Decision aid for patients requiring stroke prevention in AF .

NHS Wiltshire Clinical Commissioning Group

Comparator		Warfarin (variable dose od) £220 p.a.	Apixaban 5mg bd *N.B. This is preferred choice on the BCAP formulary (West Wilts)* £693	Dabigatran 110mg bd £620 p.a.	Dabigatran 150mg bd	Rivaroxaban 20mg od £657 p.a.	Edoxaban 60mg od £675 p.a.
License & NICE criteria		Prophylaxis of systemic embolism in pts with AF	NICE TA275: Prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation with one or more of the following risk factors: • Previous stroke or transient ischemic attack • Age ≥ 75 years • Diabetes mellitus, symptomatic heart failure (NYHA ≥ 2) or hypertension	NICE TA249: Prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation with one or more of the following risk factors: • Previous stroke or transient ischemic attack • Symptomatic heart failure, New York Heart Association (NYHA) ≥ Class 2 • Age ≥ 75 years • Diabetes mellitus or Hypertension ***Please note the license has been updated since NICE TA249 was published and hence the criteria for use are different. Follow the updated license criteria.***		NICE TA256: Prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation with one or more of the following risk factors: • Previous stroke or transient ischemic attack • Age ≥ 75 years • Diabetes mellitus, congestive heart failure or hypertension	NICE TA355 Prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation who have one or more of the following risk factors: • Heart failure, high blood pressure or diabetes • Had a stroke or transient ischaemic attack before, • Aged 75 years or older.
Stroke Risk			Primary outcome 1.27% per yr vs 1.60% per yr for warfarin, p<0.001 for non-inferiority.	Non-inferior to warfarin	Superior to warfarin	Non-inferior to warfarin	Non-inferior to warfarin
Mortality		No difference	11% reduction in all-cause mortality compared to warfarin (p=0.047)	No difference		No difference	No difference
Bleeding Risk	**Life-threatening bleed/ICH & major/minor bleeding**	Higher risk than 110mg Dabigatran dose, Rivaroxaban & Apixaban. Same risk as 150mg dose of Dabigatran.	Major bleeding was 2.13% per year in the apixaban group vs 3.09% for warfarin (p<0.001). ICH was 0.33% per year vs 0.8% for warfarin (p<0.001).	Lower risk for both strengths versus warfarin (p<0.05) Major bleeds: Dabigatran 110mg: Fewer patients had a major bleed vs warfarin (p=0.003) Dabigatran 150mg: Same risk as warfarin.		Lower risk versus warfarin. Significant reductions of ICH and fatal bleeding (ICH (0.5% vs 0.7%, p=0.02) and fatal bleeding (0.2% vs 0.5%, p=0.003) For major and non-major clinically relevant bleeding, the event rate was 14.9% for rivaroxaban & 14.5% for warfarin (p=0.44)	Annualized rate of major bleeding was 3.43% with warfarin vs 2.75% with high-dose edoxaban (P<0.001) and 1.61% with low-dose edoxaban (P<0.001). Significant reductions of ICH, life-threatening bleeding, and non-major clinically relevant bleeding (p<0.001) with both doses of edoxaban.
	Major Gastro-intestinal (GI) bleeding	Lower risk than Dabigatran 150mg and Rivaroxaban. No significant difference between Dabigatran 110mg or Apixaban.	No significant difference compared to warfarin.	No significant bleeding difference compared to warfarin.	Significantly higher rate of bleeding vs warfarin. RR (95% CI)= 1.50 (1.19-1.89) p<0.001.	Significantly higher rate of bleeding (3.2%) vs warfarin (2.2%) p=<0.001	Annualized rate of major GI bleeding was higher with high-dose edoxaban than with warfarin (1.51% vs. 1.23%). The rate was lowest with low-dose edoxaban (0.82%).
Elderly		Can be used in pts >80yrs	Can be used in pts >80yrs	Can be used in pts >80yrs	**DO NOT** use in pts >80yrs	Can be used in pts >80yrs	Can be used in pts >80yrs
Dossette Box		Not suitable to go in a dossette box unless as per NPSA guidance	Can go in a dossette box	Not suitable to go in a dossette box		Can go in a dossette box	Can go in a dossette box

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Comparator		Warfarin (variable dose od)	Apixaban 5mg bd	Dabigatran 110mg bd	Dabigatran 150mg bd	Rivaroxaban 20mg od	Edoxaban 60mg od
Renal Impairment	**CKD 4 and 5 Cr Cl <30ml/min**	Use with careful monitoring & specialist advice	Patients with serum creatinine ≥ 1.5mg/dl (133µmole/l) associated with age ≥ 80 years or bodyweight ≤ 60kg should receive the lower dose of 2.5mg bd.	Contra-indicated		Plasma levels may be significantly increased (average 1.6 fold) which may lead to an increased bleeding risk.	
			Cr Cl 15-29ml/min – reduce dose to 2.5mg bd.			**Cr Cl 15-29ml/min** – use with caution and reduce to 15mg daily.	**Cr Cl 15-29ml/min –** reduce dose to 30mg OD.
			Cr Cl <15ml/min – not recommended.			**Cr Cl <15ml/min** – not recommended.	**Cr Cl <15ml/min** – not recommended.
	CKD 3 Cr Cl 30-49ml/min	Safe to use	No dose adjustment needed.	Use 110mg dose if patient has a high bleeding risk		If Cr Cl 30-49ml/min, reduce the dose to 15mg od.	If Cr Cl 30-50ml/min, reduce the dose to 30mg OD.
Hepatic impairment		Monitor INR more frequently	Contraindicated in hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Not recommended in patients with **severe** hepatic impairment, and used with caution in patients with mild or moderate hepatic impairment (Child Pugh A or B, no dose adjustment is required). Use with caution in patients with elevated liver enzymes (ALT/AST >2 x ULN) or total bilirubin ≥1.5 x ULN.	No information available therefore use not recommended if liver enzymes >2 x upper limit of normal.		Contraindicated in hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B & C.	As per **Apixaban**
Antidote for haemorrhage		Vitamin K	**Not reversible**. If bleeding is uncontrolled with supportive measures, administration of recombinant factor VIIa may be considered. However there is currently no experience with its use. Potential problem where emergency surgery needed.	Dabigatran now has an antidote available called Idarucizumab (Praxbind®) which is available at all our local acute trusts on the advice of a haematologist.		**Not reversible**. Early clinical trial data suggests bleeding effects completely reversed by Prothrombin Complex Concentrate (PCC). Very limited clinical experience with this. Otherwise, supportive care only. Potential problem where emergency surgery needed.	As per **Apixaban – Not reversible**
Prescriber guides & Patient alert cards		Yellow books available via SBS (stationary order)	Available from: https://www.eliquis.co.uk/riskminimisationtools/index.aspx	Available from: http://www.boehringer-ingelheim.com/products/prescription_medicines/pradaxa/download.html		Available from: http://www.xarelto-info.co.uk/hcp.htm	Available from: http://www.lixiana.com/en/patient-resources/explaining-treatment

NOTE : Drug Safety Update Oct 2013 - http://www.mhra.gov.uk/home/groups/dsu/documents/publication/con322740.pdf Revised contraindications for all DOACs