What are NOACs used for?

Novel oral anticoagulants have been approved by NICE for the prevention of stroke and systemic embolism in the following conditions:

- **Dabigatran**: Non-valvular atrial fibrillation; elective hip or knee replacement surgery.
- **Apixaban**: Non-valvular atrial fibrillation; elective hip or knee replacement surgery.
- **Rivaroxaban**: Non-valvular atrial fibrillation; elective hip or knee replacement surgery; treatment and prevention of recurrent pulmonary embolism (PE) and deep vein thrombosis (DVT).

How do NOACs work?

Novel oral anticoagulants interrupt the production of a thrombus. Dabigatran is a direct thrombin inhibitor whereas apixaban and rivaroxaban are both direct inhibitors of clotting factor Xa. Anticoagulant monitoring (INR) is not required, however, to ensure optimum therapy and appropriate dose, kidney and liver function should be assessed before and routinely during treatment.

Missed Dose Advice

<table>
<thead>
<tr>
<th>Drug</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Taken twice a day and a missed dose can still be taken up to 6 hours prior to the next due dose. If the next dose is due in less than 6 hours, then omit missed dose and take next scheduled dose as normal.</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Taken twice daily, a missed dose should be taken as soon as remembered and the next dose taken on time as usual. If necessary the total daily dose can be taken at once.</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Taken once daily, if a dose is missed the patient should take it immediately and continue on the following day with the once daily dose as recommended. The dose should not be doubled within the same day to make up for a missed dose (see below for exception).</td>
</tr>
</tbody>
</table>

Missed Dose Advice for the initial 21 day treatment phase of an acute DVT or PE

Rivaroxaban is taken twice a day (15mg bd) for the initial 21 days. A missed dose should be taken as soon as remembered and the next dose taken on time as usual. If necessary the total daily dose can be taken at once i.e. 30mg once a day.

Other points to remember

See BNF for dosage regime when initiating NOACs, for different indications, in renal impairment and general frailty.
Lifestyle issues

- Counsel patient to reduce alcohol intake to within safe limits (women 2-3 units/day; men 3-4 units/day). NOACs do not interact with alcohol but excessive intake is best avoided due to increased bleeding risks.
- Advise patient to avoid stimulants including excessive caffeine or drug use
- Counsel patient on weight reduction if overweight. Signpost local weight management or exercise schemes (see local authority website for information)
- Advise patients who smoke of benefits of smoking cessation and refer to Pharmacy Stop Smoking services or Stop Smoking Wales if willing to stop
- Advise patient to avoid physical stress, high-intensity or contact sports

Red flags that need medical referral

- Bleeding e.g. dark stools, nose bleed. Unlike warfarin, there is no specific antidote for NOACs although steps can be taken to reverse their effects in the event of a major bleed
- Signs of stroke (numbness, weakness/paralysis, slurred speech, blurred vision, confusion & severe headache)
- Signs of DVT (pain and tenderness in one leg; both may be affected, tenderness, change of skin colour and temperature)
- Signs of PE (increasing breathlessness, chest pain, blood in sputum)

What are the common side effects to look out for?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Common side effects</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Dyspepsia</td>
<td>Advise patient to take medication with food but if ongoing/worsening dyspepsia then refer to GP</td>
</tr>
<tr>
<td></td>
<td>Nausea, diarrhoea, abdominal pain, anaemia, bleeding</td>
<td>Refer to GP</td>
</tr>
<tr>
<td>Apixaban ▼</td>
<td>Nausea, bleeding, bruising, anaemia</td>
<td>Refer to GP</td>
</tr>
<tr>
<td>Rivaroxaban ▼</td>
<td>Nausea, vomiting, diarrhoea, constipation, dyspepsia, abdominal pain, anaemia, hypotension, dizziness, headache, renal impairment, haemorrhage</td>
<td>Refer to GP</td>
</tr>
</tbody>
</table>

▼ Report all suspected adverse effects at www.yellowcardwales.org

Potential serious drug interactions?

NOACs can interact with many other medications - See BNF Appendix1: Interactions for more details

- NSAIDs, other anticoagulants, antiplatelets, SSRIs, systemic steroids – increased risk of haemorrhage
- Antifungals, diltiazem, verapamil, amiodarone, dronedarone – plasma concentration of NOAC increased
- Rifampicin, carbamazepine, phenytoin, phenobarbital, St John’s Wort – plasma concentration of NOAC decreased.

Where can you find more information?

- WCPE Cardiovascular disease- anticoagulant therapy; e-learning module (http://www.wcppe.org.uk)
- BNF sub-section 2.8.2 Oral anticoagulants (www.bnf.org)
- WeMeReC - Newer oral anticoagulants (http://www.wemerec.org)
- NICE Clinical Knowledge Summaries – anticoagulation, oral (http://www.cks.nice.org.uk) (note current licensed NOACs and their indications are being reviewed).
- NHS Choices – healthy living (www.nhs.uk/Livewell)
- Manufacturers’ Summary of Product Characteristics (SPCs) on www.medicines.org.uk

References

1. Patient alert cards - (http://www.pradaxa.co.uk/hcp/vte/educational-pack-uk.php; http://www.xarelto-info.co.uk; https://eliquis.co.uk/riskminimisationtools/)