Anticoagulation Therapy for DVT and PE

Disclaimer

See also:
• Deep Vein Thrombosis

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Assessment

1. Consider history and clinical findings to determine whether the patient requires:
   • routine anticoagulation in general practice, or
   • acute haematological or surgical management due to:
     • **DVT and its complications.**

### DVT and its complications

- **Extensive proximal DVT:**
  - DVT extends to the iliac vessels. If a proximal DVT involves the ilio-femoral segment and extends into the inferior vena cava, urgent advice and referral is required – see Management.
  - The proximal extent of DVT is not visible.
  - Disabled by swelling and pain.
- **Symptoms of pulmonary embolism (PE).**

- existing tendency to bleeding due to anticoagulation or underlying bleeding disorder.
- **conditions complicated by anticoagulation.**

#### Conditions complicated by anticoagulation

- Any active bleeding, or conditions with a high risk of haemorrhage, for example:
  - Stroke
  - Platelet count $50 \times 10^9$/L
  - Bacterial endocarditis
  - Uncontrolled or severe hypertension
  - Severe hepatic or renal disease
  - Angiodysplasia.
- **Post surgery, within one month of:**
  - Eye surgery
  - Central nervous system surgery

- pregnancy-related DVT.
- active malignancy.

2. Arrange **blood tests** to help exclude **conditions that impact on anticoagulation therapy.**
Thrombophilia testing is not recommended at the time of an acute venous thrombus or within 3 months of a thrombotic event.

#### Conditions that impact on anticoagulation therapy

- Thrombocytopenia
- Severe renal disease
- Severe liver disease
Pregnancy

Blood tests

- FBE to exclude thrombocytopenia
- INR, APTT
- Renal function tests to exclude severe renal disease
- LFTs to exclude severe liver disease
- Beta-hCG to exclude pregnancy for women of childbearing age

3. Determine renal function:
   - Use the patient’s weight and the **Cockcroft and Gault creatinine clearance formula** to calculate creatinine clearance.

**Cockcroft and Gault creatinine clearance formula**

\[
CrCL \text{ (mL/min)} = \frac{(140 – \text{age}) \times \text{ideal body weight (kg)}}{\text{plasma creatinine (mcmol/L)} \times 0.8 \text{ if male} \times 0.85 \text{ if female}}
\]

- Ideal
- body weight (males) = 50 kg + 0.9 kg for each cm over 150 cm in height.
- Ideal body weight (females) = 45 kg + 0.9 kg for each cm over 150 cm in height.
- Use actual body weight if this is lower than the ideal body weight.

[Cockcroft and Gault formula](https://www.cockcroft-hunt.com)

- Do not use the eGFR when creatinine is changing, or at extremes of weight, as it is unreliable.

Management

**Practice Point**

### Select appropriate anticoagulant agents

- **Novel anticoagulants (NOACs)**, apixaban, or rivaroxaban, can be used for the acute treatment of venous thromboembolism (VTE) and the prevention of recurrent VTE. They are the preferred agents over warfarin if there is no contraindication to the use of NOACs. Dabigatran is not available in Australia for the treatment of VTE

**Specialist management**

1. If a proximal DVT involves the ilio-femoral segment and extends into inferior vena cava, discuss with the **Emergency Department** and arrange urgent transfer.
2. If patient is not suitable for outpatient, general practice anticoagulation management, arrange immediate haematology, obstetric, or surgical referral or admission. This may include patients with any of:
   - **DVT, PE, and clotting complications**
DVT, PE, and clotting complications

➢ Extensive proximal DVT:
  o DVT extends to the iliac vessels.
  o The proximal extent of DVT is not visible.
  o Disabled by swelling and pain.
➢ Symptoms of pulmonary embolism (PE).

• Conditions complicated by anticoagulation

• Pregnancy-related DVT

Pregnancy-related DVT

➢ Oral anticoagulants are contraindicated and the patient will need long-term treatment with low molecular weight heparin (LMWH).
➢ Manage in conjunction with an obstetric service and with haematology advice.
➢ Calculate LMWH dosing based on the patient’s booking weight or early pregnancy weight.
➢ When DVT is clearly pregnancy-related, anticoagulation should continue to at least 6 weeks postpartum or usual duration for type of DVT, whichever is longer.
➢ A first episode, pregnancy-related DVT is unlikely to require long-term anticoagulation.

• Active malignancy

Active malignancy

*If active malignancy, use low molecular weight heparin (LMWH):*
➢ Warfarin has been shown to be less effective in this situation.
➢ Specialist input is recommended i.e., oncologist involved in the treatment of the patient’s malignancy.

3. Seek haematology advice or arrange urgent or routine haematology referral if:
   • needing advice about LMWH dose adjustment.
   • there is uncertainty about the duration of anticoagulation treatment

Duration of anticoagulation treatment

➢ As a general rule for deep vein thrombosis (DVT):
  o For provoked distal DVT with reversible risk factors, treat for 3 months.
  o For unprovoked distal DVT, commence for 3 to 6 months and request urgent or routine haematology referral for consideration of indefinite treatment. These patients will generally be triaged for review toward the end of the anticipated duration of anticoagulation.
  o If ongoing or non-modifiable risk factors and re-thrombosis risk is greater than the risk of bleeding from therapy, consider indefinite treatment. Seek haematology advice.
  o If recurrent DVT, consider extended treatment > 6 months or indefinite treatment. Seek haematology advice.
  o If DVT is associated with malignancy, LMWH may need to continue indefinitely, as warfarin has been shown to be less effective. Seek haematology advice.
➢ For pulmonary embolism (PE):
  o If provoked PE, treat for 3 to 6 months and request urgent or routine haematology referral for consideration of indefinite treatment. These patients will generally be triaged for review toward the end of the anticipated duration of anticoagulation
  o If unprovoked PE, treat for > 6 months and refer for urgent or routine haematology referral for consideration of indefinite treatment. These patients will generally be triaged for review toward the end of the anticipated duration of anticoagulation.
  o For PE associated with malignancy, LMWH may need to continue indefinitely, as warfarin has been shown to be less effective. Seek haematology advice.

- patient has an unprovoked DVT or unusual site of thrombosis.

**General practice management**

If no active cancer and the patient is not pregnant, manage routine anticoagulation in general practice.

1. Determine renal function:
   - Use the patient’s weight and the Cockcroft and Gault creatinine clearance formula to calculate creatinine clearance.
   - Do not use the eGFR when creatinine is changing, or at extremes of weight, as it is unreliable.

2. Determine if there are any contraindications to the general practice use of rivaroxaban or apixaban.

**Apixaban**

➢ Patients not suited to apixaban in a primary care setting:
  o Pregnant, breastfeeding, or postpartum.
  o Age < 18 years.
  o Systolic blood pressure > 180, or diastolic > 115.
  o Anticipated compliance problem, even with support.
  o Severe renal impairment – creatinine clearance < 25 mL/min.
  o Known liver failure.
  o Potential bleeding lesions e.g., gastrointestinal, genitourinary, or intracranial bleeding < 4 weeks prior to commencing anticoagulation therapy.
  o Congenital or acquired bleeding disorders or platelets < 90 x 109/L.
  o Unusual site of thrombosis, without prior advice from haematologist.
  o Antiphospholipid syndrome.
  o On drugs where the addition of apixaban is contraindicated e.g.,azole antifungal, HIV protease inhibitor.

➢ PBS streamlined authority for:
  o initial and continuing treatment of acute symptomatic DVT without PE.
  o initial and continuing treatment of PE.
  o prevention of recurrent VTE.

➢ Dose: 10 mg orally twice daily for 7 days, followed by 5 mg twice daily for the remaining duration of therapy.

➢ See New Oral Anticoagulants.
**Rivaroxaban**

- Patients not suited to rivaroxaban in a primary care setting:
  - Pregnant, breastfeeding or postpartum.
  - Age < 18 years.
  - Systolic blood pressure > 180, or diastolic > 115.
  - Anticipated compliance problem, even with support.
  - Severe renal impairment – creatinine clearance < 30 mL/min.
  - Known liver failure.
  - Potential bleeding lesions e.g., gastrointestinal, genitourinary or intracranial bleeding < 4 weeks prior to commencing anticoagulation therapy.
  - Congenital or acquired bleeding disorders, or platelets < 90 x 10⁹/L.
  - Unusual site of thrombosis, without prior advice from haematologist.
  - Antiphospholipid syndrome.
  - On drugs where the addition of rivaroxaban is contraindicated e.g., azole antifungal, HIV protease inhibitor.

- PBS streamlined authority for:
  - Initial and continuing treatment of acute symptomatic DVT without PE.
  - Initial and continuing treatment of PE.
  - Prevention of recurrent VTE.

- Dose:
  - 15 mg orally twice daily for 3 weeks, followed by 20 mg once daily for the remaining duration of therapy.
  - Advise the patient to take their doses with food.

  ➢ See New Oral Anticoagulants.

3. Start anticoagulation treatment with one of:
   - **NOACs**

**NOACs**

- **Apixaban** – 10 mg twice a day for 7 days, then 5 mg twice a day if renal function is adequate (CrCl > 30 ml/min)
- **Rivaroxaban** – 15 mg twice a day for 3 weeks, then 20 mg once a day, if renal function is adequate (CrCl > 30 ml/min)

  If using apixaban or rivaroxaban, low molecular weight heparin (LMWH) clexane is not necessary.
  If unsure about dose modification, request haematology advice.

- **Low molecular weight heparin (LMWH)** enoxaparin (Clexane)

**Low molecular weight heparin (LMWH)**

- Start anticoagulant therapy subcutaneous injections of low molecular weight heparin (LMWH), usually enoxaparin (Clexane).
- Calculate the dose and timing of enoxaparin.
Dose and timing of enoxaparin

Choose from two regimens:

- **Twice-daily dosing regimen** – 1 mg/kg twice daily subcutaneous
  - Use for patients with:
    - BMI ≥ 30
    - High risk of clotting (including pregnancy, iliac clot or active malignancy).
  - Also suitable for all other patients with proximal DVT.

- **Once-daily dosing regimen**: – 1.5 mg/kg daily subcutaneous
  - Suitable for distal DVT or proximal DVT.
  - If a calculated single daily dose is > 150 mg, change to a twice-daily regimen.

➢ Modify dosage of enoxaparin in patients with:

  - **extremes of weight** e.g., < 45 kg or > 150 kg.

**Extremes of weight**

- The specialist may advise to monitor the dose using anti-factor Xa.
- If anti-Xa testing is planned, the blood sample should be taken 4 hours after the dose, to reflect the peak level. Therapeutic levels should be checked, with the laboratory performing the test.

- **Chronic renal impairment** e.g., creatinine clearance < 50 mL/minute.

**Renal impairment**

- Dose reduction is recommended if creatinine clearance < 30 mL/minute.
- Although no adjustment is recommended for moderate renal impairment (creatinine clearance 30 to 50 mL/minute), enhanced vigilance for bleeding is required. Consider requesting renal or haematology advice.

If uncertain, request haematology advice about dose modification.

➢ Arrange:

- **first dose of enoxaparin and ongoing administration**.

**Ongoing administration**

- Teach the patient to self-administer, or a family member or carer to administer.
- Arrange for community nursing to administer.

- **blood monitoring** while the patient is on enoxaparin or other low-molecular-weight heparin (LMWH).

**Blood monitoring**

Arrange FBE to check platelets:

- If LMWH is used longer-term, there is a risk of heparin-induced thrombocytopenia (HIT), which can occur beyond day 5.
- Check platelets every second day for 2 weeks, even if LMWH is ceased during this period of time.
- If the platelets reduce by 30 to 50%, stop LMWH and request urgent or routine haematology referral.
Monitor for hyperkalaemia in a higher-risk patient e.g., chronic renal failure, diabetes.

**Warfarin**

If starting warfarin therapy, commence warfarin with 5 mg daily at the same time as enoxaparin (Day 1):

- Arrange daily INRs.
- Monitor warfarin and keep the INR between 2 and 3.
- Continue LMWH enoxaparin until INR is > 2 for two consecutive days and until at least 5 days of enoxaparin has been administered.
- Do not commence warfarin without LMWH enoxaparin due to the high rate of thrombus extension associated with initiation of warfarin therapy in a patient with an active clot.

4. Determine the **duration of anticoagulation treatment**.

5. Follow-up.

**Follow-up**

- Monitor:
  - for signs of bleeding, including anaemia, haematuria, malaena.
  - compliance and use of other medications which increase bleeding risk.
  - for signs of recurrent VTE. If VTE recurs while on anticoagulation therapy (and patient reports compliance with treatment), seek haematology advice.
- Cease treatment at the end of planned duration of therapy. If VTE recurs after cessation, seek haematology advice.
- NOACs:
  - Monitor renal function and adjust dose if indicated, routine laboratory monitoring is not possible.
  - INR is not used to monitor the anticoagulant effect of NOACs.
- LMWH:
  - Monitor renal function and adjust dose if indicated.
  - Check platelets.

  **Check platelets**
  - If LMWH is used longer-term, there is a risk of heparin-induced thrombocytopenia (HIT), which can occur beyond day 5.
  - Check platelets every second day for 2 weeks, even if LMWH is ceased during this period of time.
  - If the platelets reduce by 30 to 50%, stop LMWH and request urgent or routine haematology referral.
- Warfarin:
  - Monitor INR regularly, or as indicated, aiming for target INR 2.0 to 3.0.
  - See Warfarin – Starting and Monitoring.
Referral

- If a proximal DVT involves the ilio-femoral segment and extends into inferior vena cava, discuss with the Emergency Department and arrange urgent transfer.
- If patient is unsuitable for outpatient, general practice anticoagulation, arrange immediate haematology, obstetric, or surgical referral or admission.
- If suspected heparin-induced thrombocytopenia, request urgent or routine haematology referral.
- Seek haematology advice or arrange urgent or routine haematology referral if:
  - DVT in pregnancy.
  - needing advice about LMWH dose adjustment.
  - there is uncertainty about the duration of anticoagulation treatment.
  - patient has an unprovoked DVT or unusual site of thrombosis.

Information

For health professionals

Further information

- Australian Family Physician – Anticoagulation: A GP Primer on New Oral Anticoagulants
- Medicine Today – Practical Issues with Using Novel Oral Anticoagulants
- NSW Clinical Excellence Commission:
  - Anticoagulants
  - NOAC Guidelines

For patients

- National Blood Clot Alliance – Stop The Clot: Prevention Of Deep Vein Thrombosis and Pulmonary Embolism
- NHS Choices – Treatment: Deep Vein Thrombosis

Sources

Select bibliography


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