haematologist will be processed.

### 6.2 If persistent dyspnoea +/or RV dysfunction at 3 months

Clinical assessment of:

i. **End-organ damage** requiring onward referral.
   The following investigations will inform if referral is to cardiologist or respiratory physician:
   - Repeat echo: to assess pulmonary artery pressure
   - PFTs - for assessment of gas exchange / ? alternative diagnosis
   - Repeat CTPA/VQ – to identify ? recurrent PE or ? alternative diagnosis

ii. **Duration of anticoagulation** - Adult Inpatient Warfarin Chart [see Appendix 3]

<table>
<thead>
<tr>
<th></th>
<th>1st idiopathic VTE: proximal DVT or PE * *Review by senior clinician after this time to discuss long term anticoagulation</th>
<th>≥3 months*</th>
<th>2.5 (2-3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st proximal VTE/PE with precipitating factors e.g. trauma, surgery, pregnancy</td>
<td>3 months</td>
<td>2.5 (2-3)</td>
<td></td>
</tr>
<tr>
<td>1st idiopathic, calf vein DVT</td>
<td>3 months</td>
<td>2.5 (2-3)</td>
<td></td>
</tr>
<tr>
<td>1st calf vein DVT, with precipitating factors e.g. trauma, surgery</td>
<td>6 weeks</td>
<td>2.5 (2-3)</td>
<td></td>
</tr>
<tr>
<td>Recurrent VTE</td>
<td>Long term</td>
<td>2.5 (2-3)</td>
<td></td>
</tr>
<tr>
<td>VTE whilst taking warfarin</td>
<td>Long term</td>
<td>3.5 (3-4)</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 1

Groups for Special Consideration in Suspected Pulmonary Embolism

1. Pregnancy

In the acute setting, contact the Obstetric Registrar and/or Consultant early to ensure senior input.

When there are clinical signs/symptoms of PE, undertake investigations and treat with LMWH (unless strong contraindication to anticoagulation).

Choice of investigations will depend on local availability and should be made through discussion between clinician, radiologist and mother. Involvement in the care of the patient by a physician and obstetrician is essential and of a haematologist may be helpful.

Investigations in pregnancy

- All pregnant women with suspected PE should have a Chest xray.
- If CXR is normal, bilateral Doppler USS leg studies should be performed.
- If both CXR and Doppler are normal with persisting clinical suspicion of PE, proceed to CTPA or V/Q scan.
- The ventilation component of the V/Q scan can often be omitted during pregnancy, minimising the radiation dose to the foetus.
- When there is persisting clinical suspicion of PE with normal Doppler + normal V/Q scan or CTPA, continue LMWH and repeat testing until PE is definitively excluded.

Diagnosis of DVT may indirectly suggest a diagnosis of PE and, since anticoagulation therapy is the same in both conditions, further investigation may not be necessary. This would limit radiation doses to mother and foetus.

In terms of the risks of radiation from investigations in pregnancy, these vary for foetus and mother depending on the investigation:

- CTPA gives greater dose to mother, especially to the breast, but lower foetal dose. Average foetal radiation dose is <10% of V/Q scan in all trimesters of pregnancy. This must be offset by relatively higher risk of breast cancer in mother.
- VQ scans administer a greater dose to foetus, but less to mother than CTPA. Carry slightly higher risk of childhood cancer compared with CTPA; can affect foetal or neonatal thyroid function.

Usually what is best for the foetus is considered paramount, but when feasible women should be involved in the decision to undergo CTPA or V/Q scanning. Ideally, informed consent is obtained before these tests are undertaken.

Management of PE in pregnancy

- The use of D-dimer in pregnancy is not appropriate
- MDT input is valuable, especially when there is diagnostic uncertainty
- If CXR and Doppler USS are both normal with low level of clinical suspicion, can stop LMWH.
- If Doppler USS confirms diagnosis of DVT, continue anticoagulation.
- If Doppler is negative but clinical suspicion of PE is high, continue LMWH then repeat Doppler USS (or another diagnostic test) within 1 week; if repeat testing is negative and clinical review suggests low risk of PE, discontinue anticoagulation.
2. Oncology patients

PE may present in 2 ways in patients with a known diagnosis of cancer:
- With clinical suspicion of PE – follow pathway as for non-cancer patients
- PE diagnosed on routine staging CT scan – continue pathway after diagnosis

Management of PE in oncology patients

- Following assessment, involvement of the patient’s oncologist is essential within 24 hours of diagnosis/clinical suspicion of PE. LMWH can be commenced until a definitive management plan is agreed by oncologist.
- When PE is diagnosed opportunistically on imaging, the radiologist will refer the patient to the on-call medical team for assessment. The medical team will then contact the patient’s Consultant Oncologist for involvement in management.
- Evidence indicates LMWH is usually superior to warfarin in cancer patients in terms of bleeding risk, recurrence/progression of thrombosis and potential interaction with chemotherapeutic agents. Therefore continue LMWH unless oncologist decides to switch to warfarin.
- Some cancer patients may be suitable for management of their PE on an ambulatory pathway, especially when detection has initially been made through routine CT scanning. Management of these patients may differ from standard practice for PE in that PESI of Class 3 or 4 may not prevent their outpatient management (see page 6 for standard practice). Discussion with the patient’s Consultant Oncologist, with consideration of relative risk/benefits, is essential.

3. IV Drug Abusers

On presentation with suspected PE, septic emboli should be considered as a cause and additional investigations with blood cultures / infection screens undertaken.

These patients may be poorly compliant, making it difficult to control their INR with warfarin. They can be treated with longer term LMWH, if appropriate.

Patients receiving longer term LMWH should have a full blood count checked at day 5 and then every 4-6 weeks to check for HIT.

4. Patients with Alcoholism

Alcoholics with diagnosed thromboembolic disease may present problems if treated with oral anticoagulants - they may be poorly compliant and binge-drinking may interfere with control of their INR. Furthermore, accidental falls or altercations pose a risk of bleeding whist on anticoagulants. Thus a team approach which may involve senior clinicians, nurses, social workers, carers and the patient is often appropriate.
Appendix 2

1. Tinzaparin for the treatment of pulmonary embolism

In the treatment of pulmonary embolism, tinzaparin should be administered subcutaneously as a single daily injection of 175 anti-Factor Xa IU/kg bodyweight once daily, for at least 6 days, and until adequate oral anti-coagulation is established.

Tinzaparin (innohep®) for treatment of DVT/PE is available as 20,000 anti-Factor Xa IU/ml in 0.5ml, 0.7ml and 0.9ml colour-coded syringes and as a multi-dose vial.

The dosing chart below indicates the volume of tinzaparin that needs to be administered when treating pulmonary embolism, and the most convenient and cost-effective formulation to use in each case (figures rounded to the nearest 0.05ml).

e.g. a 70kg patient will require 12,000 units (0.6ml) tinzaparin (20,000 anti-Factor Xa IU/ml) given via a yellow 0.7ml syringe.

Renal impairment

Caution is recommended when treating patients with renal impairment. Monitoring of anti-factor Xa activity should be considered in patients with severe renal impairment (creatinine clearance < 30 ml/min); however, available evidence suggests that no dose reduction is needed in patients with creatinine clearance levels down to 20 ml/min.

Monitoring

Risk assessment and clinical monitoring are the best predictors of the risk of potential bleeding. Routine anti-Xa activity monitoring is usually not required (see above). However, anti-Xa activity monitoring might be considered in those patients treated with LMWH who also have either an increased risk of bleeding (such as those with renal impairment, elderly and extremes of weight) or are actively bleeding. As there is a risk of antibody-mediated heparin-induced thrombocytopenia, platelet counts should be measured in patients receiving heparin treatment for longer than 5 days and the treatment should be stopped immediately in those who develop thrombocytopenia. Plasma potassium should be measured in patients at risk before starting heparin therapy and monitored regularly thereafter, particularly if treatment is prolonged beyond about 7 days.

Further information to aid prescribing is available by viewing the Summary of Product Characteristics at: http://www.medicines.org.uk/emc/medicine/5176/SPC/Innohep+20%2c000+IU+ml+and+Innohep+syringe+20%2c000+IU+ml/
**DVT and PE Treatment Dosage**

For 20,000 anti-Factor Xa IU/ml variable dose syringe or multi-dose vial

Dosage: 175 anti-Factor Xa IU/kg bodyweight once daily for at least 6 days and until adequate oral anti-coagulation is established

<table>
<thead>
<tr>
<th>Bodyweight (kg)</th>
<th>Prescribed Dose anti-Factor Xa IU</th>
<th>Injection Volume subcutaneous inj. (ml)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>innohep® 0.5 ml syringe</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32 - 37&quot;&quot;</td>
<td>6,000</td>
<td>0.30</td>
</tr>
<tr>
<td>38 - 42</td>
<td>7,000</td>
<td>0.35</td>
</tr>
<tr>
<td>43 - 48</td>
<td>8,000</td>
<td>0.40</td>
</tr>
<tr>
<td>49 - 54</td>
<td>9,000</td>
<td>0.45</td>
</tr>
<tr>
<td>55 - 59</td>
<td>10,000</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>innohep® 0.7 ml syringe</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60 - 65</td>
<td>11,000</td>
<td>0.55</td>
</tr>
<tr>
<td>66 - 71</td>
<td>12,000</td>
<td>0.60</td>
</tr>
<tr>
<td>72 - 77</td>
<td>13,000</td>
<td>0.65</td>
</tr>
<tr>
<td>78 - 82</td>
<td>14,000</td>
<td>0.70</td>
</tr>
<tr>
<td><strong>innohep® 0.9 ml syringe</strong></td>
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<td></td>
</tr>
<tr>
<td>83 - 88</td>
<td>15,000</td>
<td>0.75</td>
</tr>
<tr>
<td>89 - 94</td>
<td>16,000</td>
<td>0.80</td>
</tr>
<tr>
<td>95 - 99</td>
<td>17,000</td>
<td>0.85</td>
</tr>
<tr>
<td>100 - 105</td>
<td>18,000</td>
<td>0.90</td>
</tr>
<tr>
<td><strong>innohep® Multi-dose vial</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;105</td>
<td>175 IU/kg</td>
<td>Based on Weight</td>
</tr>
</tbody>
</table>

*These figures have been rounded to the nearest 0.85 ml.

"""No experience with children.

For patients above 105 kg in weight, the multi-dose vial can be used.

This document has been coated with an Antimicrobial Finish which reduces levels of bacteria by up to 99.0%.
### 2. Unfractionated Heparin (UFH)

#### ABERTAWE BRO MORGANWYG UNIVERSITY HEALTH BOARD

#### HEPARIN INJECTION PRESCRIPTION CHART

**INTRAVENOUS HEPARIN THERAPY TARGET APTT 1.5-2.5**

<table>
<thead>
<tr>
<th>Date</th>
<th>Dose</th>
<th>Dr's Sig</th>
<th>Given by</th>
<th>Checked by</th>
<th>Date &amp; Time Infusion started</th>
<th>Pharm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**2. HEPARIN INFUSION DOSE INITIATION.** (See guidelines)

Infusion strength 20,000 units in 20ml (1000 units per ml)

<table>
<thead>
<tr>
<th>Date</th>
<th>Date &amp; Time APTT sample taken</th>
<th>APTT</th>
<th>Dr's Sig</th>
<th>Infusion Rate</th>
<th>Given by</th>
<th>Checked by</th>
<th>Date &amp; Time infusion started</th>
<th>Pharm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**3. HEPARIN INFUSION MAINTENANCE DOSE:** (See guidelines)

Infusion strength 20,000 units in 20ml (1000 units per ml)

<table>
<thead>
<tr>
<th>Date &amp; Time APTT sample taken</th>
<th>APTT</th>
<th>Dr's Sig</th>
<th>Infusion Rate</th>
<th>Given by</th>
<th>Checked by</th>
<th>Date &amp; Time infusion started</th>
<th>Pharm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Heparin Infusion Schedule - Guidelines

- Before starting heparin a coagulation screen and baseline APTT should be done.
- **1. HEPARIN LOADING DOSE:**
  - Give Loading Dose: Heparin 5,000 units i.v. over 5 mins
  - (Patients below 65Kg = 4,000 units)
  - (in severe pulmonary embolism 10,000 units may be used)

- **2. COMMENCE HEPARIN INFUSION:**
  - USP INFUSION STRENGTH 20,000 UNITS IN 20ML (1000 UNITS PER ML) only.
  - Start on an initial infusion rate of 18 units/kg/hour (> 0.018ml/kg/hr)
  - Due to the limitations of some syringe drivers round to the nearest 0.1ml.

- **3. HEPARIN INFUSION MAINTENANCE DOSE:**
  - Check APTT ratio after SIX HOURS
  - (Adjust dose according to APTT ratio as follows...)

<table>
<thead>
<tr>
<th>APTT Ratio</th>
<th>Infusion Rate Change</th>
<th>Recheck APTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;7.0</td>
<td>Step infuse for 3 hours and seek medical opinion, THEN REDUCE BY 6.5ml/hr (500 units/hr)</td>
<td>3 hrs</td>
</tr>
<tr>
<td>5.1-7.0</td>
<td>Step infuse for 60 mins and seek medical opinion, THEN REDUCE BY 8.5ml/hr (500 units/hr)</td>
<td>4 hrs</td>
</tr>
<tr>
<td>4.1-5.0</td>
<td>Step infuse for 30-60 mins, THEN REDUCE BY 0.5ml/hr (300 units/hr)</td>
<td>6 hrs</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>Step infuse for 30-60 mins, THEN REDUCE BY 0.2ml/hr (200 units/hr)</td>
<td>8 hrs</td>
</tr>
<tr>
<td>2.6-3.0</td>
<td>Step infuse for 30-60 mins, THEN REDUCE BY 0.1ml/hr (100 units/hr)</td>
<td>8 hrs</td>
</tr>
<tr>
<td>1.5-2.5</td>
<td>NO CHANGE</td>
<td>Within 24hrs</td>
</tr>
<tr>
<td>1.2-1.4</td>
<td>Consider further IV loading dose of 2500 IU</td>
<td>INCREASE BY 0.2ml/hr (200 units/hr)</td>
</tr>
<tr>
<td>&lt;1.2</td>
<td>Consider further IV loading dose of 5000 IU</td>
<td>INCREASE BY 0.4ml/hr (400 units/hr)</td>
</tr>
</tbody>
</table>

Platelet counts should be monitored in patients receiving heparin for more than 4 days. APTT must be checked a minimum of every 24 hours for every heparin patient. After every dose change check APTT ratio as per ‘Recheck APTT’ column.
Warfarin

Please refer to the Warfarin anti-coagulation guidelines (Appendix 3).

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Warfarin loading dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients with organ dysfunction / sepsis</td>
<td>Treat as an inpatient.</td>
</tr>
<tr>
<td></td>
<td>Discuss loading dose with senior clinician</td>
</tr>
<tr>
<td>All patients &lt; 75 years old and &gt; 60kg body weight and not taking potentiating drugs</td>
<td>Follow rapid initiation of warfarin for under 75 years (Fennerty scale) see appendix 3 Adult in-patient warfarin chart</td>
</tr>
<tr>
<td>Any patient who is either &gt; 75 years old, or &lt; 60 kg body weight or who is receiving potentiating drugs</td>
<td>Follow rapid initiation of warfarin for over 75 years, cardiac failure or liver failure, see appendix 3 Adult in-patient warfarin chart</td>
</tr>
<tr>
<td>When adopting the rapid initiation of warfarin for under 75 years or over 75 years always obtain a baseline INR and daily INR’s for the first four days as per the loading protocol. Please follow the induction of warfarin guidance as per the Adult in-patient warfarin chart (appendix 3)</td>
<td></td>
</tr>
</tbody>
</table>

See BNF Appendix 1. for details of potential drug reactions

1. Thrombolysis
Alteplase can be given to patients with massive PE who fulfil criteria for administration of thrombolysis. There is no evidence for positive effects on mortality and late morbidity related to pulmonary embolism.

Risk-benefit analysis of thrombolysis
As with all thrombolytic agents, the expected therapeutic benefit should be weighed up particularly carefully against the possible risk.

In Pulmonary Embolism, a total dose of 100 mg of alteplase should be administered in 2 hours. Most experience is available with the following dose regimen:

<table>
<thead>
<tr>
<th>Concentration of alteplase</th>
<th>1 mg/ml</th>
<th>2 mg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 mg as an intravenous bolus over 1 - 2 minutes</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>followed by an intravenous infusion of 90 mg over 2 hours</td>
<td>90</td>
<td>45</td>
</tr>
</tbody>
</table>

The total dose should not exceed 1.5 mg/kg in patients with a body weight below 65 kg.

Adjunctive therapy:

After treatment with alteplase (Actilyse), heparin therapy should be initiated (or resumed) when aPTT values are less than twice the upper limit of normal. The infusion should be adjusted to maintain aPTT between 50 - 70 seconds (1.5 to 2.5 fold of the reference value).
Contraindications to Thrombolysis

Hypersensitivity to the active substance or to any of the excipients.

Alteplase (Actilyse) is contraindicated in cases where there is a high risk of haemorrhage such as:
- significant bleeding disorder at present or within the past 6 months
- known haemorrhagic diathesis
- patients receiving oral anticoagulants, e.g. warfarin sodium
- manifest or recent severe or dangerous bleeding
- known history of or suspected intracranial haemorrhage
- suspected subarachnoid haemorrhage or condition after subarachnoid haemorrhage from aneurysm
- any history of central nervous system damage (i.e. neoplasm, aneurysm, intracranial or spinal surgery)
- recent (less than 10 days) traumatic external heart massage, obstetrical delivery, recent puncture of a non-compressible blood-vessel (e.g. subclavian or jugular vein puncture)
- severe uncontrolled arterial hypertension
- bacterial endocarditis, pericarditis
- acute pancreatitis
- documented ulcerative gastrointestinal disease during the last 3 months, oesophageal varices, arterial-aneurysm, arterial/venous malformations
- neoplasm with increased bleeding risk
- severe liver disease, including hepatic failure, cirrhosis, portal hypertension (oesophageal varices) and active hepatitis
- major surgery or significant trauma in past 3 months.
- any known history of haemorrhagic stroke or stroke of unknown origin
- known history of ischaemic stroke or transient ischaemic attack (TIA) in the preceding 6 months, except current acute ischaemic stroke within 3 hours.

Special warnings and precautions in acute pulmonary embolism

Thrombolytic/fibrinolytic treatment requires adequate monitoring. Actilyse should only be used by physicians trained and experienced in the use of thrombolytic treatments and with the facilities to monitor that use. It is recommended that when Actilyse is administered standard resuscitation equipment and pharmacotherapy be available in all circumstances.

The risk of intracranial haemorrhage is increased in elderly patients, therefore in these patients the risk/benefit evaluation should be carried out carefully.

As with all thrombolytic agents, the expected therapeutic benefit should be weighed up particularly carefully against the possible risk, especially in patients with:
- small recent traumas, such as biopsies, puncture of major vessels, intramuscular injections, cardiac massage for resuscitation
- conditions with an increased risk of haemorrhage

The use of rigid catheters should be avoided.

A dose exceeding 100 mg of alteplase must not be given because it has been associated with an additional increase in intracranial bleeding.

There is limited experience with readministration of Actilyse. Actilyse is not suspected to cause anaphylactic reactions. If an anaphylactoid reaction occurs, the infusion should be discontinued and appropriate treatment initiated.

The expected therapeutic benefit should be weighed up particularly carefully against the possible risk, especially in patients with systolic blood pressure > 160 mm Hg.

Further information, including special warnings and precautions for use, is available by viewing the Summary of Product Characteristics at:
http://www.medicines.org.uk/EMC/medicine/308/SPC/Actilyse/
ADULT INPATIENT WARFARIN CHART

Prescribe warfarin on the in-patient chart, write “see warfarin treatment chart” and attach this sheet securely to the chart. All doses must be given between 14.00 – 1600 hours. If warfarin temporarily withheld write “OMIT” on this chart.

### Affix addressograph label here

Name: ________________________________

Hospital Number: ______________________

Date of birth: _________________________

Ward: ________________________________

Consultant: __________________________

INR before starting warfarin

<table>
<thead>
<tr>
<th>Day</th>
<th>INR (best taken 0600-0800)</th>
<th>Warfarin dose (mg) (best given 1700-1800)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>&lt;1.4</td>
<td>10</td>
</tr>
<tr>
<td>Day 2</td>
<td>&lt;1.8</td>
<td>10</td>
</tr>
<tr>
<td>Day 3</td>
<td>&gt;1.8</td>
<td>0.5</td>
</tr>
</tbody>
</table>

### Rapid initiation of warfarin for 75 years and over

**Appendix 3**

<table>
<thead>
<tr>
<th>Day</th>
<th>INR (Best taken 0600-0800)</th>
<th>Warfarin dose (mg) (Best given 1700-1800)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>&lt;1.4</td>
<td>8</td>
</tr>
<tr>
<td>Day 2</td>
<td>&lt;1.8</td>
<td>8</td>
</tr>
<tr>
<td>Day 3</td>
<td>&gt;1.8</td>
<td>7.5</td>
</tr>
</tbody>
</table>

### Induction of warfarin for atrial fibrillation

Where atrial fibrillation is the sole indication, rapid loading with warfarin (using the nomograms across) is not required. Consider using a local low dose loading regime.

#### Induction of warfarin - Nomogram for target INR of 2.5

- Obtain a baseline INR and daily INRs for the first 4 days.
- If baseline INR >2.4, do not use the nomogram below. Review the indication for warfarin / seek haematological advice.
- If the patient is unstable (heart failure / liver disease / sepsis) consider using a therapeutic dose of low molecular weight heparin until the patient is stabilised.
- Give low molecular weight heparin for a minimum of 5 days (see SBF for special precautions) or until the INR is in the target range for 2 consecutive days (whichever is longer).

#### Nomograms for the loading and reloading of warfarin

<table>
<thead>
<tr>
<th>Date</th>
<th>INR result</th>
<th>Warfarin dose (mg)</th>
<th>Prescriber (Signature)</th>
<th>Next test (date)</th>
<th>Given by</th>
<th>Time &amp; Date</th>
</tr>
</thead>
</table>

### Induction of warfarin for over 75 years, cardiac failure or liver failure

<table>
<thead>
<tr>
<th>Day</th>
<th>INR (Best taken 0600-0800)</th>
<th>Warfarin dose (mg) (Best given 1700-1800)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>&lt;1.4</td>
<td>10</td>
</tr>
<tr>
<td>Day 2</td>
<td>&lt;1.8</td>
<td>5</td>
</tr>
<tr>
<td>Day 3</td>
<td>&gt;2.0</td>
<td>Omit</td>
</tr>
<tr>
<td>Day 4</td>
<td>&lt;2.0</td>
<td>5</td>
</tr>
<tr>
<td>Day 5</td>
<td>2.0 to 2.5</td>
<td>4</td>
</tr>
<tr>
<td>Day 6</td>
<td>2.6 to 2.9</td>
<td>3</td>
</tr>
<tr>
<td>Day 7</td>
<td>3.0 to 3.2</td>
<td>2</td>
</tr>
<tr>
<td>Day 8</td>
<td>3.3 to 3.6</td>
<td>1</td>
</tr>
</tbody>
</table>

- Miss one dose then 2 mg
- Miss two doses then 1 mg

Paper copies of this document should be kept to a minimum and checks made with the electronic version to ensure that the printed version is the most recent.
References

The following papers were used in the drafting of this guidance:

1. BTS guidelines for the management of suspected acute pulmonary embolism. Thorax 2003; 58:470-484
24. Management of Massive and Submassive Pulmonary Embolism, Iliofemoral Deep Vein Thrombosis, and Chronic Thromboembolic Pulmonary Hypertension; A Scientific Statement From the American


50. Miller AC and Boldy DAR. Pulmonary embolism guidelines: will they work? Thorax 2003;58:463


61. Drouet L, Bal dit Sollier C, Martin J.. Adding intravenous unfractionated heparin to standard enoxaparin causes excessive anticoagulation not detected by activated clotting time: Results of the STACK-on to ENOXaparin (STACKENOX) study.. American Heart Journal, 2009 Vol 158 (2) p177-184 2009;


64. Collignon F. et al. Thrombosis Research 1992 65 (Suppl 1) pS167; Abs P328

65. Thromb Haemost 2002; 87: 817–23 Dosing in Heavy-weight/Obsese Patients with the LMWH, Tinzaparin: A Pharmacodynamic Study James W. Hainer1, Jeffrey S. Barrett 2, Christopher A. Assaid1, Michael J. Fossler 2, Donna S. Cox2, Todd Leathers 1, Philip T. Leese3


72. Personal correspondence from Joanna Brindle, Medical Information Team Leader, Sanofi Avantis to Scott Pegler (May 2011)

73. Summary of Product Characteristics
   http://www.medicines.org.uk/EMC/medicine/24345/SPC/Clexane+pre-filled+syringes/

74. Unpublished pathways and guidance
   - Protocol for ambulatory management of PE at the Royal Berks, August 2011
   - Outpatient PE pathway North Teeside and Hartlepool NHS Foundation Trust
   - Pulmonary Embolism Pathway Checklist Portsmouth Hospitals NHS Trust
   - Cwm Taf Local Health Board - Emergency Care Centre Care Bundle for Pulmonary Embolism

This Guideline has been prepared by a working group chaired by Dr Jane Harrison (AMD for Primary Care) during 2012. For queries regarding it or its usage, contacts are as follows:

- Swansea Locality - Dr Chris Hudson, Clinical Director of Medicine Swansea Locality
- Neath Port Talbot Locality – Dr Firdaus Adenwalla, Clinical Director of Medicine Neath Port Talbot Locality
- Bridgend Locality – Dr Joanne Morris, Consultant Acute Care Physician, Princess of Wales Hospital
Authorisation form for items to be published onto COIN

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<tr>
<td>Name &amp; Signature of Author / Chair of Group or Committee *</td>
<td>Dr Jane Harrison, AMD (Primary Care)</td>
</tr>
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<td>December 2013</td>
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<td>December 2015</td>
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<tr>
<td>Name of Group or Committee *</td>
<td>Working group chaired by Dr Jane Harrison. Approved by Effective Practice Approval Committee</td>
</tr>
<tr>
<td>Name &amp; Signature of Lead Pharmacist*</td>
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* Mandatory