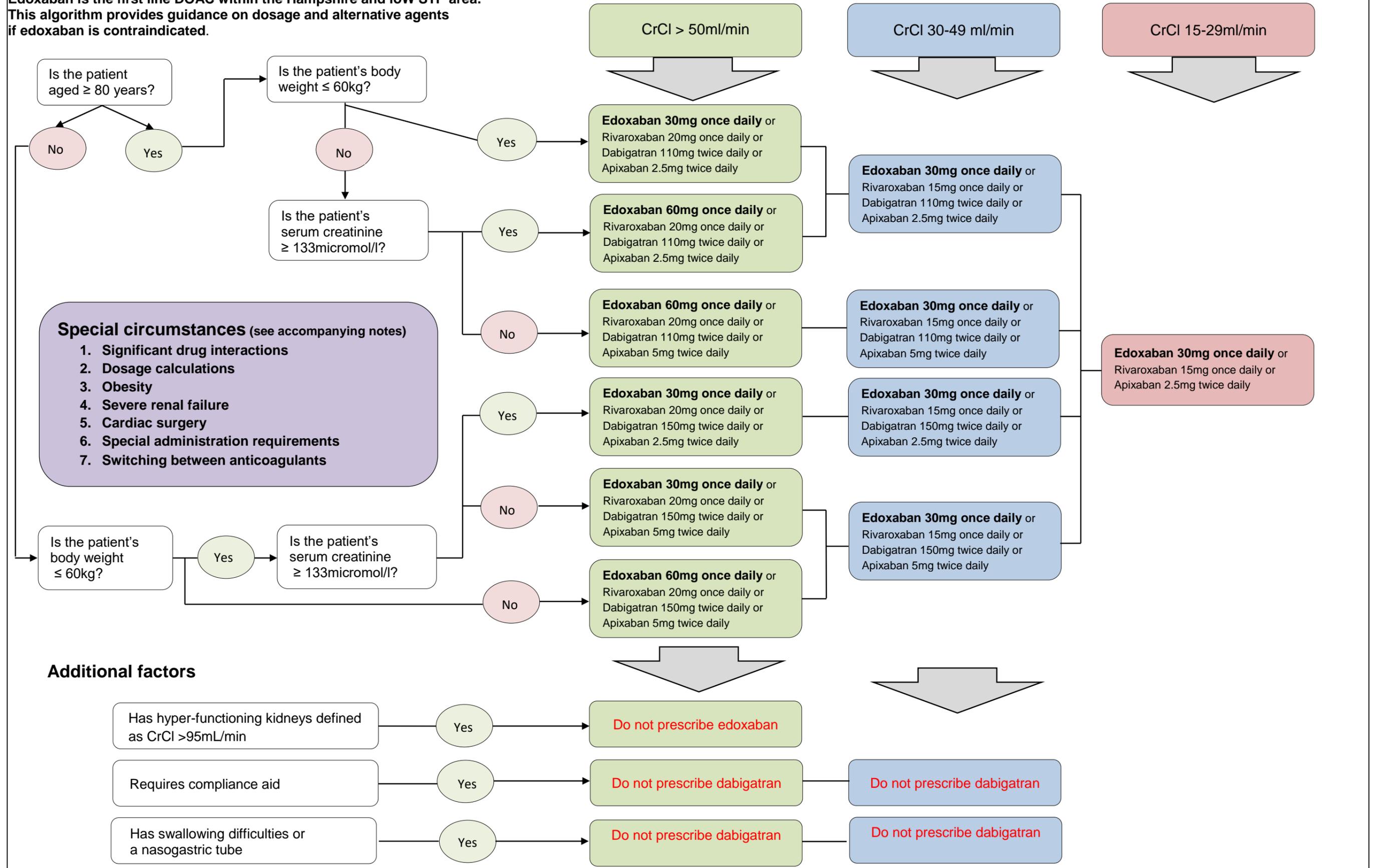


Direct Oral AntiCoagulant choices for stroke prevention in non-valvular Atrial Fibrillation Decision-making algorithm

Edoxaban is the first line DOAC within the Hampshire and IoW STP area. This algorithm provides guidance on dosage and alternative agents if edoxaban is contraindicated.



Notes to accompany the decision making algorithm: Oral anticoagulant choices for stroke prevention in non-valvular atrial fibrillation (NVAf)

1. Significant drug interactions (from Summary of medical Product Characteristics)

	P-gp inducers – reduced DOAC/ anti-thrombotic effect	P-gp inhibitors – enhanced effect of DOAC and increased bleeding risk								
DOAC	e.g. phenytoin, carbamazepine, phenobarbital, St John's wort, rifampicin	Ciclosporin, Dronedarone	Clarithromycin	Erythromycin	Quinidine	Tacrolimus	Verapamil	Amiodarone	Itraconazole, Voriconazole, Posaconazole, Ketoconazole	Protease inhibitors e.g. ritonavir
Edoxaban	Effect of edoxaban reduced	Reduce dose to 30mg daily		Reduce dose to 30mg daily					Reduce dose to 30mg daily with ketoconazole	Effect not known
Apixaban	Avoid		Dose adjustment not required		Dose adjustment not required		Dose adjustment not required	Dose adjustment not required	Avoid	Avoid
Dabigatran	Avoid	Contraindicated	Dose adjustment not required		Dose adjustment not required	Avoid	Reduce dose to 110mg twice a day	Dose adjustment not required	Contraindicated	Avoid
Rivaroxaban	Avoid	Avoid with dronedarone	Avoid in patients with high bleeding risk	Avoid in patients with high bleeding risk					Avoid fluconazole in patients with high bleeding risk	Avoid

- NSAID, SSRI and SNRI – use with caution in patients on DOACs due to increased bleeding risk, especially with chronic use of NSAIDs.
- Other anticoagulants – contraindicated with DOACs, except under specific circumstances e.g. switching anticoagulant therapy (see below)

2. Dosage calculations

The licensed doses for all DOACs should be calculated using the Cockcroft-Gault method of determining creatinine clearance (CrCl) (see <https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation>). This equation may overestimate CrCl in elderly or malnourished patients. Use **actual body weight** for **apixaban, edoxaban and rivaroxaban**. Use **ideal body weight** for **dabigatran**.

3. Obesity

Obese patients with a Body Mass Index (BMI) of more than 40 kg/m² or weight of more than 120kg: seek specialist haematological advice.

4. Severe renal failure

Dabigatran is contraindicated when CrCl is less than 30mL/min.

Edoxaban, apixaban and rivaroxaban are not recommended if CrCL is less than 15mL/min or when patient is dialysed.

5. Cardiac Surgery

Edoxaban should not be used within 3 months of cardiac surgery for tissue valve replacement or for patients where future cardiac surgery is planned.

6. Special administration requirements

Rivaroxaban 15mg or 20mg tablets should be taken with or after food. **Edoxaban** (unlicensed), **apixaban** and **rivaroxaban** may be crushed and mixed with water/ apple sauce in patients with enteral tubes/ swallowing difficulties.

Dabigatran capsules must not be opened, as this causes a substantial increase in drug bioavailability.

Dabigatran capsules are hygroscopic and should not be removed from the manufacturer's original package (e.g. to be put in a compliance aid)

7. Switching between anticoagulants

Switching to →	Edoxaban	Apixaban	Dabigatran	Rivaroxaban
Switching from ↓↓				
Warfarin	When converting patients from warfarin therapy to edoxaban, stop warfarin and start edoxaban when INR is ≤ 2.5. <i>DOACs can contribute to an elevated INR</i>	When converting patients from warfarin therapy to apixaban, stop warfarin and start apixaban when INR is < 2.0. <i>DOACs can contribute to an elevated INR</i>	When converting patients from warfarin therapy to dabigatran, stop warfarin and start dabigatran when INR is < 2.0. <i>DOACs can contribute to an elevated INR</i>	When converting patients from warfarin therapy to rivaroxaban, stop warfarin and start rivaroxaban when INR is ≤ 3.0. <i>DOACs can contribute to an elevated INR</i>

Switching to →	Warfarin
Switching from ↓↓	
Edoxaban	When converting from edoxaban to warfarin, edoxaban should be continued until the INR is ≥2 A loading dose of warfarin is not recommended. For patients currently on a 60mg dose, administer edoxaban at a dose of 30mg once daily together with an appropriate warfarin dose. For patients currently on a 30mg dose, administer edoxaban at a dose of 15mg once daily together with an appropriate warfarin dose. During the first 14 days of concomitant therapy the INR is measured at least 3 times, just prior to taking the daily dose of edoxaban
Apixaban	When converting from apixaban to warfarin, continue apixaban for at least 2 days after starting warfarin. After 2 days of co-administration of apixaban and warfarin, obtain an INR prior to the next scheduled dose of apixaban, Co-administration of apixaban and warfarin should be continued until the INR is ≥2.
Dabigatran	When converting from dabigatran to warfarin, adjust the starting time of warfarin according to creatinine clearance as follows: For CrCL ≥50mL/min, start warfarin 3 days before discontinuing dabigatran. For CrCL ≥30-<50mL/min, start warfarin 2 days before discontinuing dabigatran.
Rivaroxaban	When converting from rivaroxaban to warfarin, rivaroxaban should be continued until the INR is ≥2. 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. 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.

Switching from DOAC to DOAC	Discontinue original DOAC and commence new treatment at the time that the next scheduled dose of original drug would be due.
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