# Comparison of Novel Oral Anticoagulants (NOACs) and Warfarin

*NOACs are also referred to as Direct Oral Anticoagulants (DOACs)*

<table>
<thead>
<tr>
<th>ACTION</th>
<th>APIXBAN</th>
<th>DABIGATRAN</th>
<th>RIVAROXABAN</th>
<th>WARFARIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor Xa inhibitor.</td>
<td>Direct thrombin inhibitor.</td>
<td>Factor Xa inhibitor.</td>
<td>Inhibits synthesis of Vitamin-K dependent clotting factors.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>INDICATION (PREVENTION OF)</th>
<th>APIXBAN</th>
<th>DABIGATRAN</th>
<th>RIVAROXABAN</th>
<th>WARFARIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE in hip or knee replacement.</td>
<td>VTE in hip or knee replacement.</td>
<td>VTE in hip or knee replacement.</td>
<td>Prevention and treatment for VTE.</td>
<td></td>
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<table>
<thead>
<tr>
<th>ONSET AND HALF-LIFE</th>
<th>APIXBAN</th>
<th>DABIGATRAN</th>
<th>RIVAROXABAN</th>
<th>WARFARIN</th>
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<tbody>
<tr>
<td>Onset of action 30 minutes.</td>
<td>Onset of action 30 minutes.</td>
<td>Onset of action 30 minutes.</td>
<td>Onset of action 30 minutes.</td>
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<tr>
<td>Half-life 12 hours.</td>
<td>Half-life 7-9 hours in young adults, 12-14 hours in elderly people. Prolonged in renal impairment.</td>
<td>Half-life 5-9 hours in young adults, 11-12 hours in elderly people.</td>
<td>Onset of action 36-72 hours.</td>
<td></td>
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<td></td>
<td>Half-life 20-60 hours.</td>
<td><strong>Reversal Agent</strong></td>
<td><strong>Not available in Australia (andexanet alfa).</strong></td>
<td>Vitamin K.</td>
</tr>
</tbody>
</table>

## Should a patient be switched from Warfarin to a NOAC?

Although NOACs are being used more widely, they may not always be the most optimal medication. Warfarin may be more favourable in the following circumstances:

- Stable patients with INR largely within therapeutic range (annual time in therapeutic range >65%) in whom INR testing doesn’t present a challenge, may not benefit from switching.
- Poor adherence. NOACs have shorter half-lives and missed doses therefore may cause a complete loss of antithrombotic effect. Non-adherence is also difficult to measure with NOACs as opposed to warfarin – as there is no validated laboratory method to measure anticoagulant response.
Patients who may benefit from switching to a NOAC from warfarin:

- poorly controlled INR
- unable to access INR testing
- unable to tolerate regular INR (dementia and behavioural issues, pain related to blood tests)
- unable to tolerate warfarin
- unwilling to take warfarin

NOACs - Advantages and Disadvantages

<table>
<thead>
<tr>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
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<tbody>
<tr>
<td>Convenience (No INR testing)</td>
<td>Lack of available monitoring of blood levels and compliance</td>
</tr>
<tr>
<td>Small absolute intracranial haemorrhage (ICH) risk reduction</td>
<td>Lack of data in patients with severe chronic kidney disease</td>
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<tr>
<td>Not affected by diet</td>
<td>Higher cost</td>
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<tr>
<td>Low number of drug interactions</td>
<td>Potential that unanticipated side effects will become evident</td>
</tr>
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</table>

Which NOAC To Use?

- There are no direct head-to-head trials comparing NOACs against one another to facilitate a direct comparative evaluation between agents.
- Therefore, there no recognised guidelines on how to choose one over another.

Based on available evidence however, the following may be helpful in choosing a NOAC:

High risk of GI bleed ➔ **apixaban** (agent with lowest incidence of GI bleed)

High overall bleeding risk ➔ **dabigatran 110mg, apixaban** (agents with lowest incidence of bleeding)

Ischaemic stroke while on warfarin ➔ **dabigatran 150mg** (greatest superiority over warfarin)

Dyspepsia ➔ **apixaban** (avoid dabigatran and rivaroxaban)
Renal impairment ➔ if warfarin is not suitable, **apixaban** (lowest bleeding risk)

Patient prefers once daily dosing ➔ **rivaroxaban**

Patient cannot take whole medication ➔ **avoid dabigatran** as it must be taken whole. Chewing or opening the capsule increases the risk of bleeding.

### NOAC Dosage Guidelines

<table>
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<tr>
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<th>Apixaban</th>
<th>Rivaroxaban</th>
<th>Dabigatran</th>
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</table>
| **Prevention of emboli in AF** | 5 mg twice daily.  
 If at least 2 of:  
 Weight <60 kg, age >80 years, serum creatinine >133 micromol/L, reduce dose to 2.5 mg twice daily.  
 Contraindicated when CrCL < 25 mL/minute. | 20 mg once daily.  
 CrCl 30–49 mL/minute, 15 mg once daily.  
 Contraindicated when CrCL < 30 mL/minute. | 150 mg twice daily.  
 >75 years, reduce dose to 110 mg twice daily.  
 Increased risk of major bleeding or CrCL 30–50 mL/minute, consider reducing dose to 110 mg twice daily.  
 Contraindicated when CrCL < 30 mL/minute |
| **Treatment of acute VTE and prevention of subsequent VTE** | 10 mg twice daily for 7 days, then 5 mg twice daily.  
 Reduce dose after 6 months (2.5 mg bd) for prevention of subsequent VTE if long-term treatment is needed.  
 Contraindicated when CrCL <25 mL/minute. | 15 mg twice daily for 3 weeks, then 20 mg once daily.  
 Contraindicated when CrCL < 30 mL/minute. | 150 mg twice daily.  
 >75 years, 110 mg twice daily.  
 Increased risk of major bleeding or CrCL 30–50 mL/minute, consider reducing dose to 110 mg twice daily.  
 Contraindicated when CrCL <30 mL/minute |
**Aspirin Monotherapy vs. Warfarin**

- Evidence doesn’t support the use of aspirin as monotherapy for the prevention of thromboembolic events in patients with AF.
- A 2007 meta-analysis found that aspirin, compared to placebo or no therapy, reduced the risk of stroke by about 20 percent, although this effect was not statistically significant. Further, aspirin had little effect on reducing the risk of disabling stroke.
- In an observational study (2014), treatment with aspirin was associated with a higher incidence of stroke and thromboembolism compared to no therapy.

**Atrial Fibrillation and CKD**

CKD is an independent risk factor for stroke as well as bleeding.

**eGFR 30-59mL/min (Stage 3 CKD)**
- NOACs preferred to warfarin – equal efficacy and possible greater safety.

**eGFR 15-29mL/min (Stage 4 CKD)**
- Anticoagulant likely to have a net clinical benefit, and use recommended for those not at high risk of bleeding.
- Warfarin preferred to NOACs, due to greater clinical experience.
- If patient cannot tolerate warfarin, apixaban is used. Less dependent on kidney function compared to other NOACs.

**eGFR <15mL/min but not on Dialysis (Stage 5 CKD)**
- Minimal data.
- Suggest treating same as eGFR 15-29mL/minute.

**Dialysis (Stage 5 CKD)**
- In most cases, no anticoagulation is suggested, based on limited data reporting no thromboembolism benefit, and higher bleeding risk.

**Combination Anticoagulant and Antiplatelet Therapy**

- In patients with STABLE coronary artery disease, who develop an indication for an anticoagulant, consider ceasing the antiplatelet, once anticoagulant is commenced.
- For patients at very HIGH RISK of coronary events, combination therapy can be considered.
- If a person on an antiplatelet develops DVT-combination with anticoagulant can be continued for a minimum of 3 months. If there is an intermediate-high bleeding risk, consider stopping the antiplatelet.
- In patients with non-valvular AF, who have an acute coronary syndrome or undergo percutaneous coronary intervention, combination therapy can be continued for 12 months following, then the anticoagulant may be ceased.
- In patients with valvular heart disease, the addition of an antiplatelet reduces the risk of valve thrombosis and arterial thromboembolism but increases the risk of major bleeding.

**REFERENCES**

- **Atrial Fibrillation: Anticoagulant therapy to prevent embolization, UpToDate**
- **Management of bleeding in patients receiving direct oral anticoagulants, UpToDate**
- **Management of thromboembolic risk in patients with atrial fibrillation in the NOAC era, Hammersley, D., Signy, M. Therapeutic Advances in Chronic Disease. 2017 Dec; 8 (12): 165-176.**
- **Indications for anticoagulant and antiplatelet combined therapy, Floyd, C. N. British Medical Journal, October 2017**
- **Anticoagulant Therapy. In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2018 July.**