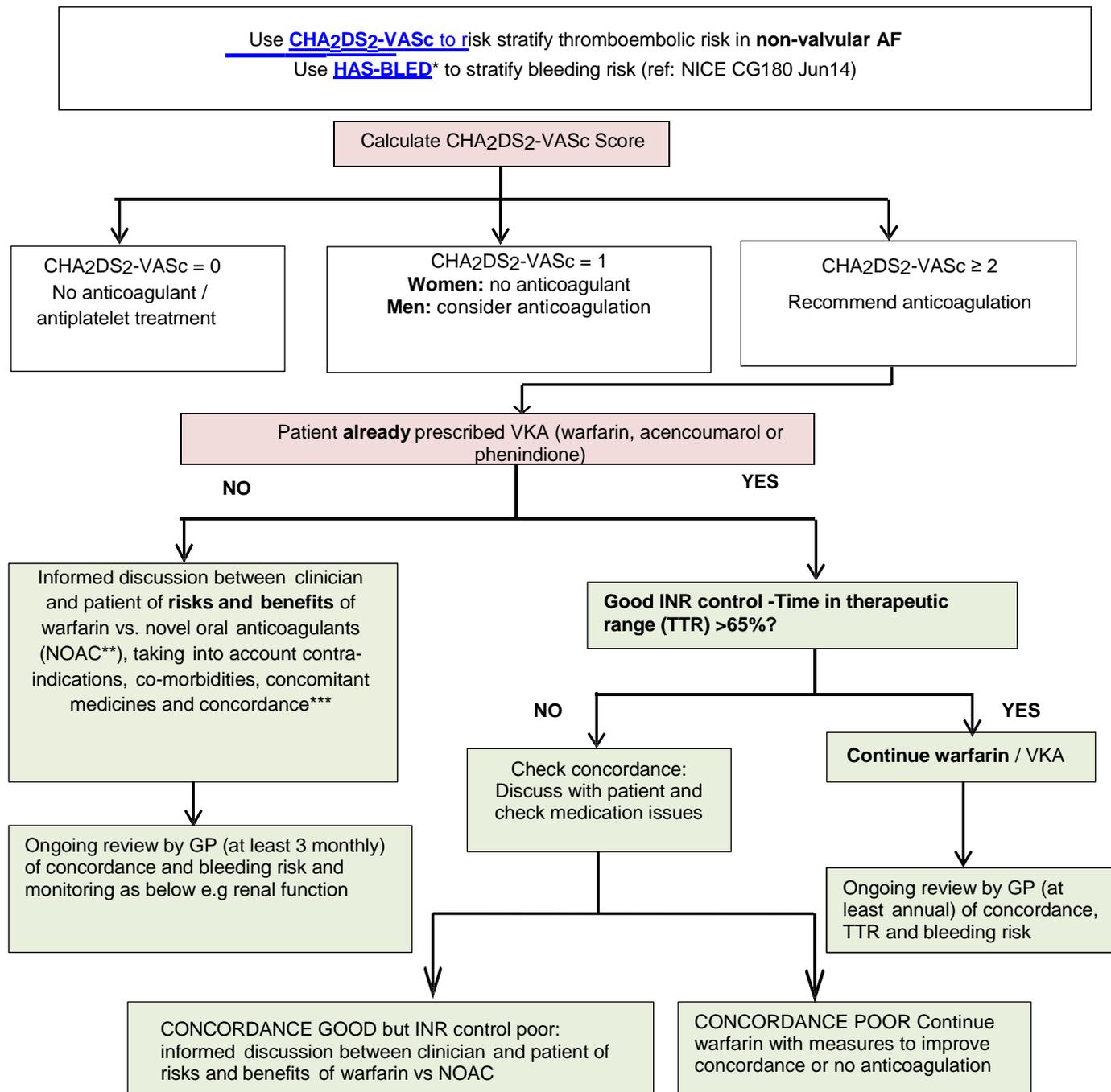


**Anticoagulant Treatment Pathway: Prevention of stroke and systemic embolism in adults with non-valvular atrial fibrillation**



\* Use HAS-BLED score to assess bleeding risk. Offer modification and monitoring of: uncontrolled Hypertension, Labile (poor) INR control, concurrent Drugs (e.g. aspirin, NSAID), harmful alcohol consumption.

\*\*Patients initiated on NOACs should be supplied with the Northern England Strategic Clinical Network **NOAC Alert Card**, plus advice on importance of adherence, potential side effects and their management. It may also be useful to provide the patient with a patient information booklet (this is published by the drug manufacturer).

\*\*Caution with NOAC in patients with high bleeding risk including: very elderly (age >80), previous bleeding event, HAS-BLED ≥3, low body weight <60Kg, renal impairment (see information on renal dosing in appendix 1)

**Please note these guidelines only refer to the use of anticoagulants in patients with non-valvular AF and do NOT cover other indications (e.g. mechanical heart valves, VTE)**

**NICE Guideline CG180 Atrial Fibrillation (Update June 2014):**

The NICE updated AF [Clinical Guideline 180](#) June 2014 advises the following interventions to prevent stroke:

- Use the CHA<sub>2</sub>DS<sub>2</sub>-VASc stroke risk score to assess stroke risk in people with atrial fibrillation and use the HAS-BLED score to assess the risk of bleeding in people who are starting or have started anticoagulation
- 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
- Anticoagulation may be with warfarin or another Vitamin K antagonist; or with a NOAC - apixaban, dabigatran etexilate, rivaroxaban, edoxaban. Discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences (*see comparison below*). The approved patient decision aid can be used as a tool when discussing treatment options with the patient.
- **Do not offer aspirin monotherapy for stroke prevention to people with AF**
- For people who are not taking an anticoagulant, review stroke and bleeding risks annually and ensure that all reviews and decisions are documented
- For people who are taking an anticoagulant, 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
- Assess the anticoagulation control in people taking vitamin K antagonists at each review and anticoagulant monitoring appointment
- Do not withhold anticoagulation solely because the person is at risk of having a fall

**RISK STRATIFICATION TOOLS**

**CHA<sub>2</sub>DS<sub>2</sub>-VASc (Stroke risk assessment):**

Feature	Score	Score	Adjusted stroke risk (at 1 year) % <sup>(4)</sup>
Congestive Heart Failure / LV dysfunction	1	0	0.78
Hypertension	1	1	2.01
Age >75 years	2	2	3.71
Diabetes mellitus	1	3	5.92
Stroke/TIA/TE	2	4	9.27
Vascular disease (previous MI, peripheral arterial disease or aortic plaque)	1	5	15.26
Age between 65 and 74 years	1	6	19.74
Sex category (i.e. female gender)	1	7	21.50
		8	22.38
		9	23.64

**HAS-BLED (Bleeding risk assessment):**

Feature	Score	Notes <sup>(4)</sup>
Hypertension (Systolic $\geq$ 160mmHg)	1	<i>Uncontrolled hypertension (e.g. systolic BP &gt;160mmHg)</i>
Abnormal renal function or liver function (1 point each)	1 or 2	<i>Abnormal renal function: presence of chronic dialysis, renal transplantation, or serum creatinine &gt;200umol/L</i>  <i>Abnormal liver function: chronic hepatic disease, or biochemical evidence of significant hepatic derangement (e.g. bilirubin &gt;2x ULN, in association with AST/ALT/ALP &gt;3x ULN)</i>
Stroke	1	
Bleeding tendency or predisposition	1	<i>Previous bleeding history and/or predisposition to bleeding (e.g. bleeding diathesis, anaemia, etc.)</i>
Labile INRs (if taking warfarin / VKA)	1	<i>Unstable INRs or poor TTR</i>
Elderly (e.g. age >65, frail condition)	1	
Drugs (concomitant aspirin, NSAID, etc.) or alcohol abuse(1 point each)	1 or 2	

## Oral anticoagulants (OACs) in AF - FAQs

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
<b>How do OACs do work?</b>	Inhibits the production of vitamin K dependent clotting factors II, VII, IX and X.	Acts as a direct thrombin (factor IIa) inhibitor. It is formulated as dabigatran etexilate, a pro-drug converted to dabigatran after administration.	Acts as a selective direct factor Xa inhibitor. Inhibition of Factor Xa interrupts the intrinsic and extrinsic pathway of the blood coagulation cascade, inhibiting both thrombin formation and development of thrombi.	Inhibits free and clot-bound factor Xa, and prothrombinase activity. Prevents thrombin generation and thrombus development. No direct effects on platelet aggregation, but indirectly inhibits aggregation induced by thrombin.	Inhibits free factor Xa, and prothrombinase activity. Reduces thrombin generation, prolongs clotting time and reduces the risk of thrombus development.
<b>What are their main contraindications?</b>	<ul style="list-style-type: none"> <li>Known hypersensitivity to warfarin or any excipients</li> <li>Haemorrhagic stroke</li> <li>Clinically significant bleeding</li> <li>Within 72 hours of major surgery with risk of severe bleeding</li> <li>Within 48 hours postpartum</li> <li>Pregnancy (first and third trimesters)</li> <li>Drugs where interactions may lead to a significantly increased risk of bleeding</li> </ul>	<ul style="list-style-type: none"> <li>Hypersensitivity to the active substance or any excipients.</li> <li>Severe renal impairment (CrCL &lt; 30 mL/min).</li> <li>Active clinically significant bleeding.</li> <li>Any lesion or condition considered a significant risk factor for bleeding.</li> <li>Concomitant treatment with any other anticoagulant</li> <li>Hepatic impairment or liver disease expected to have any impact on survival.</li> <li>Concomitant treatment with systemic ketoconazole, cyclosporine, itraconazole, tacrolimus, dronedarone.</li> <li>Prosthetic heart valves requiring anticoagulant treatment.</li> </ul>	<ul style="list-style-type: none"> <li>Hypersensitivity to the active substance or any excipients.</li> <li>Active clinically significant bleeding.</li> <li>Concomitant treatment with any other anticoagulant</li> <li>Hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C</li> <li>Pregnancy and breast feeding.</li> <li>Prosthetic heart valves requiring anticoagulation treatment</li> <li>Severe renal impairment (CrCL &lt;15ml/min)</li> <li>Dronaderone and other drug interactions</li> </ul>	<ul style="list-style-type: none"> <li>Hypersensitivity to the active substance or any excipients.</li> <li>Active clinically significant bleeding.</li> <li>Hepatic disease associated with coagulopathy and clinically relevant bleeding risk.</li> <li>Any lesion or condition considered a significant risk factor for bleeding.</li> <li>Concomitant treatment with any other anticoagulant</li> <li>Prosthetic heart valves requiring anticoagulation treatment</li> <li>Severe renal impairment (CrCL &lt;15ml/min)</li> <li>Dronaderone and other drug interactions</li> </ul>	<ul style="list-style-type: none"> <li>Hypersensitivity to the active substance or any excipients.</li> <li>Active clinically significant bleeding.</li> <li>Hepatic disease associated with coagulopathy and clinically relevant bleeding risk.</li> <li>Any lesion or condition considered a significant risk factor for bleeding.</li> <li>Uncontrolled severe hypertension</li> <li>Concomitant treatment with any other anticoagulants</li> <li>Prosthetic heart valves requiring anticoagulation treatment</li> <li>Pregnancy and breast-feeding</li> <li>End stage renal disease, or dialysis.</li> <li>Active cancer</li> </ul>
<b>Lactose and wheat content.</b>	Lactose Maize starch (Marevan®)	No lactose or wheat	Lactose No wheat	Lactose No wheat	No lactose Maize starch

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
<b>When should individual OACs be avoided?</b>	Intolerance to warfarin including allergy and rash. Demonstrated impossibility of monitoring arrangements Warfarin is teratogenic and should not be given in the first trimester of pregnancy	<b>AVOID</b> in patients with a history of poor medication adherence (unless poor adherence relates to e.g. difficulty managing flexible warfarin dosage that may be addressed through a fixed dose regime) The NOACs are <b>not</b> a suitable alternative to warfarin in patients with bleeding complications associated with warfarin treatment, contraindications to warfarin therapy due to a high bleeding risk, alcohol abuse, drug overdose or trivial side effects related to warfarin. <b>Dabigatran is not stable in compliance aids such as blister packs.</b>  Manufacturers advise to avoid use in pregnancy.			
<b>What dose should be used?</b>  (CrCl above 50 mL/min)	For patients who require rapid anticoagulation the usual adult induction dose of warfarin is 5–10 mg on the first day (elderly patients should receive a lower induction dose). For patients who do not require rapid anticoagulation, a lower loading dose can be used over 3–4 weeks. In both cases subsequent doses depend upon the prothrombin time, reported as INR	<ul style="list-style-type: none"> <li>Patients under 80 years: 150 mg twice daily</li> <li>Patients &gt;80 years: 110 mg twice daily (due to the increased risk of bleeding in this population)</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 (e.g. CrCL 30-50 mL/min) or patients weigh &lt;50kg.</li> </ul>	<ul style="list-style-type: none"> <li>20 mg once daily with food</li> </ul>	<ul style="list-style-type: none"> <li>5 mg twice daily</li> <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>Age ≥80 years</li> <li>Body weight ≤60kg</li> <li>Serum creatinine ≥1.5 mg/dL (133 micromoles/L)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>60 mg once daily</li> <li>Reduce to 30 mg once daily in patients with:               <ul style="list-style-type: none"> <li>Body weight ≤60 kg</li> <li>Concomitant P-gp inhibitors (cyclosporin, dronedarone, erythromycin, ketoconazole)</li> </ul> </li> <li>A trend towards decreasing efficacy with increasing creatinine clearance was observed compared to well-managed warfarin.</li> <li>In the US, edoxaban is not licensed in patients with CrCL &gt;95 mL/min, due to reduced efficacy.</li> </ul>
<b>CrCl 30-49 mL/min</b>	Renal insufficiency is a risk factor for bleeding.	110-150 mg twice daily	Reduce dose to 15 mg daily	Use normal dose	Reduce dose to 30 mg daily
<b>CrCl 15-29 mL/min</b>	Consider apixaban in preference to warfarin with CrCl of 30–50 mL/min/1.73 m <sup>2</sup> .	Do not use		Reduce dose to 2.5 mg 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)			

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
<b>What pre-treatment testing and ongoing monitoring is required?</b>	<p><b>Tests prior to starting treatment</b></p> <p>Clotting screen, U&amp;Es, LFTs, FBC, BP, CrCl, Thyroid status</p> <p>Ongoing monitoring requires adjustment to the individual needs of the patient and therefore requires regular monitoring using blood tests.</p>	<p><b>Tests prior to starting treatment</b></p> <p>Clotting screen, U&amp;Es, LFTs, FBC, BP, CrCl</p> <p><b>Monitoring until patient is stabilised</b></p> <p>Ideally assess every 3 months to:</p> <ul style="list-style-type: none"> <li>• Assess compliance and reinforce advice regarding regular dosing schedule.</li> <li>• Enquire about adverse effects such as bleeding.</li> <li>• Assess for the presence of thromboembolic events</li> <li>• Enquire about other medicines, including OTC medicines.</li> </ul> <p><b>Ongoing monitoring</b></p> <p>U&amp;Es, LFTs, FBC at least once a year especially in elderly and patients with renal impairment.</p> <p>Repeat U&amp;Es every 6 months if CrCl 30–60 mL/min, patient &gt; 75 years or fragile.</p> <p>Repeat U&amp;Es every 3 months if CrCl 15–30 mL/min.</p> <p>More frequent U&amp;Es /LFTs advised where intercurrent illness may impact on renal or hepatic function.</p>	<p><b>Tests prior to starting treatment</b></p> <p>Clotting screen, U&amp;Es, LFTs, FBC, BP, CrCl</p> <p><b>Monitoring until patient is stabilised</b></p> <p>Ideally assess every 3 months to:</p> <ul style="list-style-type: none"> <li>• Assess compliance and reinforce advice regarding regular dosing schedule.</li> <li>• Enquire about adverse effects such as bleeding.</li> <li>• Assess for the presence of thromboembolic events</li> <li>• Enquire about other medicines, including OTC medicines.</li> </ul> <p><b>Ongoing Monitoring</b></p> <p>U&amp;Es, LFTs, FBC at least once a year.</p> <p>Repeat U&amp;Es every 6 months if CrCl 30–60 mL/min or every 3 months if CrCl 15–30 mL/min.</p> <p>More frequent U&amp;Es /LFTs advised where intercurrent illness may impact on renal or hepatic function.</p>		

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban										
<b>Does the risk of a bleed vary between OACs?</b>	See respective agent for comparison	<p><i>Major bleeding:</i> No difference between dabigatran 150 mg BD and warfarin. Less common with dabigatran 110 mg BD than warfarin</p> <p><i>GI bleeding:</i> More common with dabigatran 150 mg BD than warfarin (p=0.0008). No difference between dabigatran 110 mg BD and warfarin.</p> <p><i>Intracranial bleeding:</i> Less common with both doses of dabigatran than with warfarin (p&lt;0.001). Bleeding risk high in the frail and elderly, particularly with renal impairment and low body weight.</p>	<p><i>Major bleeding:</i> No difference between rivaroxaban and warfarin.</p> <p><i>GI bleeding:</i> More common with rivaroxaban than warfarin (p&lt;0.001)</p> <p><i>Intracranial bleeding:</i> less common with rivaroxaban than warfarin (p=0.02)</p>	<p><i>Major bleeding:</i> Less common with apixaban than warfarin (p&lt;0.001)</p> <p><i>GI bleeding:</i> No difference between apixaban and warfarin</p> <p><i>Intracranial bleeding:</i> Less common with apixaban than warfarin (p&lt;0.001)</p>	<p><i>Major bleeding</i> Less common with edoxaban than warfarin (p&lt;0.001).</p> <p><i>GI bleeding</i> More common with edoxaban than warfarin (p=0.03)</p> <p><i>Intracranial bleeding</i> Less common with edoxaban than warfarin (p&lt;0.001)</p>										
<b>Can bleeding be reversed?</b>	Effective and well known antidote, should a severe bleed occur whilst being treated	<p>Patients with bleeding risk factors excluded from pivotal trial.</p> <p>Clearance can be increased with haemodialysis.</p> <p>Prolonged bleeding has increased morbidity and possibly contributed to deaths.</p> <p>Antidote available</p>	Antidote in phase III trials	Antidote in phase III trials	Antidote in phase III trials										
<b>What are the half-lives of the OACs?</b>	About 40 hours	<table border="1"> <thead> <tr> <th>GFR [mL/min]</th> <th>half-life in hours (range)</th> </tr> </thead> <tbody> <tr> <td>≥ 80</td> <td>13.4 (11.0-21.6)</td> </tr> <tr> <td>≥ 50 - &lt; 80</td> <td>15.3 (11.7-34.1)</td> </tr> <tr> <td>≥ 30 - &lt; 50</td> <td>18.4 (13.3-23.0)</td> </tr> <tr> <td>&lt; 30</td> <td>27.2 (21.6-35.0)</td> </tr> </tbody> </table>	GFR [mL/min]	half-life in hours (range)	≥ 80	13.4 (11.0-21.6)	≥ 50 - < 80	15.3 (11.7-34.1)	≥ 30 - < 50	18.4 (13.3-23.0)	< 30	27.2 (21.6-35.0)	5 to 9 hours in young individuals, 11 to 13 hours in the elderly.	12 hours	10 to 14 hours
GFR [mL/min]	half-life in hours (range)														
≥ 80	13.4 (11.0-21.6)														
≥ 50 - < 80	15.3 (11.7-34.1)														
≥ 30 - < 50	18.4 (13.3-23.0)														
< 30	27.2 (21.6-35.0)														

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
<b>What are the common side effects?</b>	Nausea, vomiting, diarrhoea, jaundice, alopecia, rash, hepatic dysfunction, pyrexia.	<p>Dyspepsia more frequent with both doses of dabigatran than warfarin. GI adverse events frequently led to drug discontinuation (7%, 6.5% and 3.9% in the dabigatran 150 mg, 110 mg and warfarin groups respectively).</p> <p>The rate of myocardial infarction (MI) was numerically, but not statistically significantly, higher with dabigatran in the pivotal trial (0.82% for 110 mg and 0.81% for 150 mg vs. 0.64% p=0.12).</p> <p>Two meta-analyses showed that dabigatran was associated with a significantly higher risk of MI. The control groups varied and included enoxaparin, warfarin and placebo.</p>	<p>There were no significant differences in the incidence of any adverse event other than bleeding in the pivotal rivaroxaban trial.</p> <p>The rate of MI was numerically, but not statistically significantly lower, in the rivaroxaban arm compared with warfarin.</p>	There were no significant differences between warfarin and apixaban in the incidence of any adverse events in the pivotal trial.	There were no significant differences between warfarin and edoxaban in the incidence of any adverse events in the pivotal trial.

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
<p><b>How do you switch between anticoagulants?</b></p> <p><i>There is a potential for inadequate anticoagulation during the transition between NOACs and warfarin. Continuous adequate anticoagulation should be ensured during any transition to an alternative anticoagulant.</i></p>	<p>When converting patients from warfarin therapy to a NOAC, discontinue warfarin and start:</p> <ul style="list-style-type: none"> <li>dabigatran when the INR is below 2.0</li> <li>rivaroxaban when INR is below 3.0</li> <li>apixaban when INR is below 2.0</li> <li>edoxaban when INR is <math>\leq 2.5</math></li> </ul> <p>INR values may be falsely elevated after the intake of NOACs.</p>	<p>When converting from dabigatran to warfarin, adjust the starting time of warfarin based on creatinine clearance as follows:</p> <p>For CrCl <math>&gt;50</math> mL/min, start warfarin 3 days before discontinuing dabigatran.</p> <p>For CrCl 31-50 mL/min, start warfarin 2 days before discontinuing dabigatran.</p> <p>For CrCl 15-30 mL/min, start warfarin 1 day before discontinuing dabigatran</p> <p>For CrCl <math>&lt;15</math> mL/min, no recommendations can be made – consult with haematologist.</p> <p>Because dabigatran can contribute to an elevated INR, the INR will better reflect warfarin's effect after dabigatran has been stopped for at least 2 days.</p>	<p>When converting from rivaroxaban to warfarin, rivaroxaban should be continued until the INR is <math>\geq 2.0</math>.</p> <p>For the first two days of the conversion period, standard initial dosing of warfarin should be used followed by warfarin dosing guided by INR testing.</p> <p>While patients are on both rivaroxaban and warfarin, the INR should not be tested earlier than 24 hours after the previous dose but prior to the next dose of rivaroxaban. Once rivaroxaban is discontinued INR testing may be done reliably at least 24 hours after the last dose</p>	<p>When converting from apixaban to warfarin, continue apixaban for at least 2 days after starting warfarin therapy.</p> <p>After 2 days of co-administration of apixaban and warfarin, obtain an INR prior to the next scheduled dose of apixaban.</p> <p>Continue co-administration of apixaban and warfarin until the INR is 2 or more</p>	<p>When converting from edoxaban to warfarin, continue edoxaban until the INR is <math>\geq 2.0</math>.</p> <p>A loading dose of warfarin is <b>not</b> recommended.</p> <p>For patients currently on a 60 mg dose, administer edoxaban at a dose of 30 mg once daily together with an appropriate VKA dose.</p> <p>For patients currently on a 30 mg dose, administer edoxaban at a dose of 15 mg once daily together with an appropriate VKA dose.</p> <p>During the first 14 days of concomitant therapy measure the INR at least 3 times, just prior to the daily dose of edoxaban. Edoxaban can contribute to an elevated INR.</p>
<p><b>Converting from parenteral anticoagulants</b></p>	<p>The exact regimen depends on individual circumstances. Parenteral anticoagulants are generally continued until the INR is in the desired range.</p>	<p>Discontinue the parenteral anticoagulant and start dabigatran 0-2 hours prior to the time that the next dose of the alternate therapy would be due, or at the time of discontinuation in case of continuous treatment.</p>	<p>For patients currently receiving a parenteral anticoagulant, rivaroxaban should be started 0 to 2 hours before the time of the next scheduled administration of the parenteral medicinal product (e.g. low molecular weight heparins) or at the time of discontinuation of a continuously administered parenteral medicinal product (e.g. intravenous unfractionated heparin).</p>	<p>Switching treatment from parenteral anticoagulants apixaban (and vice versa) can be done at the next scheduled dose. These agents should not be administered simultaneously.</p>	<p>These agents should not be administered simultaneously.</p> <p><i>Subcutaneous anticoagulants:</i></p> <p>Discontinue the parenteral anticoagulant and start edoxaban at the time of the next scheduled dose.</p> <p><i>Intravenous anticoagulants</i></p> <p>Discontinue the infusion and start edoxaban 4 hours later.</p>

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
What are the main drug interactions?	<p><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).</p> <p><b>Drug-drug interactions</b> Many interactions requiring additional INR monitoring.</p>	<p><b>Drug-food interactions</b> There are no known food interactions.</p> <p><b>Drug-drug interactions</b> <b>Contraindicated</b> with the strong P-gp inhibitors ketoconazole, cyclosporine, itraconazole, tacrolimus and dronedarone. Use with <b>caution</b> if co-administered with mild to moderate P-gp inhibitors such as amiodarone, quinidine, verapamil, &amp; ticagrelor. Co-administration with P-gp inducers such as rifampicin, St John's Wort, carbamazepine or phenytoin) should be avoided. SSRIs and SNRIs increased the risk of bleeding in RE-LY in all treatment groups.</p>	<p><b>Drug-food interactions</b> There are no known food interactions.</p> <p><b>Drug-drug interactions</b> <b>Not recommended</b> with concomitant systemic administration of strong inhibitors of both CYP3A4 and P-gp, such as ketoconazole, itraconazole, voriconazole, posaconazole or HIV protease inhibitors. Strong inducers of both CYP3A4 and P-gp (such as rifampicin, phenytoin, carbamazepine, phenobarbital or St John's Wort) should be co-administered with <b>caution because of the risk of a loss of effectiveness.</b></p>		<p><b>Drug-food interactions</b> There are no known food interactions.</p> <p><b>Drug-drug interactions</b> <i>P-gp inhibitors:</i> use with ciclosporin, dronedarone, erythromycin, or ketoconazole requires edoxaban dose reduction. No dose reduction required with quinidine, verapamil or amiodarone. Other P-gp inhibitors have not been studied. <i>P-gp inducers:</i> <b>use with caution.</b> Chronic use with NSAIDs not recommended.</p>
<p>Concomitant administration with any other anticoagulants is <b>contraindicated</b> (some overlap may be necessary whilst transferring between anticoagulants). Consult the SPCs for full details of interactions.</p>					

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
<b>OAC use with no clinically important bleeding risk</b>	Dental procedures — outpatient dental surgery (including extractions) can usually be undertaken without temporarily stopping or reducing the dose of warfarin. It is recommended that the INR is checked 72 hours before dental surgery. The risk of significant bleeding in people with a stable INR within the range of 2 to 4 is very small, but the risk of thrombosis may be increased if oral anticoagulants are temporarily discontinued	The procedure can be performed just before the next dose of dabigatran, rivaroxaban or apixaban is due, or approximately 18–24 hours after the last dose was taken (treatment should be restarted 6 hours later). For dental procedures, consider prescribing tranexamic acid 5% mouth wash; instruct the person to use 10 mL as a mouth wash four times a day for 5 days.			
<b>OAC use and undergoing surgery with a low bleeding risk<sup>21</sup></b>	Surgery — in general, warfarin is usually stopped 5 days before planned surgery, and once the person's international normalised ratio (INR) is less than 1.5 surgery can go ahead. Warfarin is usually resumed at the normal dose on the evening of surgery or the next day if haemostasis is adequate.	Dabigatran should be stopped 24 hours before the procedure. If the person has creatinine clearance 50–80 mL/min dabigatran should be stopped 36 hours before the intervention If the person has creatinine clearance 30–50 mL/min dabigatran should be stopped 48 hours before the intervention	Rivaroxaban should be stopped 24 hours before the procedure. If the person has a creatinine clearance between 15–30 mL/min rivaroxaban should be stopped 36 hours before the procedure.	Apixaban should be stopped 24 hours before the procedure. If the person has a creatinine clearance between 15–30 mL/min, apixaban should be stopped 36 hours before the procedure.	Edoxaban should be stopped 24 hours before the procedure.
<b>OAC use and undergoing surgery with a high bleeding risk</b>		Dabigatran should be stopped 48 hours before the procedure. If the person has creatinine clearance 50–80 mL/min dabigatran should be stopped 72 hours before the intervention If the person has creatinine clearance 30–50 mL/min dabigatran should be stopped 96 hours before the intervention	Rivaroxaban should be stopped 48 hours before the procedure.	Apixaban should be stopped 48 hours before the procedure.	
<b>Restarting OACs after surgery</b>	See local guidelines. Treatment should be restarted after the invasive procedure or surgical intervention as soon as possible <b>provided the clinical situation allows and adequate haemostasis has been established as determined by the treating physician.</b> Onset of action of NOACs is much faster than that of warfarin.				

**Table taken from:** Common Questions and Answers on the Practical Use of Oral Anticoagulants in Non-Valvular Atrial Fibrillation (2015). South West Medicines Information and Training and Regional Drug and Therapeutics Centre (Newcastle)

### **Additional points regarding warfarin:**

Patients initiated on warfarin should have the relevant patient information supplied i.e. a "yellow book" plus advice on importance of adherence, potential side effects and their management.

### **Additional points regarding NOACs:**

Patients initiated on NOACs should be supplied with the Northern England Strategic Clinical Network NOAC Alert Card, plus advice on importance of adherence, potential side effects and their management. It may also be useful to provide the patient with a patient information booklet (this is published by the drug manufacturer).

### **KEY COUNSELLING POINTS WHEN INITIATING A NOAC**

- Name of the drug and purpose i.e. to prevent blood clots or stroke
- Dosing and whether to take with or without food (N.B. rivaroxaban must be taken with food)
- The NOAC must be taken exactly as prescribed – missing doses may reduce protection
- Do not stop taking the NOAC without talking to your doctor as you are at a risk of suffering from a stroke or blood clot if you do.
- If you miss a dose take it as soon as you remember and check your medicine information leaflet for instructions. Do not take a double dose to compensate for a missed dose.
- All anticoagulants increase the risk of bleeding and you should report any bleeding symptoms to your doctor.
- Inform your pharmacist, dentist, surgeon or doctor before any procedure or new drug prescription.
- Do not take over the counter medicines without first checking with the pharmacist

### **EMERGENCY INFORMATION**

Explain to patient who to contact in the event of a bleeding emergency and write contact telephone number(s) on the NOAC card.

Signs and symptoms of bleeding include

- Tar coloured stools, blood in urine, prolonged nose-bleed lasting >10 minutes, bleeding of gums or from cuts that take a long time to stop
- Bruising or bleeding under the skin with swelling or discomfort
- Headache, dizziness, tiredness, paleness or weakness
- Coughing up blood or vomiting blood or material that looks like coffee grounds
- Loss of consciousness or drowsiness.

In the event of a bleeding event which does not stop on its own **immediately seek medical attention** and do not take any more doses until this has been reviewed.

### **BLOOD SAMPLING**

- Routine monitoring of anticoagulation level is not required.
- Yearly (at least) blood tests are required to check blood, kidney and liver function. Or, in patients with reduced kidney function, more frequent monitoring of kidney function is needed.

### **Summary of Product Characteristics (SPC)\***

*\*Please refer to the relevant SPC and patient information leaflet (PIL) provided by the manufacturers with regards to dosing, cautions, contra-indications, interactions and side-effect profile so as to ensure the most current information is referred to. SPC links: [Apixaban](#) [Dabigatran](#) [Rivaroxaban](#) [Edoxaban](#) [Warfarin](#)*

**NICE Technology Appraisals (TAs)** for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation:

**NICE [TA275](#): Apixaban.**

**NICE [TA249](#): Dabigatran etexilate**

**NICE [TA256](#): Rivaroxaban**

**NICE [TA355](#): Edoxaban**

**NICE [CG180](#): The management of Atrial Fibrillation, June 2014.**

**References:**

NICE Clinical Guideline CG180: Atrial Fibrillation: Management (June 2014) <http://www.nice.org.uk/guidance/cg180>

Anticoagulant Treatment Pathway: prevention of stroke and systemic embolism in adults with non-valvular atrial fibrillation (2014). Wye Valley NHS Trust and NHS Hertfordshire Clinical Commissioning Group. <http://www.herefordshireccg.nhs.uk/cardiovascular>

Common Questions and Answers on the Practical Use of Oral Anticoagulants in Non-Valvular Atrial Fibrillation (2015). South West Medicines Information and Training and Regional Drug and Therapeutics Centre (Newcastle)

European Society of Cardiology: Atrial Fibrillation (Management of) (2010). European Heart Journal (2010) 31, 2369–2429

'Common questions and answers on the practical use of oral anticoagulants in non-valvular atrial fibrillation', North of Tyne APC, September 2015