

DOAC Prescribing Support for NCL AF and VTE

Disclaimer

This guideline is registered at North Central London (NCL) Joint Formulary Committee (JFC) and is intended solely for use by healthcare professionals to aid the treatment of patients within NCL. However, clinical guidelines are for guidance only, their interpretation and application remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Clinicians are advised to refer to the manufacturer's current prescribing information before treating individual patients.

The authors and NCL JFC accept no liability for use of this information from this beyond its intended use. While we have tried to compile accurate information in this guideline, and to keep it updated in a timely manner, we cannot guarantee that it is fully complete and correct at all times. If you identify information within this guideline that is inaccurate, please report this to the admin@ncl-jfc.org.uk. If a patient is harmed as a consequence of following this guideline, please complete a local incident report and inform admin@ncl-jfc.org.uk.

This guideline should not be used or reproduced for commercial or marketing purposes.

NCL JFC is funded by and provides advice to Acute Trusts and Clinical Commissioning Groups in NCL.

Document control

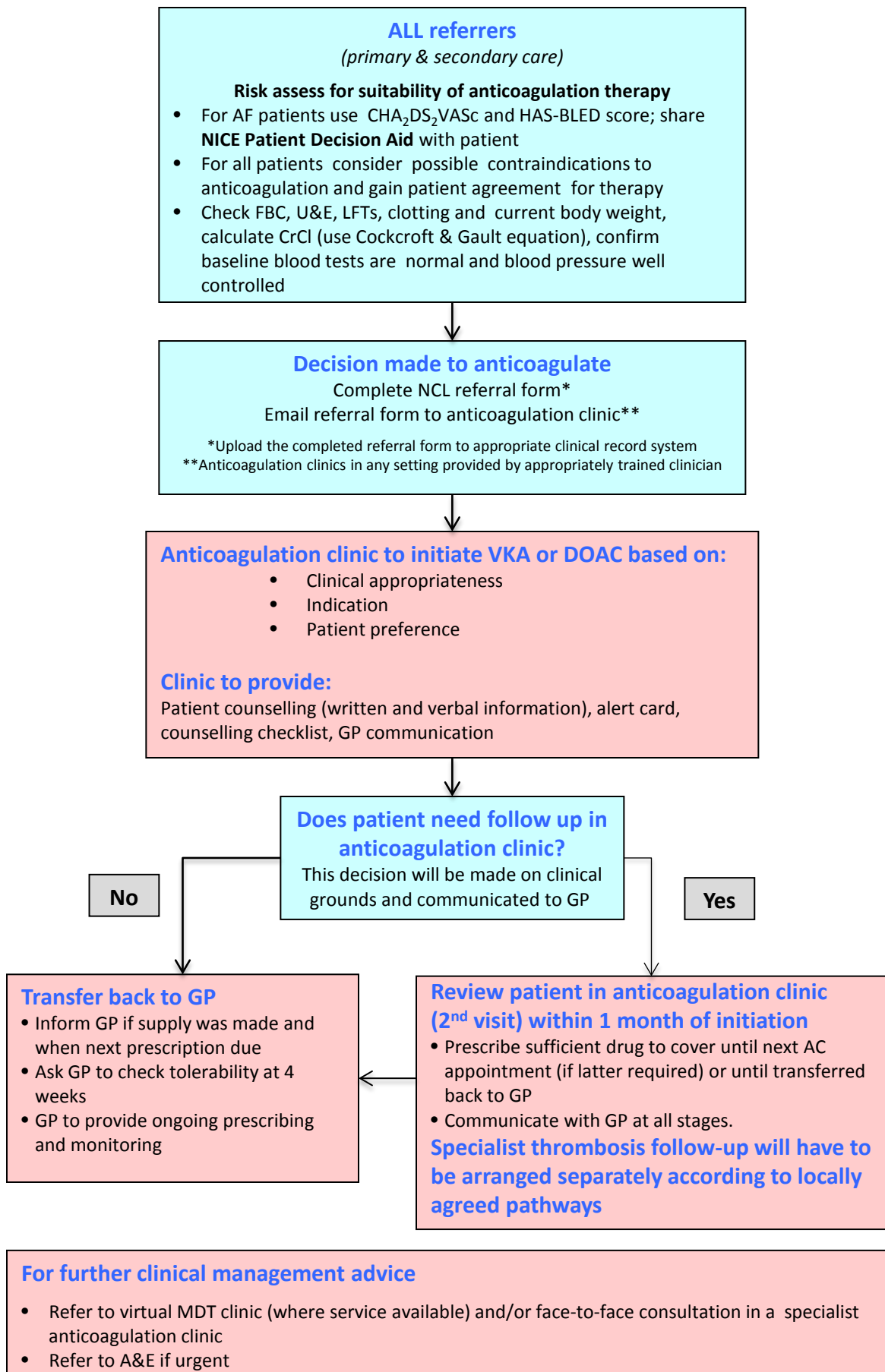
Date	Version	Amendments
20Dec16	1	New document

Document management

Groups / Individuals who have overseen the development of this guidance:	Dr Anja Drebes, Consultant Haematologist, Royal Free London NHS Foundation Trust Ms Carolyn Gates, Thrombosis and Anticoagulation Pharmacist, University College London NHS Foundation Trust
Groups and individuals which were consulted:	NCL Joint Formulary Committee, NCL Heads of Medicines Management, Dr A Bakhai, RFL Consultant Cardiologist Dr A Chandratheva, UCLH Consultant Neurologist Mr M Chevli, RFL Principle Pharmacist Dr H Cohen, UCLH Consultant Haematologist Dr C Lopez-Pieg, Enfield CCG GP Mr I Man, WH Pharmacist Dr C Mitchell, NCUH Consultant Haematologist Dr S Morgan, Camden CCG GP Dr R Sofat, UCLH Consultant Clinical Pharmacologist Dr M Thomas, UCLH Consultant Haematologist Ms B Packham, RFL Nurse Consultant Anticoagulation Ms J Walker, UCLH Clinical Nurse Specialist Anticoagulation
File name:	DOAC Prescribing Support for NCL: AF and VTE
Version number:	1
Available on:	NCL JFC Website
Disseminated to:	NCL CCGs NCL Formulary Pharmacists
Equality impact assessment:	Low
NCL Joint Formulary Committee Approval date:	December 2016
Review date:	December 2018

Disclaimer: This document is for informational purposes only and does not, itself, constitute medical advice. It is not a replacement for careful medical judgments by qualified personnel. There may be information in the document that does not apply to or may be inappropriate for the medical situation at hand.

Summary treatment pathway: Anticoagulation for non-valvular AF and VTE (adults)



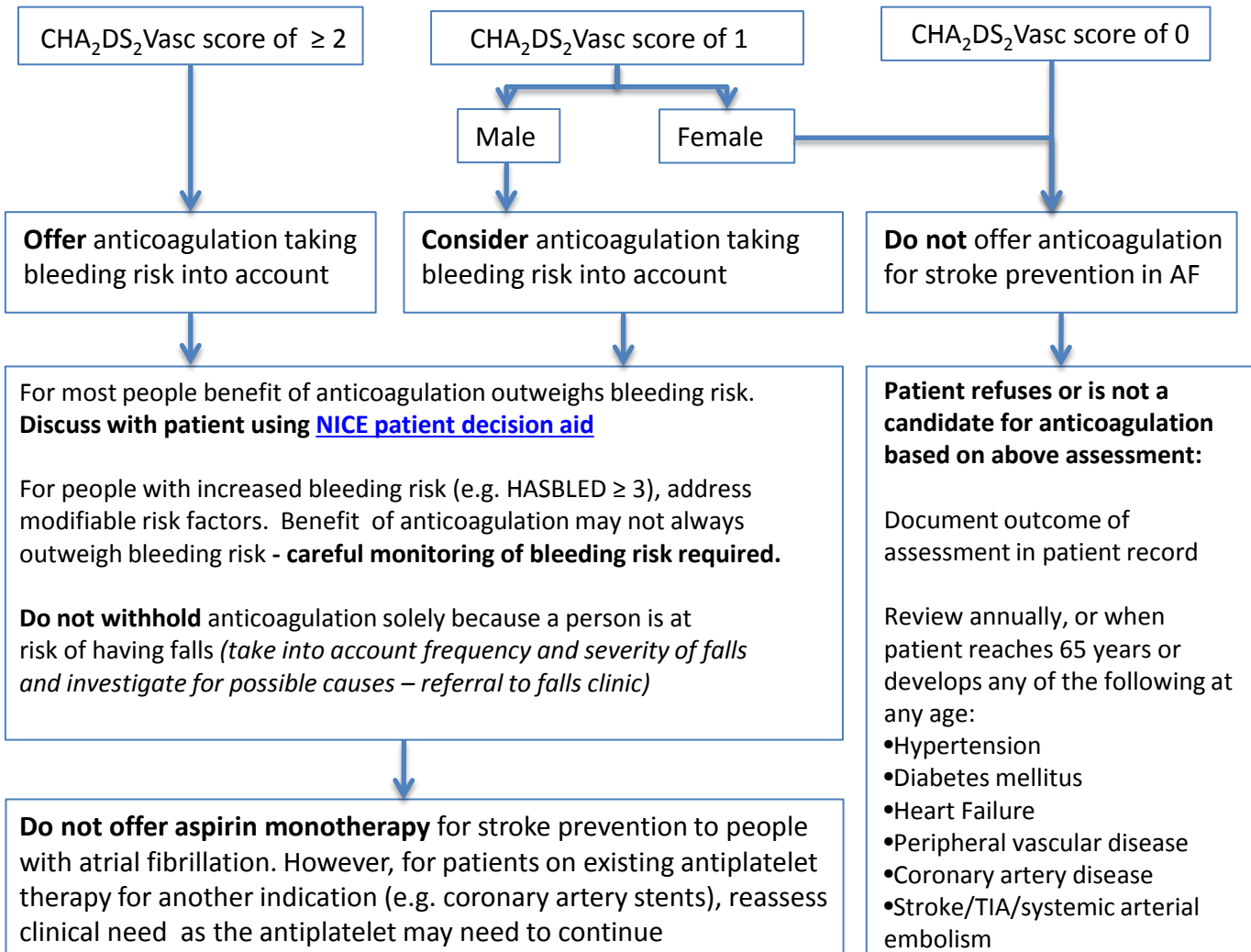
Assessing stroke/bleeding risk for patients with non-valvular AF

CHA ₂ DS ₂ Vasc	Score	HASBLED	Score
Congestive heart failure/LV dysfunct.	1	Hypertension (uncontrolled, > 160 mmHg systolic)	1
Hypertension	1	Chronic liver disease or Bili 2xULN with AST/ALT/ALP 3x ULN	1
Age ≥ 75	2	Abnormal renal function (creatinine ≥200 umol/L, renal transplant or chronic dialysis)	1
Diabetes mellitus	1	Stroke	1
Stroke/TIA/systemic arterial embolism	2	History of major bleeding ¹ or predisposition	1
Vascular disease (prev. MI, peripheral arterial disease, aortic plaque)	1	Labile INRs, time in range less than 60%	1
Age 65 -74	1	Elderly (age ≥ 65 or frail condition)	1
Sex (male 0, female 1)	F 1	Drugs (concomitant antiplatelet, NSAIDs etc) or alcohol abuse (1 point each)	1 or 2
Total score (maximum score 9)		Total score (maximum score 9)	

CHA ₂ DS ₂ -VAsc score	Adjusted stroke rate (%/year)
0	0%
1	1.3%
2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
9	15.2%

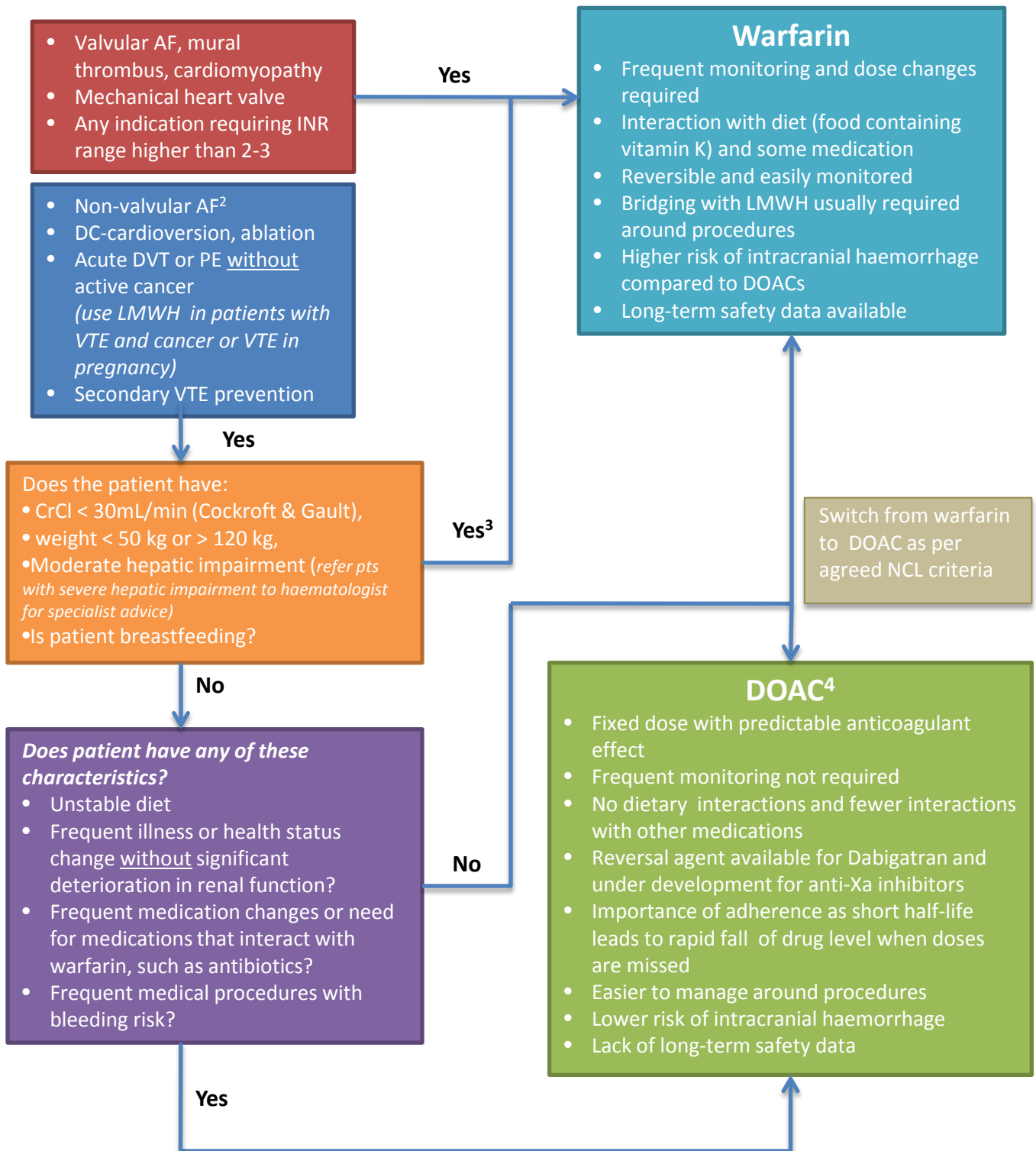
HAS-BLED score	Major bleed s per 100 pt years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.50
6-9	Insufficient data

¹Bleeding requiring hospitalisation and/or causing decrease in Hb >20 g/L and/or requiring ≥2 units blood transfusion



Anticoagulant Selection Tool¹

Indication for anticoagulation



1. Flow-chart adapted from toolkit produced by Michigan Anticoagulation Quality Improvement Initiative version 1.5/updated on 19/2/16
2. Non-valvular AF refers to AF that occurs in the absence of mechanical prosthetic heart valves and in the absence of moderate to severe mitral stenosis (usually of rheumatic origin)
3. Patients with CrCL <30mL/min were excluded from clinical trials (CrCL <25mL/min for apixaban). DOAC should not be used unless specifically advised by consultant haematologist. Patients with ALT/AST 2xULN or Bili ≥ 1.5xULN were excluded from the main clinical trials. DOACs are either contraindicated or are to be used cautiously depending on degree of liver impairment.
4. Each DOAC is only approved for certain indications and may have warnings for use in specific populations (i.e. renal impairment/hepatic failure) and with certain concurrent medications (P-gp/CYP3A4 inducers or inhibitors).

Choice of oral anticoagulant based on patient characteristics

Patient characteristic	Drug choice	Rationale
Mechanical heart valve	Warfarin	Increased risk of thrombosis/bleeding reported with dabigatran compared warfarin; other DOACs not studied in this setting
AF with valvular disease	Warfarin	All trials excluded patients with mechanical valves or moderate to severe (haemodynamically significant) mitral stenosis
Any indication requiring higher range INR than 2-3	Warfarin	
Moderate hepatic impairment (Child-Pugh B)	Warfarin	Patients with ALT/AST 2 x ULN (ALT 3 x ULN for rivaroxaban) or Bili ≥ 1.5 x ULN were excluded from the main clinical trials. Use of DOACs in patients with moderate hepatic impairment is not recommended (see SPCs for more details)
Severe hepatic impairment (Child-Pugh C)	Refer to Haematologist for advice	All DOACs are contraindicated in patients with severe hepatic disease associated with coagulopathy and clinically relevant bleeding risk, including cirrhotic patients
CrCl <30 mL/min	Warfarin	Patients with CrCl <30mL/min were excluded from clinical trials (CrCl <25mL/min for apixaban). ESC guidance from 2016 suggests that warfarin should be preferred anticoagulant in this patient group
Extremes of body weight <50 kg or >120 kg	Warfarin	Limited trial data – avoid use of DOACs (local recommendation) unless d/w haematologist
Antiphospholipid syndrome	Haematologist to advise	Refer to haematology consultant for advice on anticoagulation management.
Previous intracranial bleed (<i>Decision to anticoagulate as per neurosurgical advice</i>)	Haematologist to advise	Risk of intracranial bleeding less with DOACs than Warfarin. Patients with previous intracranial bleed excluded from trials.
Dyspepsia	Warfarin Apixaban Rivaroxaban Edoxaban	Dyspepsia in up to 10% of patients on dabigatran.
History of gastrointestinal bleed or ulcer (<i>Check that underlying cause has been treated</i>)	Warfarin Apixaban	More GI bleeds with dabigatran (150mg), edoxaban (60mg) or rivaroxaban than with warfarin. Warfarin easier to reverse if there is a further bleed.
Requirement for compliance aid such as blister pack/dosette box	Rivaroxaban Apixaban Edoxaban	Dabigatran capsules must be kept in their original container. Warfarin should not be dispensed into a sealed compliance aid (due to variable dosing)

DOAC initiation checklist

Checklist	Comments
<p>Assess bleeding risk:</p> <p>HASBLED score - alcohol consumption should not exceed nationally recommended amount (address risk factors for bleeding where possible)</p> <p>Check for lesions or conditions considered to be significant risk factors for major bleeding</p> <p>Frequency and severity of falls</p> <p>Check clotting, FBC (last 4 weeks)</p>	<p><u>Clinical management of patients with any of the following conditions should be discussed with a Haematologist:</u></p> <ul style="list-style-type: none"> • Current/recent upper or lower GI ulceration, oesophageal varices (known or suspected), malignant neoplasms at high risk of bleeding • Surgery/trauma or bleed affecting head/brain, eyes or spine within last 4 weeks • AV malformations, vascular aneurysms or major intraspinal / intracerebral vascular abnormalities • Stroke in last 14 days/severe stroke in last 6 months (unless advised by designated stroke neurology cons) • Thrombocytopenia $<50 \times 10^9/L$ • Congenital or acquired bleeding disorder (abnormal baseline clotting screen, haemophilia, low fibrinogen)
<p>Ensure DOAC use is licensed for required indication</p> <p>Establish length of anticoagulation based on indication</p>	<p>DOACs are currently only approved for stroke prevention in patients with non-valvular atrial fibrillation and treatment/prevention of VTE</p> <p>DOACs are contraindicated in patients with mechanical heart valves and should not be used for:</p> <ul style="list-style-type: none"> • indications requiring higher intensity anticoagulation e.g. INR target greater than 2.5 (range higher than 2.0 – 3.0) if on warfarin • patients with co-existing myeloproliferative disorders, nephrotic syndrome, sickle cell disease, antiphospholipid syndrome, cancer (limited clinical evidence – D/W haematologist)
<p>Check renal function (last 4 weeks) (CrCl > 30mL/min, C&G)</p>	<p>DOACs rely on renal function for elimination and should be used with caution in patients with significant renal disease. DOAC dosing is adjusted according to renal function – avoid if CrCl less than 30 mL/min</p>
<p>Check liver function (last 4 weeks)</p>	<p>DOACs are contraindicated in patients with significant hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C</p>
<p>Check blood pressure control</p>	<p>Good blood pressure control should be achieved before initiation of anticoagulation</p>
<p>Check body weight</p>	<p>There is limited trial evidence in patients at the extremes of body weight (< 50 kg or >120 kg) – avoid use (local recommendation)</p>
<p>Review medication for potential drug interactions</p>	<p>While DOACs have fewer drug interactions, there are still medications that increase or decrease drug exposure. Consider addition of proton pump inhibitor if essential for patient to remain on medication that increases bleeding risk (i.e. antiplatelet agents)</p>
<p>Consider patient's compliance with medication</p>	<p>Since DOACs have a short half-life compared to warfarin and do not require monitoring, compliance may be a more important concern. Dabigatran must not be dispensed into reminder devices</p>
<p>Pregnancy test for women of childbearing age - advise on adequate contraception</p>	<p>DOACs are contraindicated in pregnancy and when breastfeeding (crosses placenta and into breast milk).</p>

Switching from warfarin to DOAC

Indications for switch from warfarin to DOACs in patients requiring long term anticoagulation	Comments
Known allergy / intolerance to warfarin or other vitamin K antagonist	e.g. alopecia with no other cause (such as iron deficiency anaemia, hypothyroidism etc)
Significant technical difficulties with INR monitoring and/or accessing A/C clinic that raises safety concerns	Consider alternatives such as community A/C services, domiciliary monitoring/input or self-testing
Patient-time in range < 65% once established on warfarin (not due to wilful non-compliance).	Non-compliance will not necessarily improve with switch to a DOAC and will be more difficult to detect.
INR \geq 8.0 on 1 occasion or INR \geq 5.0 on 2 occasions over a period of 6 months (once A/C is established), with a high likelihood of recurrence (i.e. unsafe)	
Awaiting DC-cardioversion or urgent AF ablation within 4 weeks	
Specific clinical indication as per locally designated consultant in stroke medicine / thrombosis / cardiology	
Patient preference (if clinically appropriate)	
<p>Switching patients from warfarin or low molecular weight heparin (LMWH) to DOAC</p> <ul style="list-style-type: none"> • Only secondary care or GP led anticoagulation clinics should switch patients to DOAC • If taking warfarin: <ul style="list-style-type: none"> • Stop warfarin • Check INR in two days and start appropriate DOAC if INR < 2.0 • If taking LMWH: <ul style="list-style-type: none"> • Stop LMWH • If LMWH dosing is once daily, start appropriate DOAC approximately 24hours after the last dose of LMWH • If LMWH is twice daily, start DOAC approximately 12hours after the last dose of LMWH • Do not 'cross-cover' LMWH with DOAC 	

DOAC dosing in non-valvular AF

Renal function	CrCL > 50 mL/min					
	Age < 75y and wt > 50 kg	Age 75-79y and wt > 50 kg	Age ≥ 80y and wt > 60 kg	Age ≥ 80y and 50 - ≤ 60 kg	HASBLED ≥3 Or ↑ bleeding risk	Any age and < 50 kg or > 120 kg
Rivaroxaban	20 mg od				Consider 15 mg od	Do not use*
Apixaban	5 mg bd			2.5 mg bd	Consider 2.5mg bd	Do not use*
Edoxaban <i>Avoid if CrCL >95mL/min**</i>	60 mg od 30 mg od if ≤ 60kg or if taking P-gp inhibitor e.g. ciclosporin, dronedarone, erythromycin, ketoconazole (see also drug interaction table)			30 mg od	Consider 30mg OD	Do not use*
Dabigatran	150 mg bd 110mg bd if also on verapamil OR at ↑risk of bleeding (e.g. GI risks)	110 mg bd	110 mg bd			Do not use*

* Unless specifically advised by local haematology consultant. **↑rate of ischaemic stroke vs warfarin (AF)

NB: Certain drug interactions (other than those stated above / below) may also require consideration of dose reduction (see drug interaction table)

NB: Haematologist may advise individualised doses other than those detailed within these tables

Renal function	CrCL 30 - ≤ 50mL/min				Cr CL 15 - 29 mL/min	Cr CL < 15 mL/min
	Age < 75y and wt > 50 kg	Age 75 - 79y and wt > 50 kg	Age ≥ 80y and wt > 50 kg	Any age and wt < 50 kg or > 120 kg	Any age / wt	Any age / wt
Rivaroxaban	15 mg od			Do not use*	Do not use*	Contra-indicated
Apixaban	5mg bd if > 60 kg 2.5mg bd if 50 - ≤ 60kg (consider 2.5mg bd if HASBLED ≥3 OR at ↑risk of bleeding)		2.5mg bd	Do not use*	Do not use*	
Edoxaban	30 mg od			Do not use*	Do not use*	
Dabigatran	150 mg bd 110 mg bd if on verapamil OR at ↑risk of bleeding (e.g. HASBLED ≥3 or GI risks)	110 mg bd	Consider alternative drug	Do not use*	Contra-indicated	

DOAC dosing in VTE

Renal function	CrCL ≥ 30 mL/min			
	Initiation	Maintenance	Secondary prevention after 6 months	wt < 50 kg or > 120 kg
Rivaroxaban	15 mg bd for 21 days	20 mg od Consider 15mg od, if CrCL 30-49mL/min and the risk of bleeding outweighs risk for recurrent VTE		Do not use*
Apixaban	10 mg bd for 7 days	5 mg bd	2.5 mg bd	Do not use*
Edoxaban	Therapeutic dose LMWH for 5 days	60mg od 30 mg od with one or more of the following: • CrCL 30-50mL/min • body weight ≤ 60kg • concomitant P-gp inhibitor e.g. ciclosporin, dronedarone, erythromycin, ketoconazole (<i>see also drug interaction table</i>)		Do not use*
Dabigatran	Therapeutic dose LMWH for 5 days	150 mg bd 110mg bd if age ≥ 80y or concomitant verapamil Consider 110 mg bd if thrombotic risk low, but bleeding risk high: e.g. age 75-80y, CrCL 30-50mL/min or at other increased risk of bleeding (e.g. GI)		Do not use*

* Unless specifically advised by local haematology consultant.

NB: Certain drug interactions (other than those stated above) may also require consideration of dose reduction (see drug interaction table)

NB: Haematologist may advise individualised doses other than those detailed within these tables

Renal function	CrCL 15 - < 30mL/min	CrCL < 15 mL/min
Rivaroxaban	Do not use*	Contra- indicated
Apixaban	Do not use*	
Edoxaban	Do not use*	
Dabigatran	Contra- indicated	

DOAC frequency of follow-up

DOACs are predominantly eliminated by the renal route, it is therefore prudent to regularly monitor renal function and adjust dosing accordingly.

The renal function is assessed using **creatinine clearance, which must be calculated** by Cockcroft Gault formula (<http://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation/>) eGFR is **not** a suitable alternative, especially in the frail elderly.

Baseline blood tests

Patient group	U/Es (calculate CrCl)	weight	FBC	LFTs	Clotting screen
All patients	✓	✓	✓	✓	✓

Frequency of follow-up blood tests

Patient group	U/Es (calculate CrCl)	weight	FBC ²	LFTs	Clotting screen ³
CrCl >60 mL/min	annually ¹	annually	annually ²	At least annually or more frequently during illness affecting liver function Seek advice if AST/ALT >2x or bilirubin >1.5x ULN	APPT, PT and INR will not provide information on intensity of anticoagulation effect ³
CrCl 40- 60 mL/min	6 monthly	6 monthly	6 monthly ²		
Any of the following: CrCl <40 mL/min, high bleeding risk, Age ≥75, wt <60 kg Rapid deterioration in renal function	at least 3 monthly	at least 3 monthly	at least 3 monthly ²		
CrCl <30 mL/min	dabigatran contraindicated apixaban, edoxaban, rivaroxaban - NCL guidance is not to use , unless advised by haematologist				
Cr Cl <15 ml/min	apixaban, edoxaban, rivaroxaban - do not use (dabigatran contraindicated if CrCL less than 30ml/min)				

¹if edoxaban is used for AF, review choice of agent if CrCl >95 mL/min as reduced efficacy

² in addition to general clinical surveillance, laboratory testing of haemoglobin could be of value to detect occult bleeding, especially in patients at higher risk of bleeding complications

³ routine monitoring of anticoagulant effect of DOACs is **not** required. Standard coagulation parameters (APTT, PT, INR) may be affected to varying degrees by the different DOACs, but will **not** provide quantitative information on the level of anticoagulation achieved (poor correlation)

Managing deterioration of renal function

Any acute illness that MAY affect renal function	Check U/Es and calculate creatinine clearance. Reduce dose or withhold treatment if required. Consider seeking specialist advice regarding restarting treatment.
Significant reduction in renal function	Reduce dose as appropriate (see dosing guidance), increase frequency of routine follow-ups. Close monitoring will be required during any intercurrent illness and perioperatively. If renal function continues to worsen seek specialist advice.
Fall of CrCl to <30mL/min	Stop DOAC, assess for bleeding and seek specialist advice as to whether specific assays are indicated/alternative anticoagulation required (i.e. switch to warfarin).

DOAC follow-up checklist

At each follow-up visit	Comments
Assess compliance	<p>Review prescribing schedule, calculate and document average adherence</p> <p>If patient has stopped taking DOAC, establish whether this was secondary to side-effects, accidental stoppage, temporary/permanent cessation by another clinician.</p> <p>Re-educate on importance of strict intake schedule</p> <p>Inform about compliance aids (e.g. dosette box, blister pack, reminder charts, smartphone applications)</p> <p>NOTE: Dabigatran must remain in original packaging</p>
Assess for thrombotic complications	History of stroke/TIA, DVT/PE in last treatment interval
Assess for bleeding complications	<p>Repeat HASBLED score if ≥ 3. If at increased bleeding risk</p> <ul style="list-style-type: none"> -Correct potentially reversible risk factors -Ensure more frequent reviews are in place <p>Check for any bleeding episodes</p> <p>“nuisance bleeding” – are preventative measures possible?</p> <p>Reinforce importance of carrying ‘patient alert’ card at all times</p>
Assess for other side-effects	<p>Dyspepsia common with dabigatran; consider PPI or alternative agent</p> <p>Other side effects: Review dose? Switch to alternative agent?</p> <p><i>NB: DOACs are ‘black triangle’ drugs – All adverse drug events must be reported to MHRA via https://yellowcard.mhra.gov.uk/</i></p>
Assess risk versus benefit of anticoagulation and decide whether ongoing anticoagulation is still appropriate.	
Ensure that current dose of DOAC is still optimal in light of age, weight and renal function, liver function etc.	<p>See guidance on DOAC dosing in AF/VTE</p> <p>NCL guidance: avoid use of DOACs if CrCL <30 mL/min (dabigatran contraindicated) and/or weight is <50 kg or >120kg. If edoxaban is used for AF, review choice of agent if CrCL >95mL/min as efficacy is reduced)</p>
Review concurrent medication, including over the counter medication, herbal remedies	Check for possible drug interactions with new medication or medication that may increase bleeding risk or merit dose reduction
Managing bleeding complications	
Haemorrhage	Stop DOAC and refer patient immediately to A&E if serious bleeding occurs eg GI-bleeding, epistaxis lasting more than 1 hr
Serious Trauma (especially to the head)	Withhold DOAC and refer to A&E
Unexplained acute drop in Hb or BP	Withhold DOAC and refer for urgent investigations
Excessive bruising	Seek urgent specialist advice

Cockcroft & Gault (C&G) formula

- eGFR and calculated CrCL are NOT interchangeable, but in practice and for most adult patients of average build and height, eGFR can be used to determine dosing in place of CrCL
- Calculated CrCL rather than eGFR should be used (with caution) in the following patient populations:
 - the elderly
 - reduced muscle mass
 - poor nutritional status
 - BMI <18.5 or >30
 - eGFR ≤50mL/min

Example of electronic CrCL (C&G) calculator

<http://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation/>

Manual calculation of CrCL (mL/min) using C&G formula

$$\text{CrCL (mL/min)} = \frac{(140 - \text{age}) \times \text{weight (kg)} \times \text{constant}}{\text{serum creatinine } (\mu\text{mol/L})}$$

- Constant = 1.23 (male) or 1.04 (female)
- Weight (kg) = **current weight** or **adjusted body weight (ABW)** if obese*
 - *Obese defined as >20% over ideal bodyweight (IBW) (see table)
- Adjusted body weight (ABW) =**
Ideal body weight + 0.4 (current body weight - ideal body weight)

HEIGHT		IDEAL BODY WEIGHT (kg)	
feet	cm	Male	Female
5ft 1in	155	52.3	47.8
5ft 2in	158	54.6	50.1
5ft 3in	160	56.9	52.4
5ft 4in	163	59.2	54.7
5ft 5in	165	61.5	57.0
5ft 6in	168	63.8	59.3
5ft 7in	170	66.1	61.6
5ft 8in	173	68.4	63.9
5ft 9in	175	70.7	66.2
5ft 10	178	73.0	68.5
5ft 11	180	75.3	70.8
6ft	183	77.6	73.1
6ft 1in	185	79.9	75.4
6ft 2in	188	82.2	77.7

Management of DOAC around elective MINOR procedures

- The management of anticoagulation around elective procedures is a balance of thrombosis (venous/arterial) vs the risks of bleeding. DOACs are simpler to manage peri-procedurally than warfarin, and LMWH bridging is generally not required
- **Patients at high risk of thrombosis (e.g. VTE/CVA within the previous 3 months, antiphospholipid syndrome or antithrombin deficiency) should be discussed with the patient's haematologist**

Suggested management for MINOR PROCEDURES that are considered to carry **no clinically important bleeding risk and /or where adequate local haemostasis is possible**:

Examples include:

- **Dental interventions:** e.g. tooth extraction (1-3 teeth), root canal procedures, incision of abscess, implant positioning, periodontal surgery
- **Superficial surgery** e.g. abscess incision, small dermatologic excisions etc
- **Ophthalmology:** cataract or glaucoma intervention
- Procedure can usually be undertaken at trough drug level i.e. 12 hours post BD dose (*but see table for dabigatran*), or 24hrs post OD dose. (If taking evening doses of edoxaban or rivaroxaban, it may be more practical to schedule the intervention 18-24h after the last dose).
- **If estimated CrCL <30mL/min:** discuss with local haematologist (*NB: dabigatran contraindicated*)
- **If unsure as to the management of a particular patient:** discuss with local haematologist

DOAC	Day before procedure	Day of procedure	Day 1 post*
Apixaban BD	Take AM and PM doses	No DOAC	Restart AM
Dabigatran BD	Take AM dose; <u>omit</u> PM dose	No DOAC	Restart AM
Edoxaban Rivaroxaban (OD)	If usually takes AM, take dose	No DOAC	Restart AM
	If usually takes PM, then take dose no later than 6pm	No DOAC <i>(schedule procedure ~18-24h post dose)</i>	Restart evening

Post-procedure

- Optimise local haemostasis
- *Delay restarting DOAC if there are any concerns re bleeding; discuss with local haematologist as appropriate
- Peak drug levels (i.e. therapeutic anticoagulation) are reached 2-4 hours post oral dose

- **For patients undergoing more complex procedures with higher bleeding risks** e.g. in-patient procedures (including day surgery) or major surgery: management plans should be arranged by the pre-assessment clinic or the responsible speciality team of the trust where the procedure will be undertaken. These patients will need to be assessed in terms of thrombosis and bleeding risk and DOAC withheld as per local secondary care guidelines.

References:

Assessing stroke/bleeding risk for patients with non-valvular AF

NICE CG180: The Management of Atrial Fibrillation. June 2014

Pisters et al, A novel user-friendly score (HAS-BLED) to assess 1-Year risk of major bleeding in patients with Atrial Fibrillation

CHEST 2010; 138(5); 1093-1100

Flow diagram adapted from AF (non-valvular): prescriber decision support for anticoagulation, Nottinghamshire Area Prescribing Committee

Nice Patients Decision Aid

<https://www.nice.org.uk/guidance/cg180/resources/patient-decision-aid-243734797>

Anticoagulant selection tool

Adapted from toolkit produced by Michigan Anticoagulation Quality Improvement Initiative

Choice of oral anticoagulant based on patient characteristics

Keeling D., Alikhan R. Management of venous thrombembolism – controversies and the future

BJHaem, 2013, 161, 755 – 763

Diener et al. Choosing a particular anticoagulant and dose for stroke prevention in NVAf part 2. EHJ Feb 2016

Heidbuchel et al. Updated European Heart Rhythm Association practical guide on the use of non-VKA antagonist anticoagulants in patients with non-valvular AF: Executive summary – revision 1 EHJ June 2016

Adapted from toolkit produced by Michigan Anticoagulation Quality Improvement Initiative version 1.5/updated 19/2/16

DOAC frequency of follow-up

Adapted from AF (non-valvular): prescriber decision support for anticoagulation, Nottinghamshire Area Prescribing Committee

Cockcroft & Gault formula

Cockcroft DW and Gault H. Nephron 1976;16: 31-41.

Basic Clinical Pharmacokinetics 4th edition; 2004. Michael Winter. Editor: DB Troy. Lippincott Williams & Wilkins, Philadelphia

Electronic medicines compendium www.emc.medicines.org.uk

Summary of product characteristics. Eliquis (apixaban) 5mg & 2.5mg film coated tablets. Bristol-Myers Squibb-Pfizer. Accessed April 2016.

Summary of product characteristics. Lixana (edoxaban) 30mg & 60mg film coated tablets. Daiichi Sankyo UK Limited. Accessed April 2016.

Summary of product characteristic. Pradaxa (dabigatran etexilate) 150mg & 110mg capsules. Boehringer Ingelheim Ltd. Accessed April 2016.

Summary of product Characteristics. Xarelto 20mg & 15mg film coated tablets. Bayer Pharma AG. Accessed April 2016.

Camm AJ et al. 2012 focused update of the ESC guidelines for the management of atrial fibrillation. Eur. Heart J. 2012. 33:2719-2747

MHRA Drug Safety Update October 2013: New oral anticoagulants apixaban (Eliquis ▼), dabigatran (Pradaxa) and rivaroxaban (Xarelto ▼): risk of serious haemorrhage—clarified contraindications apply to all three medicines. Available at: <http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON322347>