Prescribing Criteria for Apixaban (Eliquis®) in Stroke Prevention in (non-valvular) AF

NHS Wiltshire Clinical Commissioning Group

Apixaban is licensed for prevention of stroke and systemic embolism in ADULT 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**

Apixaban has been approved as a GREEN drug across Wiltshire and is the preferred choice in the BCAP formulary which covers West Wiltshire.
Any potential use of Apixaban outside of NICE and/or license should be discussed with the CCG Medicines Management Team

The NICE TA275 (published February 2013) allows Apixaban to be used as an option in stroke prevention in AF as per the license above. **The CHADS2-VASc score can be used to assess a patient's stroke risk**.

Please use the following checklists in order to prescribe Apixaban appropriately and safely.

These lists are not exhaustive and professional judgment should be used on an individual patient basis

1. Does the patient have any of the following contra-indications * (from Summary of Product Characteristics)? *(tick any that apply)*	
	Hepatic disease associated with coagulopathy and clinically relevant bleeding risk.
	Active clinically significant bleeding
	Hypersensitivity to Apixaban or to any of the excipients
	Lesion or condition at significant risk of major bleeding such as current or recent gastrointestinal ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities.
	Concomitant treatment with any other anticoagulant agent e.g. unfractionated heparin (UFH), low molecular weight heparins (enoxaparin, dalteparin, etc.), heparin derivatives (fondaparinux, etc.), oral anticoagulants (warfarin, rivaroxaban, dabigatran, etc.) except under the circumstances of switching therapy to or from apixaban or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter.
If any of the contra-indications apply to your patient do not prescribe apixaban and seek advice.	
2. Patient groups where specialist advice should be sought before prescribing * *(tick any that apply)*	
	Previous history of intracranial haemorrhage – *some AF patients especially those considered at high risk of stroke may benefit from anti-thrombotic therapy, seek the opinion of a stroke specialist.*
	Pregnancy & breastfeeding. Apixaban is not recommended during pregnancy. See SmPC for full details.
	Recent major extracranial bleed within the last 6 months where the cause has not been identified or treated – *seek opinion of specialist*
	Patient with recent history of recurrent falls who are at higher bleeding risk.
	Patients with prosthetic heart valves - Safety and efficacy of Apixaban have not been studied in patients with prosthetic heart valves, with or without atrial fibrillation. The use of Apixaban is not recommended in this setting.

3. Assess your patient's bleeding risk. - The following risk factors can increase the risk of bleeding: The HAS-BLED score can be used to assess the bleeding risk of the patient (see reverse of 'Choosing the most suitable oral anticoagulant' document for further information)

	Age > 65 years		Recent brain spinal or opthalmic surgery
	Previous history bleed or predisposition to bleeding (e.g. diverticulitis)		Chronic alcohol abuse- especially if associated with binge drinking.
	Congenital or acquired coagulation disorders		Uncontrolled hypertension
	Recent biopsy or major trauma		Bacterial Endocarditis
	Moderate & severe renal impairment		Acute hepatic impairment (e.g. bilirubin > 2 x ULN + LFTS > 3x ULN), chronic liver disease (e.g.cirrhosis)
	Low platelet count < 80 x 10^9/L or a thrombocytopenia or anaemia of undiagnosed cause		On concomitant drugs associated with an increased bleeding risk e.g. SSRIs, oral steroids, NSAIDs, clopdiogrel, methotrexate or other immune-suppressant agents
	Active ulcerative gastrointestinal (GI) disease or recent GI ulcerations		Intraspinal or intracerebral vascular abnormalities
	Recent intracranial or intracerebral haemorrhage		Bronchiectasis or history of pulmonary bleeding

It might be worth considering co-prescription of a PPI to add gastroprotection in certain patient groups on concomitant medications which increase bleeding risk.

Dose is 5mg twice daily; reduce to 2.5mg twice daily if patient has two of the following:
age ≥ 80 years, body weight ≤ 60kg or serum creatinine ≥ 133 micromole/l

Other prescribing considerations

Renal Function – As renal function declines, drug clearance is reduced.	
Creatinine Cl (ml/min)	**Recommended dose**
Mild and Moderate renal impairment (30 to ≤80ml/min)	No dose adjustment
Severe renal impairment (Cr Cl<30ml/min)	Use with caution in pts with a Cr Cl 15-29ml/min and **reduce the dose to 2.5mg twice daily**. Use is not recommended in pts with Cr Cl <15ml/min.
There are no requirements to monitor urea & creatinine in the SPC but it may be worth checking intermittently to ensure that the renal function has not declined	

Weight of patient
Reduce to 2.5mg twice daily if patient has **two** of the following: age ≥ 80 years, body weight ≤ 60kg or serum creatinine ≥1.5mg/dl (133 micromole/l)

Patients being switched from warfarin
Warfarin should be stopped & then apixaban started once INR is below 2.0, so INR monitoring is needed initially.

Other important considerations:

- A bleeding risk that would lead to a contra-indication to warfarin would also contra-indicate apixaban.
- Sub-optimal compliance with warfarin may not be improved by switching to apixaban as many of the causes of non-compliance with warfarin may also result in non-compliance with apixaban (e.g. alcoholism, chaotic lifestyle, wilful non-compliance). As apixaban has a relatively short half-life (12hrs) missing a dose could be associated with an increased risk of stroke.
- Ensure that the patient is given an alert card by the pharmacy and that the patient knows to carry it around with them.
- Apixaban is stable in monitored dosage systems (e.g. dossette) (unlike warfarin and Dabigatran).
- Apixaban has no antidote and so haemorrhages are dealt with by supportive care.
- For patients with **swallowing difficulties or PEG tubes** etc, please contact the Medicines Management Team for specific advice.

Drug Interactions (See SPC for full details, this list is not exhaustive)	
Interacting Drug	**Management**
Anti-platelets (e.g. aspirin, clopidogrel)	Concomitant use increases the risk of bleeding and hence should be used with caution.
NSAIDs	Concomitant use increases the risk of bleeding and hence should be used with caution.
P-gp inhibitors:e.g. Itraconazole & Ketoconazole	Combination thought to result in **increased** apixaban plasma concentrations. Concomitant use not recommended.
P-gp inducers: e.g. Rifampicin, St. John's wort, Phenobarbital, Carbamazepine, or Phenytoin	Expected to result in **decreased** apixaban concentrations. Concomitant use with caution.
Protease Inhibitors e.g. Ritonavir	Not recommended for concomitant treatment with apixaban

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