



NON-VITAMIN K ANTAGONIST ORAL ANTICOAGULANTS (NOACs)

Top tips for MURs

- Check patient/carer understands the purpose of the NOAC*
- Counsel patient on the need to take medication regularly and address any compliance issues
- Advise patient on managing missed doses (see below)
- Check patient has been supplied with a medication alert card and encourage them to carry card at all times (available from individual product manufacturer - see reference overleaf)
- Check patient has had at least one routine blood test for kidney function in the last year
- Advise patient not to use over the counter NSAIDs or aspirin which could increase bleeding risk
- Advise patients taking dabigatran that they must not remove the capsule from the original packaging until administered; it is not suitable for supply in a multi-compartment compliance aid
- Advise patients to take rivaroxaban with food as this significantly affects plasma levels. Apixaban, dabigatran and edoxaban can be taken with/without food (with food can reduce dyspepsia)
- NOACs should be avoided in pregnant patients and those who are breast feeding. Women of child bearing potential should be counselled appropriately.
- Counsel patient on signs and symptoms that need referral (see red flags overleaf)
- Counsel patients on common side effects (see overleaf)
- Report any relevant adverse drug reactions to the Yellow Card Scheme

* Also known as 'Novel Oral Anticoagulants' or 'direct Oral Anticoagulants' (DOACs)

What are NOACs used for?

Four non-vitamin k antagonist oral anticoagulants (NOACs) 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; treatment and secondary prevention of recurrent pulmonary embolism (PE) and deep vein thrombosis (DVT). |
| Apixaban | Non-valvular atrial fibrillation; elective hip or knee replacement surgery; treatment and secondary prevention of recurrent pulmonary embolism (PE) and deep vein thrombosis (DVT). |
| Rivaroxaban | Non-valvular atrial fibrillation; elective hip or knee replacement surgery; treatment and secondary prevention of recurrent PE and DVT. |
| Edoxaban | Non-valvular atrial fibrillation; treatment and secondary prevention of recurrent PE and DVT. |

How do NOACs work?

Non-vitamin K antagonist oral anticoagulants (NOACs) interrupt the production of a thrombus. Dabigatran is a direct thrombin inhibitor whereas apixaban, edoxaban and rivaroxaban are direct inhibitors of clotting factor Xa. Anticoagulant monitoring (INR) is not required, however, a coagulation/ clotting screen should also be performed before treatment and kidney and liver function should be assessed before and routinely during treatment.

Missed Dose Advice

| | |
|-------------|---|
| Dabigatran | 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. |
| Apixaban | Taken twice daily, a missed dose should be taken as soon as possible on the same day and twice daily administration should be resumed; the dose should not be doubled to make up for a missed dose. |
| Rivaroxaban | 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). |
| Edoxaban | 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. |

Missed Dose Advice for rivaroxaban in the initial 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 information on duration of therapy and dosage regime when initiating NOACs, for different indications, in renal impairment and general frailty.

Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 more days, with several alcohol free days)
- Counsel patient on healthy eating, exercise & weight loss (if BMI > 25kg/m²) – reduce saturated fat and salt intake, avoid salt substitutes, increase oily fish intake, complete 30 minutes of aerobic exercise three to five times a week, reduce caffeine intake to no more than 5 cups a day and recommend 5 portions of fruit and vegetables a day
- 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. There is no specific antidote for rivaroxaban, apixaban and edoxaban, there is a licensed antidote for dabigatran - Idarucizumab (Praxbind)
- 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)
- Pregnancy, as NOAC's safety in pregnancy has not been established

What are the common side effects to look out for?

| Drug | Common side effects | Recommendation |
|-------------|--|--|
| Dabigatran | Dyspepsia | Advise patient to take medication with food but if ongoing/worsening dyspepsia then refer to GP. |
| | Nausea, diarrhoea, abdominal pain, anaemia, bleeding | Minor bleeding - refer to GP. Major bleeding - i.e. haemorrhage - refer to A+E |
| Apixaban | Nausea, bleeding, bruising, anaemia | Minor bleeding - refer to GP Major bleeding - i.e. haemorrhage - refer to A+E |
| Rivaroxaban | Nausea, vomiting, diarrhoea, constipation, dyspepsia, abdominal pain, anaemia, hypotension, dizziness, headache, renal impairment, haemorrhage | Minor bleeding - refer to GP Major bleeding - i.e. haemorrhage - refer to A+E |
| Edoxaban | Nausea, rash, anaemia, minor bleeding | Minor bleeding - refer to GP Major bleeding - i.e. haemorrhage - refer to A+E |

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.

* exception for rivaroxaban - prophylaxis of atherothrombotic events in acute coronary syndromes - rivaroxaban is used with aspirin alone or aspirin and clopidogrel

Where can you find more information?

- WCPPE Cardiovascular disease- anticoagulant therapy; e-learning module (<http://www.wcppe.org.uk>)
- WCCPE - Safe use of oral anticoagulants (<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)
- EHRA Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation: executive summary (www.escardio.org)
- Manufacturers' Summary of Product Characteristics (SPCs) (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/>; <http://www.lixiana.co.uk/en-gb/practical-guide/patient-alert>)