

# Non-valvular Atrial Fibrillation: Anticoagulation Colour Comparison Chart

Drug / BRAND	Vitamin K Antagonist	DOACs			
	Warfarin COUMADIN, g	Thrombin Inhibitor Dabigatran PRADAXA, g	Rivaroxaban XARELTO, g	Factor Xa Inhibitors Apixaban ELIQUIS, g	Edoxaban LIXIANA, SAVAYSA
<b>Landmark AF RCTs Comparing to Warfarin non-inferiority analysis; superiority if appropriate</b>	<b>Active comparator.</b> Efficacy / safety demonstrated in multiple RCTs (e.g. ACTIVE-W) & meta-analyses.	N=18,113 randomized 1:1:1 dabi 110mg or 150mg BID vs warf (TTR 64%) ITT; open-label RCT Note: 75mg dose not studied	N=14,264 riva 20mg* daily vs warf (TTR 55%) ITT; double-blind, RCT *20% (n=1474) on riva had CrCl 30-49mL/min → 15mg daily	N=18,201 apix 5mg* BID vs warf (TTR 62%) ITT; double-blind RCT *4.7% (n=428) on apix had ≥2: ≥80yr, ≤60kg, SCr ≥133 umol/L → 2.5mg BID	N=21,105 randomized 1:1:1 edox 30mg* or 60*mg daily vs warf (TTR 65%) ITT; double-blind RCT *↓dose by 50% (i.e. to 15mg or 30mg) if ≥1 of: CrCl 30-50mL/min, or ≤60kg, or on verapamil/quinidine/dronedaron
<b>↓ Stroke / Systemic Embolism</b>	✓ absolute differences minimal when TTR≥65%	✓✓? NNT=88/2yrs 2.2% dabi 150mg vs 3.4% warf; dabi 110mg vs warf NS	✓? riva vs warf NS only per-protocol met non-inferiority, not ITT	✓✓? NNT=167/1.8yrs 2.3% apix vs 2.9% warf	✓✓? NNT=141/2.8yrs 2.6% edox 60mg vs 3.3% warf ITT non-infer, mITT superior; edox 30mg vs warf NS
<b>Intracranial Hemorrhage</b>	✗ low incidence but ↑ rates in RCTs vs DOACs	✓ ↓ rate vs warfarin NNT=116/2yrs 0.6% dabi 150mg vs 1.5% warf	✓ ↓ rate vs warfarin NNT=250/1.6yrs 0.8% riva vs 1.2% warf	✓ ↓ rate vs warfarin NNT=128/1.8yrs 0.6% apix vs 1.4% warf	✓ ↓ rate vs warfarin NNT=99/2.8yrs 0.9% edox 60mg vs 1.9% warf
<b>Major GI Bleed</b>	✓	✗ NNH=100/2yrs 3.1% dabi 150mg vs 2.1% warf; 2.3% dabi 110mg vs 2.1% warf NS (but less benefit)	✗ NNH=100/1.6yrs 3.2% riva vs 2.2% warf	✓ no difference vs warfarin 1.2% apix vs 1.3% warf [observational data: apixaban ↓ GI bleed vs other DOACs] <sup>10</sup>	✗ NNH=166/2.8yrs 3.3% edox 60mg vs 2.7% warf; 1.8% edox 30mg vs 2.7% warf NNT=111/2.8yrs (but less benefit)
<b>Major Bleed</b>	✓	✓ no difference vs warfarin 6.6% dabi 150mg vs 7% warf	✓ no difference vs warfarin 5.6% riva vs 5.4% warf	✓✓ ↓ bleeds vs warfarin NNT=67/1.8yrs 3.6% apix vs 5.1% warf	✓✓ ↓ bleeds vs warfarin NNT=67/2.8yrs 6% edox 60mg vs 7.5% warf
<b>Bleed Management</b>	✓ Vitamin K, PCC	✓ idarucizumab PRAXBIND	✗ Antidote: andexanet alfa ONDEXXYA x®; ANDEXXA FDA'18		
<b>Discontinuation Rates</b>	–	✗ NNH=25/2yrs 21% dabi vs 17% warf	– no difference vs warfarin	✓ NNT=45/1.8yrs 25% apix vs 28% warf	– no difference vs warfarin
<b>Renal function (CrCl &lt;30mL/min)</b>	RCTs ongoing. Observational data conflicting, benefit may not outweigh harm, esp. in ESRD	✗ Contraindicated <30mL/min	very limited data avoid <15mL/min	very limited data avoid <15mL/min	very limited data avoid <15mL/min (see side panel for >95ml/min)
<b>Half-life Pros/Cons</b>	Half-life of DOACs is shorter than warf. <b>Con:</b> nonadherence (missed doses) will result in earlier loss of anticoagulation status vs warfarin. <b>Pro:</b> anticoagulation is achieved <b>faster</b> after starting, & when managing bleeds coagulation status returns to normal <b>faster</b> after stopping.				
<b>Other</b>	INR monitoring ✓ tailor dose re: stroke vs bleed risk ✗ ? inconvenient	✗ ? ↑ MI see RxFiles Q&A ✗ ↑ Dyspepsia NNH=18/2yrs vs warf	–	↓ All-Cause Mortality NNT=132/1.8yrs 6.6% apix vs 7.4% warf	–
<b>Drug Interactions</b>	Warfarin has ↑↑ drug interactions; however, very few interactions with warfarin are absolutely contraindicated - warfarin dose can be tailored in response to INR; Generally avoid 3A4 & P-gp induc/inhibs with DOACs, but some monographs offer dosing guidance to manage.				
<b>Cost per month</b>	✓✓ \$15	✗ (\$98 g ✗ ▼) - \$120	✓ \$35 g (brand=\$105)	✓ \$37 g (brand=\$118)	✗ \$107

Indirect costs with warfarin include INR monitoring and time/travel to the patient.

✓✓ An Advantage
✓
Neutral
✗
✗✗ A Disadvantage
? Unknown/Ongoing

## Comments

- There is a positive correlation between warfarin's efficacy / safety and its **Time in Therapeutic Range (TTR)**. Consider local context.
- **Renal function** (also see row in table): All OAC have limited RCT data with ↓renal function (CrCl <30mL/min). Warfarin: observational data for safety & efficacy is conflicting. Dabigatran is contraindicated (**CI**) if CrCl <30ml/min; 80-85% renally cleared. Apixaban & rivaroxaban have limited RCT data down to CrCl 15mL/min. **RENAL-AF:** apixaban vs warfarin n=154 (planned for n=760) hemodialysis patients, ended early; risk of bleeding & benefit similar. OAC not routinely recommended in Stage 5 CKD (eGFR <15mL/min). **CCS AF WR, LQ** Edoxaban & CrCl >95mL/min: ↑ risk of ischemic stroke; FDA recommends to avoid, but Health Canada does not.
- **Valvular atrial fibrillation** (AF in presence of mechanical heart valve, or of moderate–severe mitral stenosis, rheumatic or nonrheumatic): warfarin is the preferred agent<sup>CCS'20</sup>; dabigatran contraindicated (↑ rates of bleeding & thrombotic events in **RE-ALIGN** trial); avoid other DOACs.
- **Canadian differences:** international trials with few Canadian patients; in general, most Canadian sites would be expected to have better TTR with warfarin than average,<sup>8</sup> & less absolute risk of intracranial hemorrhage.<sup>7</sup> These factors potentially limit DOAC advantages.
- **Importance of dose:** efficacy & bleed risk are both dependent on dose; e.g. dabigatran 110mg BID & edoxaban 30mg daily had ↓ bleeding, but also ↓ efficacy, vs dabigatran 150mg BID<sup>1</sup> & edoxaban 60mg daily,<sup>4</sup> respectively.
- **Life-threatening/ fatal bleed** was ↓ in dabi / riva / edox trials vs warfarin.

Trials were designed as non-inferiority, with option for superiority analysis. Only direct comparisons of individual DOACs with warfarin have been studied; comparisons above are indirect & have inherent limitations; however, they are the best data available.

apix=apixaban dabi=dabigatran edox=edoxaban DOAC=direct oral anticoagulant → apix, dabi, edox, or riva PCC=prothrombin complex concentrate riva=rivaroxaban thrombin=aka Factor IIa warf=warfarin wt=weight

## Anticoagulation Colour Comparison Chart

This editorial synthesis was based on interpretation of data from RCTs ([RELY](#), [ROCKET-AF](#), [ARISTOTLE](#), ENGAGE-AF), CADTH reports, product monographs & clinical consultation.

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### Search Terms

Anticoagulant	22
Apixaban	22
Atrial Fibrillation	22
COUMADIN	22
Dabigatran	22
DOACs	22
Edoxaban	22
ELIQUIS	22
LIXIANA	22
PRADAXA	22
Rivaroxaban	22
Warfarin	22
XARELTO	22
Andexanet alfa	22
ONDEXXYA	22

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