NOACs for stroke prevention in AF – Drug Comparisons Chart

Licensed indications:
Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors.

**Renal function should be assessed prior to initiation and at least once a year, or more frequently as needed in certain situations when it is suspected that the renal function could decline or deteriorate e.g. hypovolaemia, dehydration, and in case of concomitant use of certain medicinal products such as:*
[a] *ketoconazole, cyclosporin, itraconazole, tacrolimus, dronedarone*
[b] *amiodarone, quinidine, verapamil and ticagrelor*
[c] *rifampicin, St John's Wort, carbamazepine or phenytoin*

		Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Usual dose		Usual dose: 150 mg twice daily Reduce to 110 mg twice daily: ≥80 years, verapamil, thromboembolic risk low and the bleeding risk high (e.g. CrCL 30 - 50 mL/min, <50kg or patients with gastritis, oesophagitis or gastro-oesophageal reflux)	20 mg daily	5 mg twice daily Reduce to 2.5 mg twice daily in patients with two or more of the following characteristics: age ≥80 years, body weight ≤ 60kg, serum creatinine ≥1.5 mg/dL (133 micromole/L)	60 mg daily Reduce dose to 30 mg: moderate to severe renal impairment, ≤60kg, concomitant use of P-gp inhibitors
Renal Impairment	CrCl <15ml/min	Contra-indicated	Not recommended	Not recommended	Not recommended
	CrCl 15 – 29ml/min	Contra-indicated	15 mg daily and caution	2.5 mg twice daily	30 mg daily
	CrCl 30 – 49ml/min	No dosage adjustment unless bleeding risk	15 mg daily	No dosage adjustment	30 mg daily
Hepatic impairment	(Hepatic disease-coagulopathy, bleeding risk inc. cirrhotic patients with child pugh B and C)	Contra-indicated where expected to have impact on survival	Contra-indicated in hepatic disease	Severe – not recommended Mild to moderate - caution	Measure LFTs prior to initiating Contra-indicated in hepatic disease and severe hepatic impairment. Caution with mild to moderate hepatic impairment
	Patients with elevated liver enzymes >2 ULN	Not recommended	Not stated	Caution (including total bilirubin ≥1.5 x ULN)	Caution (including total bilirubin ≥1.5 x ULN)
Drug interactions	Strong CYP 3A4 and P-gp inhibitors[a]	Contra-indicated	Not recommended	Not recommended	Reduce to 30 mg
	Mild to moderate P-gp inhibitors[b]	Caution	Not stated	No dosage adjustment	No dosage adjustment
	Co-administration with P-gp inducers[c]	Avoid	Avoid	Not recommended	Caution
Reversibility		Idarucizumab (Praxbind®)	No licensed antidote Phase 3 trials ongoing Activated charcoal may be considered	No licensed antidote. Phase 3 trials ongoing Prothrombin complex concentrates or recombinant factor VIIa may be considered for life threatening conditions	No licensed antidote. Phase 3 trials ongoing 4-factor prothrombin complex concentrate or recombinant factor VIIa can also be considered for life threatening conditions
Half- life (t ½)		Healthy elderly - 11 hours; multiple doses - 12 - 14 hours If renal impairment: GFR (ml/min) / Half-life (range, hours) ≥80 / 13.4 (11.0 - 21.6) ≥50 - <80 / 15.3 (11.7 - 34.1) ≥30 - <50 / 18.4 (13.3 - 23) <30 / 27.2 (21.6 - 35)	Young individuals: t ½ 5 - 9 hours, t ½ 11 - 13 hours in the elderly	Approximately 12 hours	10 -14 hours
Switching from NOAC to warfarin		Adjust the starting time of the warfarin based on CrCL as follows: ▪ CrCL ≥50 mL/min, start warfarin 3 days before discontinuing dabigatran ▪ CrCL ≥30 - <50 mL/min, start warfarin 2 days before discontinuing dabigatran Because dabigatran can increase INR, the INR will better reflect warfarin's effect only after dabigatran has been stopped for at least 2 days. Until then, INR values should be interpreted with caution	Warfarin should be given concurrently until the INR is ≥2.0. For the first two days of the conversion period, standard initial dosing of warfarin should be used followed by warfarin dosing, as 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	Continue administration of apixaban for at least 2 days after beginning warfarin therapy. After 2 days of co-administration of apixaban with warfarin therapy, obtain an INR prior to the next scheduled dose of apixaban. Continue co-administration of apixaban and warfarin therapy until the INR is ≥2.0	**60 mg dose:** administer 30 mg + warfarin **30 mg dose**: administer 15 mg + warfarin Do not give a loading dose of warfarin in order to promptly achieve INR 2 - 3. It is recommended to take account of maintenance dose of warfarin and if patient was previously taking warfarin or to use validated INR driven warfarin treatment algorithm. INR ≥2, discontinue edoxaban. Most patients should be able to achieve INR ≥2 within 14 days of edoxaban + warfarin. After 14 days discontinue edoxaban and titrate warfarin to achieve INR 2 - 3

Mechanical/ prosthetic	Contra-indicated	Contra-indicated	Contra-indicated	Not studied in the first 3 months. May be used with bioprosthetic heart valves after 3 months
NICE guidance: Considered as option in line with licensed indications	TA 249	TA 256	TA 275	TA 355
Bleeding risk (see NICE TAGs, available at www.nice.org.uk)	RE-ly (n = 18,113) Major bleeding: 110 mg was associated with a statistically significant reduction compared to warfarin GI bleeding: 150 mg had higher rate compared to warfarin Life threatening: Both doses of dabigatran were associated with statistically significant reductions in the incidence of life-threatening bleeds compared with warfarin; Intracranial haemorrhage: both doses were associated with fewer cases (including haemorrhagic stroke) than warfarin (p <0.001)	ROCKET-AF trial (n = 14,264). Major bleeding: No significant differences between rivaroxaban and warfarin for major and non-major clinically significant bleeding GI bleeding: More often than warfarin (p <0.001) Intracranial haemorrhage rates: lower with rivaroxaban than with warfarin (p = 0.02)	ARISTOTLE (n = 18,201) Major bleeding: Significantly fewer events than warfarin (p <0.001) (and also intracranial major bleeding, other location major bleeding and clinically relevant non major bleeding) GI bleeding – difference between apixaban and warfarin was not statistically significant (p = 0.37)	ENGAGE AF TIMI-48 (n = 21,105) Major bleeding: Reduced rate compared to warfarin (p <0.001) (also reduced for fatal, intracranial and non-major bleeds) Major GI bleeding : more frequent in edoxaban 60 mg/30 mg arm than warfarin arm (p = 0.03)
Compliance Aids	Unsuitable as it needs to be kept in original pack to protect from moisture	No special precautions for storage	No special precautions for storage	No special precautions for storage
Cost/28 days at usual dose (Drug Tariff, MIMS December 2016)	£51.00	£50.40	£53.20	£51.80 (less rebate)

This information is a summary guide – for further information please consult individual SPCs at www.medicines.org.uk