NOACs for DVT and PE in adults

Prescribing criteria for Rivaroxaban (Xarelto®) or Dabigatran (Pradaxa®) in the treatment of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) and prevention of recurrent DVT and PE in adults

- Although Dabigratran has recently received NICE approval for this indication, Rivaroxaban will continue to be the first line NOAC of choice as it is an established treatment for this indication
- Dabigratran also requires at least 5 days loading with a parenteral anticoagulant before use which is a disadvantage
- For dosage information see SPC

Hospital DVT treatment pathways

- The hospital treatment pathways found via the links below advise the GP how to deal with suspected DVTs according to which local hospital trust the patient is to be sent to for further investigation
- The treatment pathways should be used in conjunction with our documents about Rivaroxaban if that particular anticoagulant is being considered

RUH (Bath)


SFT (Salisbury)

A large range of documents regarding VTE can be accessed via:
The DVT pathway can be found here:
http://www.icid.salisbury.nhs.uk/clinicalmanagement/vascular/documents/suspecteddeepvenenthrombosisreferralformaugust%202012.doc

GWH (Swindon)

- See treatment pathway overleaf

Pulmonary Embolism

- NICE recommends rivaroxaban as a possible treatment for adults with pulmonary embolism and to prevent a further deep vein thrombosis or pulmonary embolism (June 2013)
- Follow this link for further information: http://www.nice.org.uk/guidance/ta287
- The above treatment pathways only discuss treatment of DVT. However, if a patient needs to have Rivaroxaban for a PE, the following documents are applicable to that situation as well and Rivaroxaban is on our local formularies for this indication
- Dabigatran has also been approved as a possible treatment for adults with deep vein thrombosis or pulmonary embolism (but not used locally as a first-line option) and further information can be found here:
  - https://www.nice.org.uk/guidance/ta327
NOACs for DVT and PE in adults

GWH OP DVT Treatment Flowchart

Patient (NHS Swindon or NHS Wiltshire) attends single point of access (SEQOL) for initial assessment including FBC, Urea and electrolytes, eGFR, LFT’s D-Dimer, Wells score and +/- Doppler ultrasound. If appropriate commence treatment dose LMWH (Dalteparin) given s/c once daily until result of Doppler scan known

Scan Positive

Refer to anticoagulant clinic for on-going anticoagulation with either Warfarin or Rivaroxaban. Continue LMWH until patient is seen by anticoagulant team

Rivaroxaban:
NICE TA261 for DVT and NICE TA287 for PE recommend:
Rivaroxaban is an option for the treatment of DVT and PE and prevention of recurrent DVT and PE in adults.
Both rivaroxaban and warfarin are available as options for the treatment of VTE patients.
Rivaroxaban will be considered for use first-line for all patients with distal DVT, provoked DVT, any other forms of DVT or PE.

Anticoagulant team to consider warfarin or rivaroxaban for each patient:
1.) Use “warfarin and rivaroxaban decision aid for DVT and PE” to help decide the optimum treatment for the patient.  (See p.3)
2.) If Rivaroxaban is being considered, use the “Rivaroxaban prescribing criteria for DVT & PE” to ensure that it is prescribed safely & that the NICE criteria are fulfilled. (See p.5)

Treat with Rivaroxaban

- Fully counsel patient re: anticoagulation
- Prescribe Rivaroxaban 15mg b.d issuing a 21 day pack (42 tabs)
- Issue patient with information leaflet and alert card
- For Swindon patients: Arrange to review patient in the anticoagulant clinic in 3 weeks time to reduce the dose of Rivaroxaban to 20mg daily issuing a further 28 days prescription.
- For Wilts patients : Arrange appointment with GP in 3 weeks time to reduce dose and check compliance
- Transfer care to GP for further supplies
- For all patients fax all details to patients GP

Scan negative

SEQOL team will liaise with patients GP to further investigate symptoms, LMWH discontinued

Considerations – warfarin may be more appropriate:
1.) For patients with a Cr CL below 30ml/min or eGFR below 30ml/min/1.73m
Refer to the “Rivaroxaban prescribing criteria for DVT & PE” document for further advice in any patient with a Cr CL below 50ml/min or eGFR below 50ml/min/1.73m³.
2.) If HAS bled score > 3 (although this should not be used as a decision not to anticoagulate).

Treat with Warfarin

- Fully counsel patient re anticoagulation, including information leaflet and alert card
- Prescribe warfarin and continue with LMWH until INR>2 on two consecutive occasions.
- Either: Review patient in the anticoagulant clinic until LMWH can be discontinued
- Or: Arrange for follow up with patients GP and or D/N services to monitor INR’s and discontinue LMWH when appropriate

N.B. Dabigatran not included in flowchart as it is not a first-line option.

NOACs for DVT & PE
Updated December 2014. Review due July 2016
NHS Wiltshire CCG Medicines Management Team
### NOACs for DVT and PE in adults

**Warfarin and Rivaroxaban Decision Aid for DVT and PE**

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Warfarin (variable dosing od)</th>
<th>Rivaroxaban 15mg bd for 3/52 loading (provided by hospital), then 20mg od.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cost</strong></td>
<td>£220 p.a. (inc. monitoring)</td>
<td>£766.50 p.a.</td>
</tr>
<tr>
<td><strong>Licensed indication &amp; NICE criteria</strong></td>
<td>Prophylaxis &amp; treatment of venous thrombosis &amp; pulmonary embolism; Prophylaxis of systemic embolism in pts with rheumatic heart disease and AF; prophylaxis after insertion of prosthetic heart valves; transient attacks of cerebral ischaemia.</td>
<td><strong>NICE TA261</strong> and <strong>NICE TA287</strong> for PE allow rivaroxaban to be used as an option in the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent VTE in adults. Rivaroxaban is also licensed for prevention of stroke and systemic embolism in adult patients with non valvular AF, and prophylaxis of venous thromboembolism in adults after total hip or total knee replacement surgery.</td>
</tr>
<tr>
<td><strong>Clinical Experience</strong></td>
<td>Has been used for &gt;50yrs.</td>
<td>Long term safety data is limited to the duration of treatment exposure of up to 2 years in the clinical trials, EINSTEIN-DVT &amp; EINSTEIN-EXT. EINSTEIN-PE had a mean study duration of 9 months. Available as an anticoagulant since Nov 2011.</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>Regular INR tests are needed in order to ensure the correct dose is being taken.</td>
<td>No anticoagulation monitoring is needed (therefore unable to check adherence). No requirement in Summary of Product Characteristics (SPC) to do U&amp;Es but it may be useful to monitor renal function as the dose needs adjusting if renal function declines.</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>Variable dose once daily dose according to INR.</td>
<td>15mg bd for 3/52 loading, then reduce to 20mg once daily (duration depends on the type of DVT or PE).</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td>See Rivaroxaban information</td>
<td>Non-inferior to warfarin in EINSTEIN-DVT (n=3449 pts). 2.1% of rivaroxaban-treated pts had recurrent VTE compared with 3.0% of patients receiving standard treatment (hazard ratio: 0.68; 95% CI 0.44 to 1.04). Non-inferior to std therapy (p=0.003) in the treatment of PE in EINSTEIN-PE.</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td>See Rivaroxaban information</td>
<td><strong>EINSTEIN-DVT:</strong> Primary safety outcome (major bleeding or clinically relevant non-major bleeding) (p=0.77) 8.1% 8.1%  <strong>EINSTEIN-PE:</strong> Major or clinically relevant non-major bleeding (HR, 0.90; 95% CI, 0.76-1.07; p=0.23). 10.3% 11.4%  <strong>EINSTEIN-PE:</strong> Major bleeding (HR, 0.49; 95% CI, 0.31 to 0.79; p=0.003). 1.1% (26pts) 2.2% (52pts)</td>
</tr>
</tbody>
</table>

Continued overleaf.
<table>
<thead>
<tr>
<th>Comparator</th>
<th>Warfarin (variable dosing od)</th>
<th>Rivaroxaban 15mg bd for 3/52 loading, then 20mg od.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Impairment</td>
<td>If anticoagulation is needed, warfarin may be used in this group of patients with very careful monitoring &amp; specialist advice.</td>
<td>Plasma levels may be significantly increased (1.6 fold in severe renal impairment) which may lead to an increased bleeding risk. A reduction of maintenance dose to 15mg once daily should be considered if assessed risk of bleeding outweighs risk of recurrent DVT and PE. Cr Cl 15-29ml/min - use with caution Cr Cl &lt;15ml/min - use is not recommended <em>It is advisable to use warfarin as an alternative in patients with a Cr Cl 15-29ml/min if renal function might be expected to deteriorate further.</em></td>
</tr>
<tr>
<td>CKD 4 or 5 Cr Cl 0-29ml/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD3 Cr Cl 30-49ml/min</td>
<td>Safe to use</td>
<td>If Cr Cl 30-49ml/min, a reduction of maintenance dose to 15mg once daily should be considered if assessed risk of bleeding outweighs risk of recurrent DVT and PE.</td>
</tr>
<tr>
<td>Administration &amp; stability</td>
<td>Not suitable to go in a dossette box unless a risk assessment has been undertaken and a management plan is in place to manage dosage changes (NPSA guidance)</td>
<td>Suitable to go into a dossette box. Take with food.</td>
</tr>
<tr>
<td>Hepatic Impairment</td>
<td>Monitor INR more frequently</td>
<td>Contraindicated in hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B &amp; C.</td>
</tr>
<tr>
<td>Antidote for haemorrhage</td>
<td>Vitamin K</td>
<td>Rivaroxaban is not reversible. Early clinical trial data suggests bleeding effects completely reversed by Prothrombin Complex Concentrate (PCC) (very limited clinical experience with this). Otherwise, supportive care only. Potential problem where emergency surgery is needed.</td>
</tr>
</tbody>
</table>
| Prescriber guides and patient alert cards | Yellow books available via SBS (stationary order) | Available from: [http://www.xarelto-info.co.uk/](http://www.xarelto-info.co.uk/)

**NOTE : Drug Safety Update Oct 2013 - Revised contraindications for all NOACs**


N.B. Dabigatran not included in decision aid as it is not a first-line option.

Warfarin contraindications:

[http://www.medicines.org.uk/emc/medicine/25626/SPC/Warfarin+0.5mg+Tablets/#CONTRAINDICATIONS](http://www.medicines.org.uk/emc/medicine/25626/SPC/Warfarin+0.5mg+Tablets/#CONTRAINDICATIONS)

Rivaroxaban contraindications:


Dabigatran contraindications:

[http://www.medicines.org.uk/emc/medicine/24839#CONTRAINDICATIONS](http://www.medicines.org.uk/emc/medicine/24839#CONTRAINDICATIONS)