Prescriber Decision Support

Novel or Non-vitamin K antagonist Oral Anti-Coagulants (NOACs)

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Prescriber Decision Support of Novel/ Non-vitamin k antagonist Oral Anti-Coagulant (NOAC)

The aim of this guidance is to summarise and compare NOACs endorsed by NICE and GMMMG and support prescriber decisions. NICE and GMMMG have issued guidance and endorsements on the specific uses of NOACs –dabigatran[1] (Pradaxa®), rivaroxaban[2] (Xarelto▼®), apixaban[3] (Eliquis▼®) and Edoxaban[4] (Lixiana▼®). NICE states:

The decision about whether to start treatment with warfarin or a NOAC should be made after an informed discussion between the prescriber and the patient about the relative risks and benefits of each agent.

If a NOAC is recommended, establish the principal reason of this suggestion over alternative anticoagulant agents. There are many factors to consider when recommending an anticoagulant. For example drug interactions, indications, bleeding risk, lifestyle issues, alcohol consumption, poor compliance, failure to comply with monitoring arrangements etc. This guidance aims to provide prescribers a personalised approach to selecting anticoagulant therapy for their patients.

INR control

Optimal INR control is defined as time in therapeutic range (TTR) ≥65%. Factors to consider in improving TTR:

- Patient education
- Concordance – identify patients with poor compliance by comparing recommended dose over 3-6 months with quantity of prescription issued
- Inconvenient or inappropriate monitoring arrangements – confirm suitability of arrangements for each patient
- Consider domiciliary monitoring arrangements for patients with reduced mobility
- Lifestyle factors e.g. alcohol consumption, diet
- Drug interactions

Take action to minimise the effect of any factors that can adversely affect INR control. For all patients deemed to have previously failed on warfarin therapy, establish all the relevant anticoagulant treatment history. Confirm the evidence to support proposed reason for treatment failure. For example:

- Failed monitoring arrangements – did the patient attend an anticoagulation monitoring service?
- Labile INR – did the patient achieve a therapeutic INR?
- Bleeding complications – was the bleed major/minor? Confirm INR at time of bleed.
- Drug interactions – any change to concurrent therapy should be considered.
- Serious ADR – was this documented in patient records?
- Severe alopecia – was the patient offered alternative vitamin K antagonist (VKA) agents?

Key points: Warfarin

- Warfarin has been the mainstay of oral anticoagulant for more than 50 years
- Warfarin activity/effect can be measured easily by an INR and may help give an indication to compliance
- Effective and well known antidote in the reversal of anticoagulant effect with vitamin K
- All NOACs are licensed for prevention of stroke in non-valvular atrial fibrillation (NVAF) plus at least one additional risk factor. Warfarin is licensed for use without additional risk factors present.
- Warfarin - time to peak effect ranges from 3-5 days.
- Warfarin has many drug-drug and certain food interactions which may require additional INR monitoring or which may prevent concurrent use.
- Patients may have difficulty around INR monitoring.

Key points: NOACs

- No requirement for INR monitoring.
- NOACs provide immediate anti-coagulant effect (time to peak effect ranges from 1-4 hours).
- NOACs currently have no known food interactions.
- NOACs have shorter half-life and missed doses may result in more time without any anticoagulation and greater risk of thromboembolic complications.
- NOAC activity/effect cannot be easily measured compared to warfarin.
- Each NOAC has a higher acquisition cost than warfarin.
- In September 2015, the European Medicines Agency (EMA) granted positive opinion to idarucizumab, the specific reversal agent to dabigatran, if rapid reversal of its effects is required. There is currently no licensed antidote in the reversal of anticoagulant effect of rivaroxaban, apixaban and edoxaban.
- Renal function should be assessed and monitored using Cockcroft and Gault formula – Creatinine Clearance (CrCL). Especially in patients with extreme BMI.

Patient groups considered to benefit from a NOAC include:

✓ Those with poor INR control on warfarin. Poor INR control defined as:
  - TTR ≤65%
  - Two or more unexplained INR results >5 OR one INR >8 within past 6 months
  - Two INR values <1.5 within past 6 months.

  Calculate TTR over a maintenance period of at least 6 months and exclude measurements taken during the first 6 weeks of treatment. Exclude all reasons for poor 'INR control' (see box above) despite good compliance before considering NOAC.

✓ Significant difficulties with INR monitoring and/or accessing anticoagulant clinics that raises safety concerns. Exclude alternatives such as community anticoagulant services, domiciliary monitoring/input or self-testing.

✓ Patients in whom warfarin is unsuitable due to contraindication or intolerance e.g. alopecia, could be offered a NOAC.

✓ Patients that consider a NOAC as their preferred anticoagulant following an informed discussion with a clinician on the risks, benefits, individual circumstances and needs.

(Note: There is currently insufficient evidence to recommend one NOAC over another, some patient characteristics, drug compliance and tolerability, and cost maybe important factors in the choice of agent)

Licensed indications	*Primary prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective hip or knee replacement surgery. Acute Trust service delivery arrangement: The full supply should be made by the responsible surgeon and **is not covered by this guidance**[5,6,7]*								
	[AF] Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) (with at least one additional risk factor) [8,9,10,11]								
	[DVT, PE] Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults [12,13, 14,15]								
	[ACS] Prevention of atherothrombotic events after acute management of acute coronary syndrome[16] *(NOTE: refer to current rivaroxaban 2.5mg tablet Summary of Product Characteristics (SPC). Efficacy and safety data based on ATLAS ACS 2-TIMI 51 trial)*								
	Dabigatran[1]		***Rivaroxaban[2] ▼***			***Apixaban[3] ▼***		***Edoxaban[4] ▼***	
Indication [NICE TA]	***AF [NICE TA 249]***	***DVT, PE [NICE TA 327]***	***AF [NICE TA 256]***	***DVT, PE [NICE TA 287]***	***ACS [NICE TA 335]***	***AF [NICE TA 275]***	***DVT, PE [NICE TA 341]***	***AF [NICE TA 355]***	***DVT, PE [NICE TA 354]***
Doses	Age < 80 yrs - 150mg twice daily Age ≥ 80 yrs or taking verapamil - **110mg twice daily** Following individual assessment of the individual risk of thromboembolism and bleeding consider **110 mg twice daily** if: - bleeding risk is high - age 75-80 yrs - patients with gastroesophageal reflux, oesophagitis or gastritis - CrCL 30-50mL/min	Following parenteral anticoagulant for at least 5 days - 150mg twice daily Duration of treatment individualised after careful assessment of the treatment benefit against the risk of bleeding	20mg once daily 15mg once daily when CrCL is 15-49 mL/min	15mg twice a day for 21/7 then 20mg daily (min. 3/12) CrCL 15-49 mL/min - 15mg twice a day for 21/7 then 20mg daily (or 15mg daily if risk of bleeding > risk of recurrent DVT & PE)	2.5mg twice daily with: -aspirin alone **Or** -aspirin plus clopidogrel or ticlopidine Use with caution if >75yrs or if <60kg Review regularly. Extension of treatment beyond 12 months should be done on an individual basis	5mg twice daily CrCL 15-29mL/min - 2.5mg twice daily Patients with two or more of the following give **2.5mg twice daily:** -age ≥80 yrs -body weight ≤60kg -serum Cr ≥133 micromole/l	Treatment dose DVT/PE - 10mg twice daily for the first 7 days followed by 5mg twice daily Prevention DVT/PE following 6/12 treatment dose – 2.5mg twice daily The duration of treatment should be individualised after careful assessment of the treatment benefit against the risk of bleeding	60mg once daily Patients with one or more of the following give **30mg daily:** - CrCL 15-50mL/min -body weight <60kg -concurrent P-gp inhibitors: ciclosporin, dronedarone, erythromycin or ketoconazole	Following parenteral anticoagulant for at least 5 days - 60mg once daily Duration of treatment individualised after careful assessment of the treatment benefit against the risk of bleeding
Mechanism of action	**Direct thrombin inhibitor**		**Direct factor Xa inhibitor**						
Assess bleeding risk in Atrial Fibrillation (HAS-BLED)	Use **HAS-BLED** score to assess 1 year major bleeding risk in people who are starting or have started anticoagulation with AF. Caution and regular review is recommended if score is ≥ 3; with efforts to offer modification and monitoring of the potentially reversible risk factors: • uncontrolled hypertension • poor INR control ('labile INRs') • concurrent medication (e.g. aspirin, NSAIDs) • harmful alcohol consumption[24]. Note: Do not withhold anticoagulation solely because the person is at risk of falls. For most people the benefit of oral anticoagulants outweighs the bleeding risks and a high HAS-BLED score should not be used to exclude anticoagulation therapy. Overtime the risks and benefits may change and clinicians should review both CHA_2DS_2-VAS_c and HAS-BLED following any changes in the individual's clinical condition and at least annually[25]. (see CHA_2DS_2-VAS_c and HAS-BLED calculator http://www.mdcalc.com/has-bled-score-for-major-bleeding-risk)								

	Dabigatran[1]	***Rivaroxaban***[2] ▼	***Apixaban***[3] ▼	***Edoxaban***[4] ▼
Interactions (***List not exhaustive. As NOACs enter more routine practice, it is likely that other drug-drug and food-drug interactions will be identified*** *– refer to electronic BNF and SPC when prescribing)*	➢ Potential for P-gp interactions e.g. amiodarone, verapamil, quinidine, ketoconazole, clarithromycin, rifampicin, phenytoin and carbamazepine ➢ SSRIs and SNRIs increased the risk of bleeding in RE-LY in all treatment groups ➢ See contraindication below	➢ Avoid concomitant treatment with strong inhibitors of both CYP3A4 and P-gp e.g. ketoconazole, itraconazole, voriconazole or HIV protease inhibitors ➢ Caution with strong CYP3A4 and P-gp inducers e.g. rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort as they may lead to reduced rivaroxaban concentrations ➢ Avoid use with dronedarone	➢ Avoid concomitant use with strong inhibitors of both CYP3A4 and P-gp e.g. ketoconazole, itraconazole, voriconazole or HIV protease inhibitors ➢ Avoid strong CYP3A4 and P-gp inducers e.g. rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort for VTE treatment since efficacy may be compromised ➢ Caution in the concurrent use with strong CYP3A4 and P-gp inducers in the prevention of stroke and systemic embolism for patients with NVAF and for the prevention of recurrent DVT and PE	➢ Potential for P-gp interactions. Recommend edoxaban 30mg daily with the concomitant use of following P-gp inhibitors: ciclosporin, dronedarone, erythromycin, or ketoconazole. Concomitant use of amiodarone, quinidine or verapamil does not require dose reduction The use of edoxaban with other P-gp inhibitors including HIV protease inhibitors has not been studied ➢ Caution with P-gp inducers e.g. rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort as they may lead to reduced edoxaban concentrations
	Close clinical surveillance (looking for signs of bleeding or anaemia) is recommended in patients treated concomitantly with NSAIDs (including acetylsalicylic acid), anti-platelets (see below) and any other drugs that can typically increase the risk of bleeding.			
Review of individuals with AF and existing cardiovascular disease taking anti-platelets	NICE CG180 advises to NOT offer aspirin monotherapy solely for stroke prevention to people with AF. It does not give specific advice on the treatment of patients with AF who have co-existing cardiovascular disease. **Where anticoagulants and anti-platelets are co-prescribed, the advice of the individual's consultant should be followed.** The decision to continue or stop anti-platelets is based on the individuals thromboembolic and bleeding risks. GPs should be vigilant in the co-prescribing of anti-thrombotic therapy and ensure anti-platelets are stopped in accordance with the consultant's treatment plan, and liaise with the consultant where there is a change in the patient's clinical condition i.e. the risk factors for stroke or bleeding and/or the addition of interacting medicines.			
Contraindications (C/I) (***List not exhaustive*** *– refer to current SPC)*	➢ Hypersensitivity ➢ A lesion or condition, if considered a significant risk factor for major bleeding ➢ Active bleeding ➢ Hepatic disease or impairment expected to impact survival ➢ Anticoagulant in use (except during switching -see below) ➢ Concomitant treatment with systemic ketoconazole, cyclosporine, itraconazole and dronedarone ➢ CrCL<30mL/min ➢ Prosthetic heart valves	➢ Hypersensitivity ➢ A lesion or condition, if considered a significant risk factor for major bleeding ➢ Active bleeding ➢ Hepatic disease associated with coagulopathy and clinically relevant bleeding risk ➢ Anticoagulant in use (except during switching -see below) ➢ Pregnancy and breast feeding ➢ Concomitant treatment of ACS with antiplatelet therapy in patients with a prior stroke or a transient ischaemic attack (TIA)	➢ Hypersensitivity ➢ A lesion or condition, if considered a significant risk factor for major bleeding ➢ Active clinically significant bleeding ➢ Hepatic disease associated with coagulopathy and clinically relevant bleeding risk ➢ Anticoagulant in use (except during switching -see below)	➢ Hypersensitivity ➢ A lesion or condition, if considered a significant risk factor for major bleeding ➢ Active bleeding ➢ Hepatic disease associated with coagulopathy and clinically relevant bleeding risk ➢ Anticoagulant in use (except during switching -see below) ➢ Pregnancy and breast feeding ➢ Uncontrolled severe hypertension
Administration	Take with or without food. Swallow whole - opening capsules increases plasma levels and may increase risk of bleeding.	The 15mg and 20mg dose **must be taken with food to increase absorption.** Maybe crushed and put through a gastric tube if required[17].	Take with or without food. Maybe crushed and suspended as per SPC instructions to be given immediately orally or via a nasogastric tube.	Take with or without food.

	Dabigatran[1]	***Rivaroxaban***[2] ▼	***Apixaban***[3] ▼	***Edoxaban***[4] ▼
Efficacy for stroke prevention	Note: The differences in efficacy compared to warfarin are due to clinical and methodological differences between the trials. We are unable to recommend an overall preferred NOAC, based on efficacy without direct comparative studies.			
	Superior to warfarin with 150mg twice daily dose. Non-inferior to warfarin with 110mg twice daily dose (RE-LY)[18].	Non-inferior to warfarin (ROCKET-AF)[19].	Superior to warfarin (ARISTOTLE)[20].	Non-inferior to warfarin (ENGAGE AF-TIMI 48)[21].
Poor adherence	NOACs have shorter half-life therefore missed doses may result in more time without any anticoagulation and greater risk of thromboembolic complications. Warfarin – longer half-life and once a day dosing.			
	Twice a day dosing.	Once a day dosing.	Twice a day dosing.	Once a day dosing.
Missed dose	Missed dose may still be taken up to 6 hours prior next scheduled dose. If within 6 hours of next dose, the missed dose should be omitted.	Missed dose should be taken immediately and then continued on the following day with once a day dosing. Do not double dose within the same day to make up for missed dose (except if taking 15mg twice daily for DVT/VTE treatment, take 2x15mg immediately to ensure a dose of 30mg daily. Continue 15mg twice daily intake as recommended on the following day).	Missed dose should be taken immediately and then continued with twice a day as before.	Missed dose should be taken immediately and then continued once daily as before. Do not double dose within the same day to make up for missed dose.
Requirement for compliance aid	Warfarin – not suitable for compliance aids unless risk assessment has been undertaken and a management plan is in place to manage dosage changes[22]			
	Capsules taken out of blister are not suitable for compliance aids. Shelf life of 3 years for blister and bottle. Once bottle is opened, the product must be used within 4 months.	**Can be used in compliance aids.** Shelf-life of 3 years and no special storage requirement.	**Can be used in compliance aids.** Shelf-life of 3 years and no special storage requirement.	**Use in compliance aid has not been studied and is not recommended.** Shelf-life of 3 years and no special storage requirement in original blister packaging.
Mechanical heart valve	Contraindicated	Not studied – not recommended	Not studied – not recommended	Not studied – not recommended
Valvular disease	Not studied – not recommended	Not studied – not recommended	Not studied – not recommended	Not studied – not recommended
Extremes of BMI	Exposure of NOACs may vary by 20-30% at extremes of bodyweight (<50 kg or >100-120 kg). This may be problematic given the difficulties in monitoring the therapeutic effects. It is recommended that Cockcroft and Gault formula is used to calculate CrCL to adjust NOAC dosage or product.			
Renal impairment *(see additional advice above in Doses)*	**Cockcroft and Gault formula: CrCL = (140-Age) X Weight X Constant / Serum creatinine** ***[Age (in years). Weight* (in kilograms). Constant = 1.23 (Men); 1.04 (Women). Serum creatinine (in micromole/litre)]*** (see BNF: Prescribing in renal impairment[23] and electronic calculator link) **NB: Ideal Body Weight (IBW) should be used if the patient is clinically obese i.e. >20% over IBW (see IBW calculator link)*			
	Patients must have a baseline renal function test before initiating NOAC. Renal function can decline while on treatment hence monitor annually or more often in high risk patients. Note: In practice eGFR and CrCL are not interchangeable; however for most drugs and for most patients (over 18 years) of average build and height, eGFR could provide some guidance. The SPC of each NOAC recommends that 'Cockcroft and Gault' formula is used for dosing and monitoring.			

	Dabigatran[1]	***Rivaroxaban***[2] ▼	***Apixaban***[3] ▼	***Edoxaban***[4] ▼
Renal impairment *(see additional advice above in Doses)*	Contraindicated in CrCL<30mL/min	Not recommended if CrCL<15mL/min Use with caution if CrCL 15-29mL/min	Not recommended if CrCL<15mL/min Use with caution if CrCL 15-29mL/min	Not recommended if CrCL<15mL/min Renal function in NVAF – A trend towards decreasing efficacy with increasing CrCL. Edoxaban should only be used in patients with NVAF and high CrCL after careful evaluation of the individual thromboembolic and bleeding risk[4]
Hepatic impairment	Not recommended in patients with elevated liver enzymes >2 upper limit of normal. Contraindicated in patients with hepatic impairment or liver disease expected to impact on survival.	Use with caution as requires hepatic metabolism. Contraindicated in hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic with Child Pugh B and C.	Not recommended in severe hepatic impairment as requires hepatic metabolism. Contraindicated in hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Caution in patients with mild or moderate hepatic impairment (Child Pugh A or B), elevated ALT/AST (>2x upper limit normal) or total bilirubin (≥1.5x upper limit normal). Check baseline LFTs prior initiation.	Not recommended in severe hepatic impairment as requires hepatic metabolism. Contraindicated in hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Caution in patients with elevated ALT/AST (>2x upper limit normal) or total bilirubin (≥1.5x upper limit normal). Check baseline LFTs prior initiation and periodic monitoring if treatment beyond 12 months.
Age (≥80 yrs)	Use reduced dose -110mg twice daily.	No dose reduction unless age related renal impairment.	Consider dose reduction in ≥80yrs – 2.5mg twice daily.	No dose reduction unless age related renal impairment.
Pregnancy & breastfeeding	Not recommended.	Contraindicated in pregnancy and breastfeeding.	Not recommended.	Contraindicated in pregnancy and breastfeeding.
Major bleed risk compared to warfarin	Similar risk with 150mg twice daily Reduced risk with 110mg twice daily (RE-LY)[18]	Similar risk (ROCKET-AF)[19]	Reduced risk (ARISTOTLE)[20]	Reduced risk (ENGAGE AF-TIMI 48)[21]
Intracranial bleed risk compared to warfarin	Reduced risk (RE-LY)[18]	Reduced risk (ROCKET-AF)[19]	Reduced risk (ARISTOTLE)[20]	Reduced risk (ENGAGE AF-TIMI 48)[21]
Major GI bleed risk compared to warfarin	Significantly increased risk with 150mg twice daily. Similar risk with 110mg twice daily (RE-LY)[18]	Significantly increased risk (ROCKET-AF)[19]	Similar risk (ARISTOTLE)[20]	Increased risk (ENGAGE AF-TIMI 48)[21]
Risk of dyspepsia/ upper GI side effects compared to warfarin	Dyspepsia was significantly more common with both doses of dabigatran (RE-LY)[18]	Similar risk of dyspepsia (ROCKET-AF)[19]	Similar risk of dyspepsia (ARISTOTLE)[26]	Similar risks of nausea, gastritis and dyspepsia[27]
Risk of MI compared to warfarin	Trend towards increased risk but did not reach statistical significance (RE-LY)[18]	Reduced risk but trend did not reach statistical significance (ROCKET-AF)[19]	Reduced risk but trend did not reach statistical significance (ARISTOTLE)[20]	Reduced risk but trend did not reach statistical significance[27]

	***Dabigatran*[1]**	***Rivaroxaban*[2] ▼**	***Apixaban*[3] ▼**	***Edoxaban*[4] ▼**
Reversibility	Data suggest dabigatran can be dialysed or reversed with prothrombin complex concentrate (PCC) however evidence and experience is limited[1, 28]. Note: The EMA granted positive opinion to idarucizumab (Sept 2015), the specific reversal agent to dabigatran, if rapid reversal of its effects are required.	Haemodialysis will not clear rivaroxaban and currently there is no antidote. Data suggest reversibility with PCC[29] may be considered but limited clinical experience.	Haemodialysis is unlikely an effective mean of clearing apixaban and currently there is no antidote.	Haemodialysis is not expected to be effective mean of clearing edoxaban and there is currently no antidote. Data suggest reversibility with PCC may be considered.
	If patient develops minor bleeding, consider withholding the NOAC and investigate source of bleeding. Patients who develop major bleeding should be referred to Accident & Emergency (A&E) upon which consultation with haematologist should be undertaken.			
Conversion from warfarin to NOAC *(consult locally agreed pathways if available)*	Discontinue warfarin and start dabigatran when the INR<2.0. Caution: INR values will be falsely elevated when taking dabigatran.	Discontinue warfarin and start rivaroxaban when: - INR ≤3.0 for prevention of stroke and systemic embolism. - INR ≤2.5 for DVT, PE and prevention of recurrence. Caution: INR values will be falsely elevated after the intake of rivaroxaban.	Discontinue warfarin and start apixaban when the INR<2.0.	Discontinue warfarin and start edoxaban when the INR<2.5.
Conversion from NOAC to warfarin/alternative NOAC *(consult locally agreed pathways if available)*	**Dabigatran to warfarin –** CrCL ≥50mL/min – Start warfarin 3 days before discontinuing dabigatran. CrCL ≥30- <50mL/min – Start warfarin 2 days before discontinuing dabigatran[5]. CrCL <30mL/min – dabigatran is contraindicated if CrCL<30mL/min. Advised to consult haematologist if converting to warfarin/alternative NOAC. Caution: INR values will be falsely elevated. INR testing should not be performed until dabigatran has been stopped for at least 2 days.	**Rivaroxaban to warfarin –** Co-administer rivaroxaban and warfarin until INR>2.0. Test INR 24hours after previous dose but prior next dose of rivaroxaban. Start warfarin as standard initial dosing followed by dosing guided by INR testing. Once rivaroxaban is discontinued, INR testing may be done reliably at least 24hours after the last dose.	**Apixaban to warfarin –** Continue with apixaban for at least 2 days after starting warfarin therapy. Check INR after 2 days of co-administration. Obtain INR before next schedule dose of apixaban. Continue co-administration until the INR ≥2.0 then discontinue apixaban.	**Edoxaban to warfarin –** For patients on 60mg dose – co-administer edoxaban 30mg daily with warfarin. Those on 30mg dose – co-administer edoxaban 15mg with warfarin. Patients should not take a loading dose of warfarin in order to promptly achieve a stable INR between 2-3. During first 14 days of concomitant therapy measure INR at least three times just before schedule dose of edoxaban to minimise influence on INR measurements. Continue co-administration until the INR is >2.0 then discontinue edoxaban. **Edoxaban to alternative NOAC –** discontinue edoxaban and start other NOAC at time of next scheduled dose of edoxaban.
	NOACs have shorter half-life and converting a NOAC to an alternative NOAC should be theoretically uncomplicated. To date, dabigatran, rivaroxaban and apixaban have little evidence of such practice and it would be advisable to seek advice from specialist anticoagulant team or GPwSI when necessary.			

	Dabigatran[1]	Rivaroxaban[2] ▼	Apixaban[3] ▼	Edoxaban[4] ▼
Before surgery *(consult specialist advice on the overall risk for thromboembolism and bleeding on an individual patient basis for any peri-procedural management - see SPC for details)*	Depending on renal function stop dabigatran 1 - 4 days prior elective surgery or invasive procedure. If acute, surgery/invasive procedure should be delayed if possible until at least 12 hours after the last dose.	If possible, based on the clinical judgement of the physician, discontinue rivaroxaban 10mg, 15mg or 20mg tablets 24 hours before surgery or invasive procedure. Rivaroxaban 2.5mg - If possible, based on the clinical judgement of the physician, discontinue 12 hours before surgery or invasive procedure.	Discontinue at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of bleeding. Discontinue at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding.	If possible, based on the clinical judgement of the physician, discontinue 24 hours before surgery or invasive procedure.
	If the procedure cannot be delayed the increased risk of bleeding should be assessed by the specialist against the urgency of the intervention.			

Key for summary table:

NOACs (VTE prevention post hip and knee replacement) – not covered in this guidance ***Common features/recommendations of NOACs***

Dabigatran ***Rivaroxaban (NVAF and DVT/PE) and Rivaroxaban (ACS)*** ***Apixaban*** ***Edoxaban***

▼ *- Newly marketed drugs and vaccines are intensively monitored for a minimum of two years, in order to confirm the risk / benefit profile of the product. Healthcare professionals are encouraged to report all suspected adverse drug reactions.*

This information is a summary to guide prescribers – for up to date information please consult individual SPCs at www.medicines.org.uk

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Further resources

1. European Heart Rhythm Association (EHRA) Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation: executive summary. April 2013.
2. Common questions and answers on the practical use of oral anticoagulants in non-valvular atrial fibrillation. South West Medicines Information and Training & Regional Drug and Therapeutics Centre (Newcastle). March 2015.
3. NICE Patient decision aid. Atrial fibrillation: medicines to help reduce your risk of stroke – what are the options. June 2014.
4. Stroke Prevention in Atrial Fibrillation Risk (SPARC) Tool.
5. NICE CG 182. Chronic kidney disease: early identification and management of chronic kidney disease in adults in primary and secondary care. July 2014.
6. Eliquis® (apixaban) – Educational risk minimisation material to help reduce the risk associated with using this medicine.
7. Lixiana® (edoxaban) – Educational risk minimisation material to help reduce the risk associated with using this medicine.

Appendix: 1

GP checklist for patients on NOACs

The following counselling checklist should be completed by the prescriber when a NOAC is being used. Further information and support may be provided by your local hospital trust and/or CCG medicines optimisation team if required.

NOAC** (please circle) **Dabigatran/ Rivaroxaban/ Apixaban/ Edoxaban				***Tick when completed***	***Date:***
CHA_2DS_2-VAS_c score:		**HAS –BLED score:**			
Patient will require a longer GP consultation time to cover all the advice.					
Give a full explanation of the indication and rationale for prescribing a NOAC.					
Explain how the drug works i.e. 'blood takes longer to clot not thinner'.					
Explain the intended duration of therapy.					
Explain the required dose and time to take NOAC.					
Explain the follow-up arrangements to assess compliance, side-effects, bleeding and monitoring.					
Explain the risk of potential drug interactions and changes, particularly antibiotics and over the counter medicines.					
Explain the risk of bleeding / bruising and what action to take in the event of bleeding, fall or head injury.					
It is essential that the patient is fully aware of the lack of reversal agents for NOACs.					
Ensure patients carry a Patient Alert Card and provide any other available information to support NOAC use i.e. locally produced patient information leaflets.					
Always inform any healthcare professional, including doctors, pharmacists and dentists that they are taking an anticoagulant and to show their Patient Alert card.					
Stress the importance of compliance, especially for patients switching from warfarin who are used to being monitored.					
Explain what to do if the patient misses a dose.					
Lifestyle advice, including contact/extreme sports should be included in the counselling.					
Explain how to get repeat prescriptions.					
Ensure patients know when to seek medical help.					
Provide the patient opportunities to ask questions and ensure his/her understanding of all advice given.					
Advice given by whom?					