

# Managing patients safely on oral anticoagulants in Primary Care

For use in Calderdale CCG

**Approved by:** Medicines Advisory Group

**Date approved:** April 2015

**Review date:** April 2016

## Introduction

This guidance provides advice to clinicians on managing patients on oral anticoagulants, specifically warfarin and novel oral anticoagulants (NOACs).

There are three NOACs available at present, apixaban, dabigatran and rivaroxaban with edoxaban expected to be licensed shortly. Unlike warfarin, the NOACs do not require regular monitoring of INR.

## Key Recommendations

When prescribing anticoagulants or treating patients who are receiving anticoagulant therapy GPs, clinicians and prescribers should take the following points into consideration:

- Warfarin remains first-line choice due to clinical experience and reversibility unless;
  - Previous confirmed allergy or alopecia with warfarin
  - Contributing factors still exist for previous unsuccessful treatment with warfarin
- Consider NOACs when
  - Time in therapeutic range (TTR) < 65% after 6-9 months warfarin treatment (check adherence)
  - INR > 8 on one occasion in 6 months (if unexplained following clinical review)
  - INR > 5 on two occasions in 6 months (if unexplained following clinical review)
  - Confirmed intolerance, allergic reaction or alopecia with warfarin
- Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences
- When discussing the benefits and risks of anticoagulation, explain that:
  - For most people the benefit of anticoagulation outweighs the bleeding risk
  - For people with an increased risk of bleeding the benefit of anticoagulation may not always outweigh the bleeding risk, and careful monitoring of bleeding risk is important
- Do not withhold anticoagulation solely because the person is at risk of having a fall
- Review the need for anticoagulation and the quality of anticoagulation at least annually, or more frequently if clinically relevant events occur affecting anticoagulation or bleeding risk
- Ensure all newly diagnosed patients are counselled by the anticoagulant service provider so they are fully aware of the reasons for anticoagulant treatment and what this therapy involves
- Use the [CHA<sub>2</sub>DS<sub>2</sub>-VASc](#) stroke risk score to assess stroke risk in people with atrial fibrillation (AF) and use the [HAS-BLED](#) score to assess the risk of bleeding in people who are starting or have started anticoagulation
- In AF, consider anticoagulation for men with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of **1** and offer anticoagulation to people with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of **2** or above, taking bleeding risk into account
- Do not offer aspirin monotherapy solely for stroke prevention to people with AF
  - This does not change other recommendations for use of aspirin in cardiovascular illness e.g. post MI

### Prescribing anticoagulants for Atrial Fibrillation (AF) in primary care

The anticoagulation effects of NOACs wear off more rapidly than warfarin; this should be considered when patients are struggling to adhere/comply with prescribed therapy.

Dose adjustment for renal function is reported using CrCl in the table below in line with manufacturers' guidance. Renal function is commonly reported as eGFR and whilst this is not interchangeable with creatinine clearance, for most patients this can be used to determine dosage adjustment. However for patients at extremes of weight (BMI < 18.5 or >30 kg/m<sup>2</sup>) CrCl should be calculated from the Cockcroft and Gault formula:

$$\text{Estimated Creatinine Clearance in mL/minute} = \frac{(140 - \text{Age}) \times \text{Weight} \times \text{Constant}}{\text{Serum creatinine}}$$

Age in years, Weight in kilograms (use ideal body-weight), Serum creatinine in micromol/litre  
Constant = 1.23 for men; 1.04 for women

	Warfarin	Dabigatran	Rivaroxaban	Apixaban
<b>*Dose:</b>	Induction: 2mg daily for maximum 7 days before INR check (consider lower initial dose for frail patients)	Patients under 80 years: 150 mg twice daily	20 mg once daily with food	5 mg twice daily
<b>CrCl above 50ml/min</b>	Subsequent doses depend upon the prothrombin time, reported as INR (international normalised ratio).	<ul style="list-style-type: none"> <li>Patients &gt;80 years: 110 mg twice daily</li> <li>Reduce to 110 mg twice daily in patients who are taking verapamil</li> <li>Consider 110 mg twice daily when the thromboembolic risk is low and the bleeding risk is high or patients weigh &lt;50kg</li> </ul>		<ul style="list-style-type: none"> <li>Reduce to 2.5 mg twice daily in patients with two or more of the following characteristics:               <ul style="list-style-type: none"> <li>o Age ≥80 years</li> <li>o Body weight ≤60kg</li> <li>o Serum creatinine ≥1.5mg/dL (133 micromoles/L)</li> </ul> </li> </ul>
<b>CrCl 30-49ml/min</b>		110-150mg twice daily	Reduce dose to 15mg daily	Use normal dose
<b>CrCl 15-29ml/min</b>		Do not use	Reduce dose to 15mg daily	Reduce dose to 2.5mg twice daily
<b>CrCl &lt; 15ml/min</b>		Do not use		
<b>Safety</b>	Long-term safety based on 50 years use in clinical practice.	No information available on long-term safety. Reduce dose in renal impairment (based on Cockcroft Gault calculation of CrCl)		
<b>Interactions</b>	<b>Drug-food interactions</b> Cranberry juice and alcohol interact with warfarin. Some foods interact with warfarin (e.g. foods containing high amounts of Vitamin K). <b>Drug-drug interactions</b> Many interactions	<b>Drug-food interactions:</b> None known <b>Drug-drug interactions:</b> <b>Contraindicated</b> with ketoconazole, cyclosporine, itraconazole, tacrolimus and dronedarone. Use with <b>caution</b> with	<b>Drug-food interactions</b> There are no known food interactions. <b>Drug-drug interactions</b> <b>Not recommended</b> with concomitant ketoconazole, itraconazole, voriconazole, posaconazole or HIV protease inhibitors.  Use with <b>caution</b> with rifampicin, phenytoin, carbamazepine, phenobarbital or St John's Wort) <b>due to risk of a loss of effectiveness.</b>	

	requiring additional INR monitoring.	amiodarone, quinidine, verapamil, & ticagrelor. <b>Avoid</b> with rifampicin, St John's Wort, carbamazepine or phenytoin. SSRIs and SNRIs may increase the risk of bleeding.	
--	--------------------------------------	--	--

*\*Different doses apply for other indications*

See BNF and individual product [SPCs](#) for more detail. All agents have important differences in doses, dosing frequency, drug-drug interactions and adjustments for doses in renal and hepatic impairment.

### Anticoagulant monitoring in primary care

All patients prior to anticoagulant treatment and at least annually thereafter should have the following monitoring:

- renal function (U&Es)
- full blood count (FBC)
- liver function (LFTs)
- clotting screen– prior to initiation only
- blood pressure
- thyroid status – prior to initiation only

#### Warfarin:

- Monitor and record INR regularly according to recommended instructions from anticoagulant Monitoring service
- It has been locally agreed in Calderdale that the 5mg tablets should not be routinely used.

Warfarin regimens with the following characteristic promote safer use;

- use constant daily dosing and not alternate daily dosing
- does not require splitting tablets in half
- doses should be expressed in mg
- clear directions on the prescription to state that they should be taken as directed according to anticoagulant booklet/blood test results

Repeat prescriptions of warfarin should only be issued if the prescriber has checked that the patient is regularly having their INR monitored and that their INR is within safe limits.

#### NOACs:

All patients should be reviewed 4-6 weeks after initiation of therapy and at least annually thereafter:

- Assess for compliance and tolerability
  - renal function (U&Es)
  - full blood count (FBC)
  - liver function (LFTs)
  - Repeat U&E's every 6 months if CrCl 30–60 mL/min or every 3 months if CrCl 15– 30 mL/min.
- More frequent U&E's/LFTs are advised where concurrent illness may impact on renal or hepatic function.

Patients switching from warfarin to NOAC:

- seek advice from the anticoagulant monitoring service before switching agents
- an international normalised ratio (INR) must be taken
- discontinue warfarin and start NOAC when
  - INR < 2:- dabigatran, apixaban
  - INR < 3:- rivaroxaban (INR values will be falsely elevated after the intake of rivaroxaban)

### **Report adverse events to the MHRA**

<http://www.mhra.gov.uk/#page=DynamicListMedicines>

### **Useful resources**

- [Apixaban for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation](#). NICE TA275
- [Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation](#). NICE TA256
- [Dabigatran etexilate for the prevention of stroke and systemic embolism in people with atrial fibrillation with one or more risk factor for stroke or systemic embolism](#). NICE TA249
- [Atrial fibrillation: the management of atrial fibrillation](#). NICE CG180
- [www.npsa.nhs.uk](http://www.npsa.nhs.uk)