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.

Cutaneous (> 50ml/min)

Is the patient aged ≥ 80 years?

No

Yes

Is the patient’s body weight ≤ 60kg?

No

Yes

Is the patient’s serum creatinine ≥ 133micromol/l?

No

Yes

CrCl 30-49 ml/min

Edoxaban 30mg once daily or Rivaroxaban 20mg once daily or Dabigatran 110mg twice daily or Apixaban 2.5mg twice daily

CrCl 15-29ml/min

Edoxaban 30mg once daily or Rivaroxaban 15mg once daily or Dabigatran 150mg twice daily or Apixaban 5mg twice daily

Special circumstances (see accompanying notes)

1. Significant drug interactions
2. Dosage calculations
3. Obesity
4. Severe renal failure
5. Cardiac surgery
6. Special administration requirements
7. Switching between anticoagulants

Additional factors

Has hyper-functioning kidneys defined as CrCl >95mL/min

Yes

Do not prescribe edoxaban

No

Requires compliance aid

Yes

Do not prescribe dabigatran

No

Has swallowing difficulties or a nasogastric tube

Yes

Do not prescribe dabigatran
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)

<table>
<thead>
<tr>
<th>DOAC</th>
<th>P-gp inhibitors – reduced DOAC anti-thrombotic effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>e.g. phenytoin, carbamazepine, phenobarbital, St John’s wort, rifampicin</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Ciclosporin, Dronedarone</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Clarithromycin</td>
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<tr>
<td></td>
<td>Erythromycin</td>
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<td></td>
<td>Quinidine</td>
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<td>Tacrolimus</td>
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<td>Verapamil</td>
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<td>Amiodarone</td>
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<tr>
<td></td>
<td>Edoxanze, Voriconazole, Posaconazole, Ketoconazole</td>
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<tr>
<td></td>
<td>Protease inhibitors e.g. ritonavir</td>
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</tbody>
</table>

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 (uncensored), 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

<table>
<thead>
<tr>
<th>Switching to --</th>
<th>Edoxaban</th>
<th>Apixaban</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>When converting patients from warfarin therapy to edoxaban, stop warfarin and start edoxaban when INR is ≤ 2.5. DOACs can contribute to an elevated INR</td>
<td>When converting patients from warfarin therapy to apixaban, stop warfarin and start apixaban when INR is ≤ 2.0. DOACs can contribute to an elevated INR</td>
<td>When converting patients from warfarin therapy to dabigatran, stop warfarin and start dabigatan when INR is ≤ 2.0. DOACs can contribute to an elevated INR</td>
<td>When converting patients from warfarin therapy to rivaroxaban, stop warfarin and start rivaroxaban when INR is ≤ 3.0. DOACs can contribute to an elevated INR</td>
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<tr>
<td>Edoxaban</td>
<td>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.</td>
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<tr>
<td>Apixaban</td>
<td>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.</td>
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<tr>
<td>Dabigatran</td>
<td>When converting from dabigatran to warfarin, adjust the starting dose of warfarin according to creatinine clearance as follows: For CrCl 250mL/min, start warfarin 3 days before discontinuing dabigatran. For CrCl 100–250mL/min, start warfarin 5 days before discontinuing dabigatran. For CrCl ≤ 100mL/min, start warfarin 10 days before discontinuing dabigatran.</td>
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<tr>
<td>Rivaroxaban</td>
<td>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.</td>
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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.