

Clinical decision-making tool for embolism prophylaxis for patients with non-valvular atrial fibrillation

CHA ₂ DS ₂ -VASc ≥ 2			ORBIT		
Congestive heart failure (inc LVD)		1	Haemoglobin < 12g/dL or Haemocrit < 36%		2
Hypertension		1	Age > 74 years		1
Aged 75 or more		2	History of GI / intracranial bleed or haemorrhagic stroke		2
Diabetes		1	GFR < 60ml/min/ 1.73m ²		1
Stroke/TIA/thromboembolism		2	Treatment with antiplatelet agents		1
Vascular disease (prior MI, PAD or aortic plaque)		1	Orbit score	Risk Group	Bleeds per 100 patient years
Aged 65-74		1	0-2	Low	2.4
Sex category: female		1	3	Medium	4.7
			4-7	High	8.1
CHA₂DS₂-VASc score			Limitations to the ORBIT tool are explained with the evidence appraisal		
Risk Group					
Stroke rate per patient per year					
0	Low	2/1000			
1	Low/ Moderate	6/1000			
2	High	22/1000			

- Anticoagulation is recommended in patients with CHA₂DS₂-VASc ≥ 2
- Consider oral anticoagulation depending on bleeding risk & patient preferences in patients with CHA₂DS₂-VASc of 1, except for female patients < 65 years & lone AF where no prophylaxis is recommended
- NICE now recommend [ORBIT bleeding risk score](#) because evidence shows it has a higher accuracy in predicting absolute bleeding risk than other bleeding risk tools.

Direct Oral Anticoagulant versus Vitamin K Antagonist (VKA)

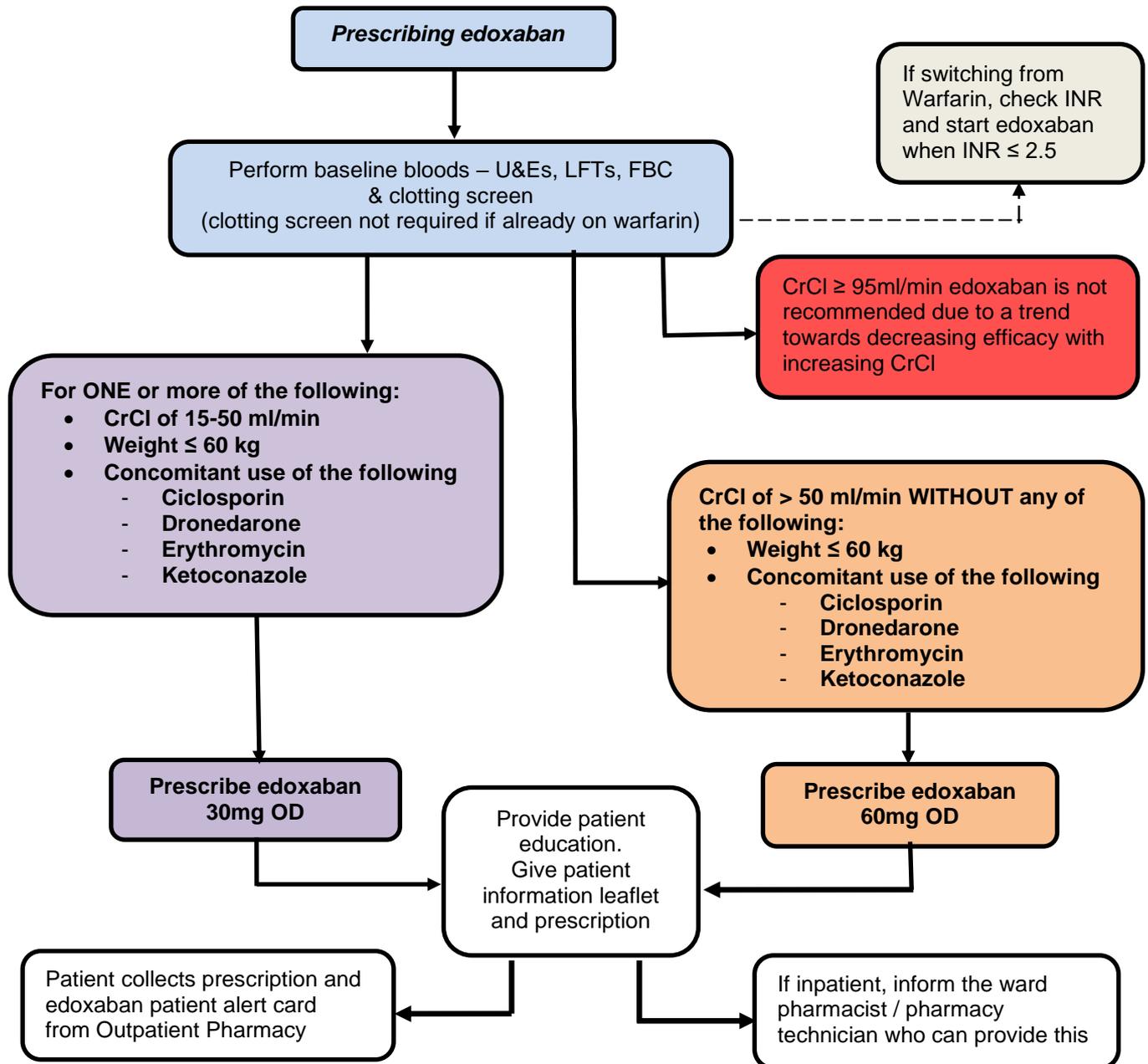
- European Society of Cardiology (ESC) and NICE guidelines recommend starting a DOAC in preference to warfarin if there are no contra-indications due to their favourable safety profile
- Non-valvular AF is defined as AF in the absence of a mechanical prosthetic heart valve or absence of moderate to severe mitral valve stenosis (usually of rheumatic origin). Patients with aortic valve disease are therefore included in the scope of this guideline.
- For patients with AF already taking a VKA and are stable, continue with their current medication and discuss the option of switching to a DOAC at their next routine appointment taking into account their therapeutic time in range (TTR)
- Calculate TTR using validated method such as Rosendaal (contact Anticoagulation clinic on ext. 3085 for Harrogate patients) over a maintenance period of at least 6 months excluding the first 6 weeks of treatment.
- Where individual patient TTR info is not available, unstable warfarin control may be indicated by two unexplained INR values >5 or <1.5 or one INR value > 8 within the past 6 months.
- When reassessing anticoagulation, take into account and if possible, address the following factors that may contribute to poor anticoagulation control: cognitive function, adherence to prescribed therapy, illness, interacting drug therapy, lifestyle factors including diet and alcohol consumption
- If poor anticoagulation control cannot be improved, evaluate the risks and benefits of alternative stroke prevention strategies and discuss these with the person

Do not prescribe a DOAC if the patient has any of the following exclusion criteria:

- Presence of contra-indication (see SPC www.medicines.org.uk)
- Age < 18 years
- >150kg. If risk outweighs benefit for warfarin therapy consider rivaroxaban but requires anti-Xa level. Contact anticoagulation pharmacist (Harrogate ext. 3085, York ext. 724328) for advice.
- Women of child-bearing age without adequate contraception
- Presence of interactions that lead to unmanageable risk
- CrCl < 15ml/min for rivaroxaban / apixaban / edoxaban & CrCl < 30ml/min for dabigatran

Use edoxaban 1st line EXCEPT in the following patient groups:

- High risk of bleeding ORBIT > 3 after attempts to adjust for modifiable risk factor (blood pressure control drugs, alcohol). Consider using apixaban 1st line
- History of GI bleed. Consider using apixaban 1st line
- Patients on concomitant antiplatelets post PCI
- > 120kg. Most experience is with rivaroxaban or apixaban in this patient group. Seek advice.
- CrCl > 95ml/min (use adjusted CrCl for BMI ≥ 30)

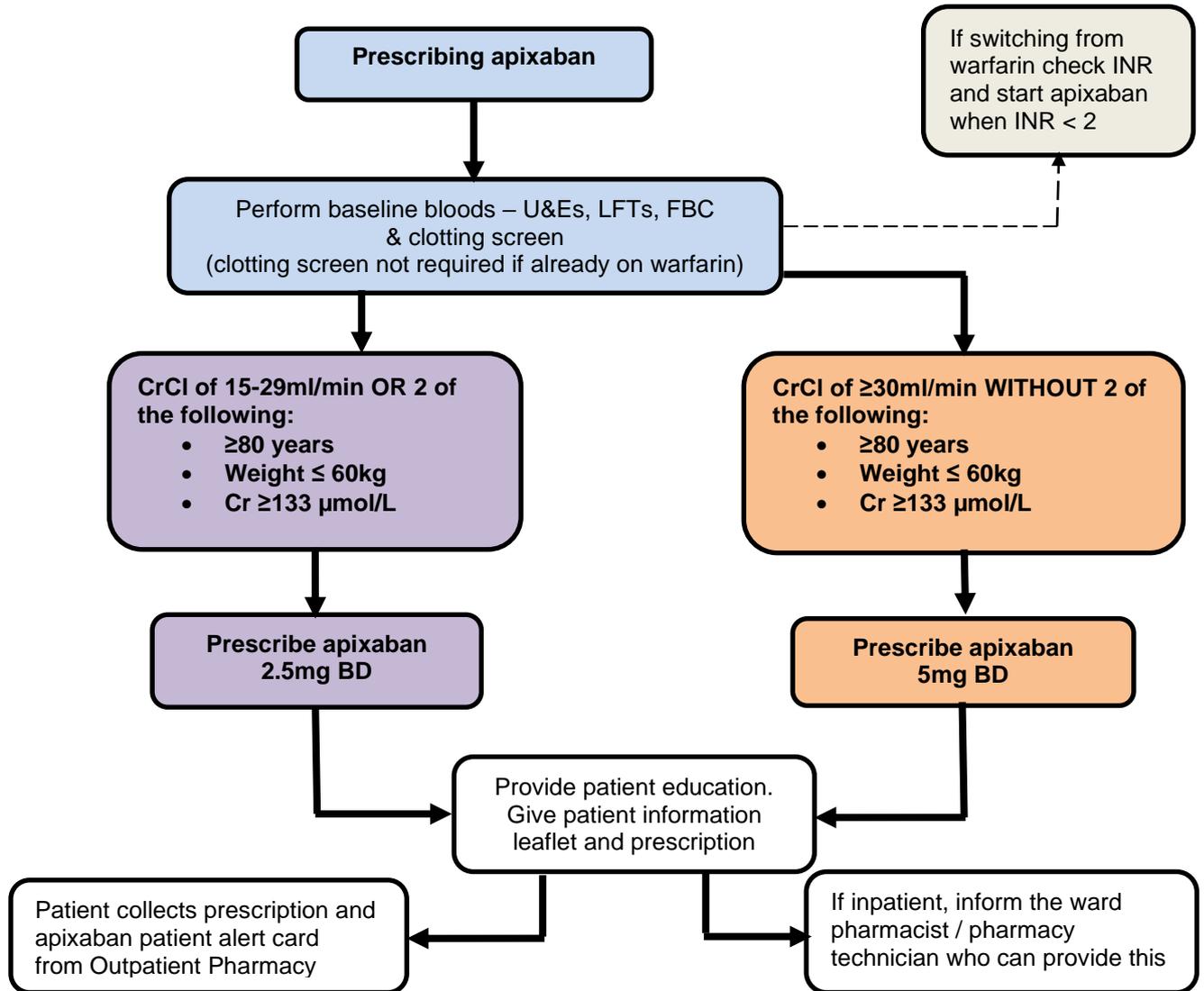


Prescribing notes for edoxaban

- Edoxaban tablets can be crushed and mixed with water if swallowing difficulties/enteral tubes.
- Manufacturers of edoxaban state that they would not expect any interaction with carbamazepine to be clinically significant so is not a contra-indication to starting edoxaban therapy.

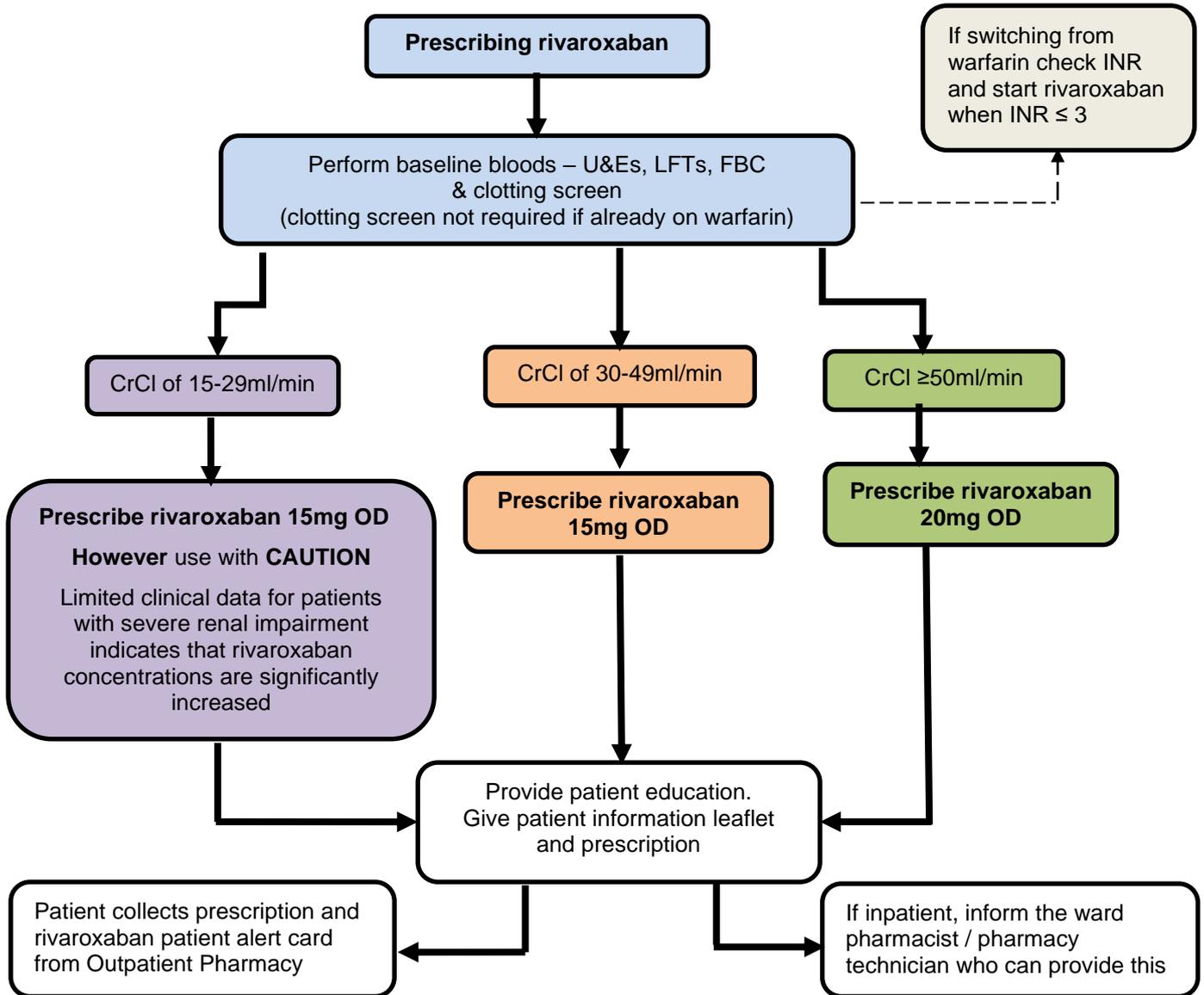
Use apixaban as first line agent in patients with the following:

- High risk of bleeding ORBIT>3 after attempts to adjust for modifiable risk factor (blood pressure control drugs, alcohol)
- History of GI bleed



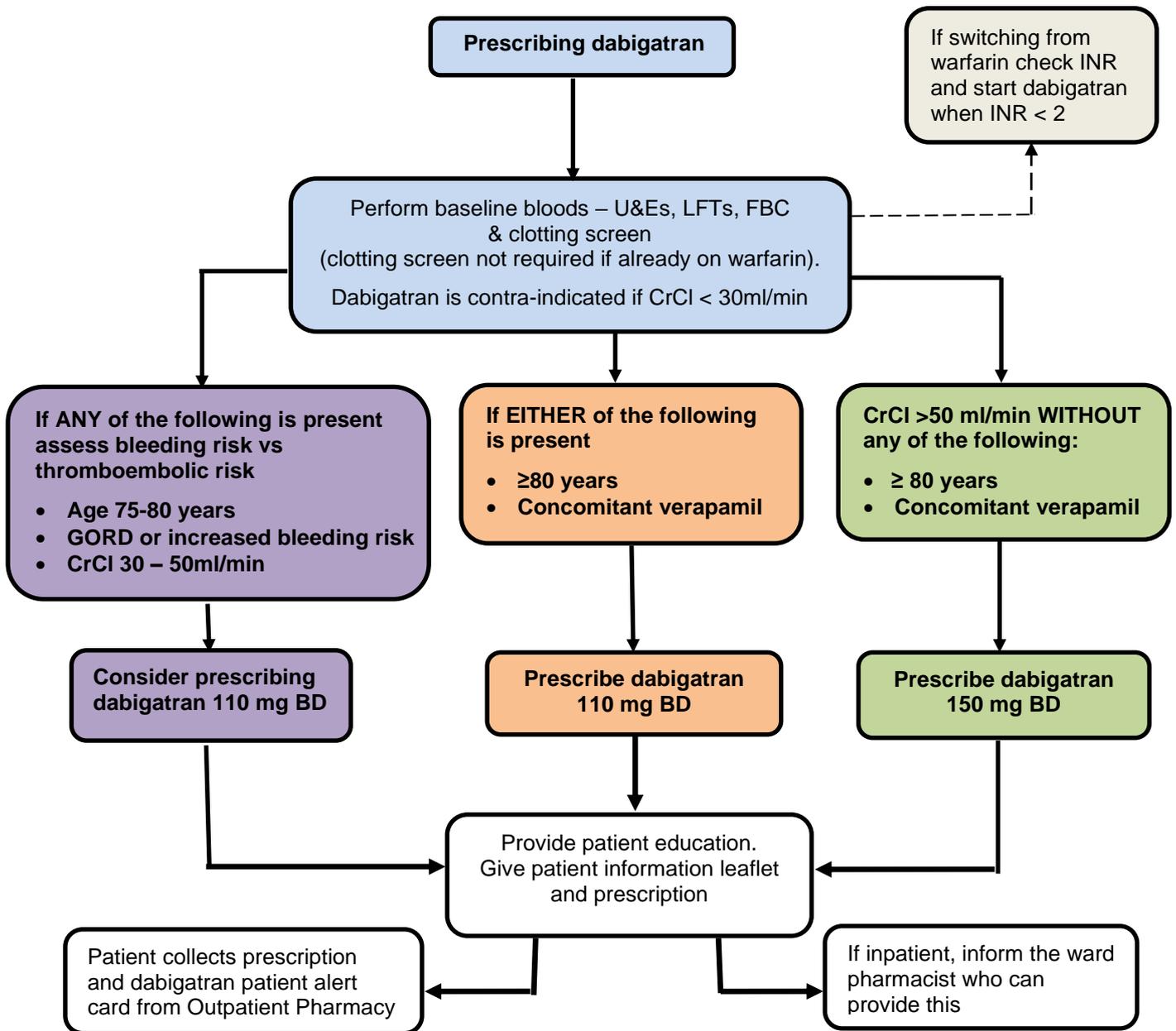
Prescribing notes for apixaban:

- Suitable for administration in compliance aids.
- Swallowing difficulties – apixaban is licensed to be crushed and dispersed in water, glucose 5%, apple juice, or apple puree immediately prior to use and administered orally
- NG-tubes – apixaban is licensed to be crushed and dispersed in water or in glucose 5% for administration (the manufacturers recommend 60mL) through nasogastric tubes – administration through other types of enteral feeding tube would be outside the product license. Flush well after each dose.
- Reversal agent andexanet alfa (Ondexxya®) available. See local reversal guidelines.



Prescribing notes for rivaroxaban:

- Suitable for administration in compliance aids.
- Swallowing difficulties - rivaroxaban is licensed to be crushed and mixed with water or apple puree immediately prior to use and administered orally. After the administration of crushed tablets, the dose should be immediately followed by food.
- NG / PEG tubes – rivaroxaban is licensed to be crushed and mixed with water for administration. Re-start the feed immediately after the dose has been given and the feeding tube flushed (15mg and 20mg doses).
- NJ / PEJ / PEGJ - Rivaroxaban is not suitable for administration via enteral feeding tubes terminating beyond the stomach (i.e. in the duodenum or jejunum) due to decreased absorption of the drug when given in this manner. Bioavailability is significantly reduced when rivaroxaban is administered beyond the stomach.
- Rivaroxaban must be taken with food to optimise its absorption. This makes it unsuitable for patients without a regular meal pattern.
- Reversal agent andexanet alfa (Ondexxya®) available. See local reversal guidelines.



Prescribing notes for dabigatran:

- Dabigatran capsules should not be opened. The capsule shell is specially formulated to release slowly at the correct point of the GI tract. The pellets inside the shell are designed to create an acidic micro-environment to improve drug dissolution and absorption. Opening the capsules may greatly affect the oral bioavailability of the drug with a risk of increased side effects (i.e. bleeding).
- Cannot be put in a compliance aid.
- Reversal agent, Idarucizumab (Praxbind®), available.

Follow up at 1 month, CHECK:

1. Adherence. Patient should bring remaining pills
2. Bleeding events. FBC to monitor Hb can be of assistance in monitoring for bleeding if clinically appropriate
3. Other side effects
4. Interactions
5. Thrombo-embolic events
6. Safety of therapy – emergence of contra-indications or complication/co-morbidities
7. Adequate contraception in women of childbearing age
8. Reinforce safe alcohol limits. (Alcohol does not interact with DOACs but will increase the risk of bleeding)

Follow up at 3 months, CHECK all of above and

9. Blood tests only if clinically indicated for CrCl > 60ml/min
10. U&Es, FBC and LFTs if CrCl 15 – 60ml/min

For GP pathway only

Concern

If
contraindication

Stop
DOAC

*CrCl – Calculate using Cockcroft & Gault equation and ABW as recommended by the manufacturers. Use adjusted CrCl if BMI ≥ 30

CrCl ≥
60ml/min

CrCl
≥30 - 59ml/min

CrCl
15 - 29ml/min

CrCl
< 15ml/min

Other biochemical parameters normal & no new interactions, evidence of bleeding or problems with adherence

Review notes and check bloods every 6 months using monitoring requirements detailed above

Continue treatment with annual review including bloods

Follow up as per NICE CKD Guideline. Consider bleeding risk may be increased. Check bloods every 3 months. NOTE: dabigatran contraindicated if CrCl < 30 ml/min

Concern

Investigate

Concern

Resolved

Contraindication

PLEASE NOTE

If CrCl is declining a follow up may be required sooner

Stop
DOAC

DOAC dosing shortcut tool

Creatinine Clearance (CrCl)	≥50 ml/min	30-49 ml/min	15-29 ml/min	<15 ml/min
Apixaban	5mg BD. Check: Age ≥80 y. Weight ≤60 kg & Creatinine ≥133µmol/L. If ≥ 2 of these features present:2.5 mg BD		2.5mg BD	
Dabigatran	150 mg BD. Check: Age ≥80y & Drugs – Verapamil. If either present: 110 mg BD If aged 75-80 y, CrCl 30-50 ml/min, GORD or increased risk of bleeding consider reduced dose 110 mg BD		<30 ml/min	
Edoxaban	60 mg OD. Check: Weight ≤60 kg & Drugs – Ciclosporin, Dronedarone, Erythromycin or Ketoconazole. If either present: 30 mg OD	30 mg OD		<15 ml/min & ≥ 95 ml/min
Rivaroxaban	20 mg OD (with food)	15 mg OD (with food)		



No dose adjustment



Dose adjustment recommended



Not recommended / contraindicated

Drug Interactions

The information provided below is based on information available at the time of writing and is not exhaustive. Refer to the BNF and SPC for further information.

	No current data available	√	Combination has been proven safe	X	Combination has been proven to be clinically unsafe
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Caution	Combination is known to / may alter plasma concentration. Approach with care and take into account other factors affecting plasma concentrations e.g. renal impairment, other concomitant interacting drugs etc. Dose adjustments may be needed.
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	Apixaban	Rivaroxaban	Dabigatran	Edoxaban
Azole antifungals:				
Itraconazole	X	X	X	Caution – may increase plasma levels of edoxaban
Posaconazole	X	X	Caution – may increase plasma levels of dabigatran	
Voriconazole	X	X	Caution – may increase plasma levels of dabigatran	
Fluconazole	√	√	Caution – may increase plasma levels of dabigatran	
Ketoconazole	X	X	X	
Anti-arrhythmics:				
Dronedarone	Caution – may increase plasma levels of apixaban	X	X	Reduce edoxaban dose by 50%
Amiodarone	Caution- may increase plasma levels of apixaban	Caution – may increase plasma levels of rivaroxaban	Caution – may increase plasma levels of dabigatran	Caution – may increase plasma levels of edoxaban
Quinidine	Caution- may increase plasma levels of apixaban		Caution – may increase plasma levels of dabigatran	Caution – may increase plasma levels of edoxaban
Verapamil	√	√	Caution – may increase plasma levels of dabigatran	Caution – may increase plasma levels of edoxaban
Other drugs:				
Tacrolimus	√	√	X	Caution – may increase plasma levels of edoxaban
Clarithromycin / Erythromycin	Caution – may increase plasma levels of apixaban	√	Caution – may increase plasma levels of dabigatran	Erythromycin - reduce edoxaban dose by 50% Clarithromycin – caution may increase plasma levels of edoxaban

Ciclosporin	Caution – predicted to increase exposure to apixaban	Caution – predicted to increase exposure to rivaroxaban	X	Reduce edoxaban dose by 50%
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Interactions with other medicinal products affecting haemostasis

<p>Anticoagulants</p> <p>Unfractionated heparins, low molecular weight heparins (e.g. tinzaparin, enoxaparin, dalteparin), heparin derivatives (e.g. Fondaparinux)</p> <p>Oral anticoagulants e.g. warfarin</p>	<p>Concomitant use of a DOAC with any other anticoagulant agent is contraindicated, except under the circumstances of switching therapy to or from a DOAC or when unfractionated heparin is given at doses necessary to maintain a patent central venous or arterial catheter</p>
<p>Platelet aggregation inhibitors and NSAIDs including acetylsalicylic acid (ASA) and platelet aggregation inhibitors</p>	<p>Care is to be taken if patients are treated concomitantly with non-steroidal anti-inflammatory drugs (NSAIDs), including ASA and platelet aggregation inhibitors because these medicinal products typically increase the bleeding risk. For patients at risk of ulcerative gastrointestinal disease an appropriate prophylactic treatment may be considered.</p> <p>Combination therapy with oral anticoagulants and anti-platelets in patients with AF/IHD/PCI must be decided / initiated on a case-by-case basis by a Cardiologist and the duration of the regime clearly documented.</p>

Additional notes:

The following drugs are contraindicated with DOACs and warfarin should be used for anticoagulation: HIV protease inhibitors (e.g. ritonavir, rifampicin).

The following drugs are contraindicated with apixaban, rivaroxaban and dabigatran. They may reduce the plasma concentration of edoxaban and should be used with caution on an individual basis: St John's Wort, carbamazepine, phenytoin, phenobarbital

References:

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- The 2021 EHRA Practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Europace (2021) 23, 1612–1676 doi:10.1093/europace/euab065 accessed 26/4/22
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- NEWT Guidelines for apixaban, dabigatran, edoxaban and rivaroxaban www.newtguidelines.com accessed 27/4/22
- Direct Oral Anticoagulant (DOAC) dosing for stroke prevention in those with non-valvular Atrial Fibrillation. GP notebook shortcuts www.gpnotebook.co.uk accessed 26/6/19
- Stockleys Drug Interaction database www.medicinescomplete.com accessed 13/5/22
- Comparison of DOACs for Non-valvular Atrial Fibrillation; Information for Prescribers. June 2022; Regional Drug & Therapeutics Centre: <https://rdtc.nhs.uk/prescribing-support-document/comparison-of-doacs-for-atrial-fibrillation/> (Registration required)
- MD-CALC: ORBIT Bleeding Risk Score for Atrial Fibrillation: <https://www.mdcalc.com/calc/10227/orbit-bleeding-risk-score-atrial-fibrillation#evidence>

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This clinical guideline has been produced after input and collaboration with: HDFT, YSTHFT, NY&Y MMT, GPs in NY & York

Adoption and approval:

Adopted and approved by NY & York APC on 3rd August 2022