# NHS South West Essex Shared Care Guideline (SCG)

Apixaban SCG for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF).

## Introduction

### Indication and Licensing

Apixaban is one of the novel oral anticoagulants (NOACs) licensed for the 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
- Hypertension
- Diabetes mellitus
- Symptomatic heart failure (NYHA Class ≥ II)

Apixaban is a direct inhibitor of activated factor X (factor Xa). Due to its selective inhibition of one clotting factor, the anticoagulation effects are more predictable and as such there is no requirement for regular monitoring (unlike warfarin that requires regular INR checking). Within the East of England, warfarin remains the drug of choice for individuals requiring anticoagulation in non-valvular AF. Apixaban can be prescribed for the management in non-valvular AF and requires prior approval (Appendix I).

### Patient Pathway

| Clinical speciality | Prescribing initiated by | Prescribing continued by | Monitored by | Duration of treatment |
|---|---|---|---|---|
| Cardiology Haematology Stroke | Hospital consultant | GP following initiation by hospital | GP following initiation by hospital | Life long* |

*temporary discontinuation for surgical procedures advised, see guidelines for the peri-operative management of drug therapy

Patients are to be initiated in the first instance via a consultant (cardiology, haematology, stroke). One month supply to be provided by hospital when initiated, followed by GP continuation.

Treatment should continue indefinitely on confirmation of non-valvular atrial fibrillation that requires anticoagulation. Treatment should be reviewed (at least annually) and an assessment made for new contra-indications to ongoing anticoagulation with apixaban

(e.g. temporary discontinuation for surgery, marked decline in renal function and increased bleeding). Where new contraindications are found, treatment is to be reviewed and anticoagulation therapy withdrawn if risks are deemed to outweigh benefits. If therapy is to be withdrawn, refer to specialist to assess and initiate suitable antithrombotic therapy.

Ongoing compliance should be reviewed on a regular basis, the duration and method of compliance assessment should be determined by the GP and patient characteristics.

**Normal dose and administration**

Apixaban is available as two strengths for the prevention of stroke and systemic embolism in atrial fibrillation, 2.5mg and 5mg film coated tablets.

**Usual dose**:
5mg twice daily* to be swallowed whole with or without food.
*Unless dose reduction indicated as below.

**Dose reduction**

The recommended dose of apixaban in patients with non-valvular atrial fibrillation and at least two of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL (133 micromol/L) is 2.5 mg taken twice daily.

Renal impairment:

-CrCl < 15 mL/min, or in patients undergoing dialysis: apixaban is not recommended as there is no clinical experience in these patients

-Severe renal impairment, CrCl 15-29 mL/min: apixaban 2.5 mg twice daily

-Mild to moderate renal impairment: no dose adjustment, apixaban 5 mg twice daily

-Serum creatinine ≥ 1.5 mg/dL (133 micromol/L) associated with age ≥ 80 years or body weight ≤ 60 kg: lower dose of apixaban 2.5 mg twice daily

**Monitoring**

| Parameter | Renal function (creatinine clearance - CrCl) |
|---|---|
| Target level | -CrCl < 15 mL/min, or in patients undergoing dialysis: apixaban is not recommended<br>-CrCl 15-29 mL/min: apixaban 2.5 mg twice daily<br>-CrCl ≥ 30 mL/min: no dose adjustment, apixaban 5 mg twice daily<br>-Serum creatinine ≥ 1.5 mg/dL (133 micromol/L) associated with age ≥ 80 years or body weight ≤ 60 kg: lower dose of apixaban 2.5 mg twice daily |
| Frequency of monitoring | Assess renal function prior to starting treatment to ensure appropriate starting dose then while on treatment renal function should be assessed at least once a year (or more frequently as needed in certain clinical situations when it is suspected that the renal function could decline or |

| | |
|---|---|
| | deteriorate such as hypovolemia and dehydration). |
| Action | Dose reduction may be required based on initial renal function.<br>If renal function declines rapidly may need to temporarily withhold therapy and review prior to restarting. |

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| Parameter | Liver function |
| Target level | |
| Frequency of monitoring | Assess liver function prior to starting treatment. |
| Action | Apixaban is contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk. It is not recommended in patients with severe hepatic impairment. It should be used with caution in patients with mild or moderate hepatic impairment (Child Pugh A or B). No dose adjustment is required in patients with mild or moderate hepatic impairment. Apixaban should be used with caution in patients with elevated liver enzymes (ALT/AST >2 x ULN) or total bilirubin ≥1.5 x ULN. |

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| Parameter | Bleeding risk |
| Target level | Although treatment with apixaban does not require routine monitoring of exposure, the Rotachrom® anti-FXa assay may be useful in exceptional situations where knowledge of apixaban exposure may help to inform clinical decisions, e.g. overdose and emergency surgery. |
| Frequency of monitoring | Patients should be carefully observed for signs of bleeding. |
| Action | It is recommended that apixaban should be used with caution in conditions with increased risk of haemorrhage. Apixaban should be discontinued if severe haemorrhage occurs. |

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| Parameter | Adherence |
| Target level | 100% |
| Frequency of monitoring | Prior to initiation, likely compliance should be considered and discussed with the patient. Following initiation, compliance should be checked and reinforced at a minimum of annually although this is left at the discretion of the physician. |
| Action | If compliance likely to be low, consider alternative anticoagulation that can be monitored. |

**Common adverse effects**

Common adverse reactions include epistaxis, contusion, haematuria, haematoma, eye haemorrhage, and gastrointestinal haemorrhage.

**Contra-indications**

-Clinically significant active bleeding

-Hepatic disease associated with coagulopathy and clinically relevant bleeding risk

-Lesion or conditions 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.

**Drug interactions**

Co-administration of apixaban with inducers of CYP3A4 and P-glycoprotein (such as rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort) may result in reduced apixiban plasma levels. No dose adjustment of apixaban is required during concomitant therapy with such agents, however strong inducers of both CYP3A4 and P-glycoprotein should be co-administered with caution.

Co-administration of apixaban with strong inhibitors of both CYP3A4 and P-glycoprotein (such as azole-antimycotics e.g. ketoconazole, itraconazole, voriconazole and posaconazole, and HIV protease inhibitors e.g. ritonavir) may result in increased apixaban plasma levels and is not recommended.

Due to an increased bleeding risk, concomitant treatment with any other anticoagulants is contraindicated

For comprehensive information on cautions, contra-indications and interactions, please refer to the current British National Formulary and Summary of Product Characteristics.

**Pregnancy and breast feeding**

The safety of apixaban has not been established in pregnant or lactating women; as such use in these patients is not recommended.

**Shared care guideline**

SCG is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets out responsibilities for each party. The intention to shared care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and cooperation in the management of patients. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use.

**Consultant**

1. Ensure that the patient/carer is an informed recipient of apixaban.
2. Ensure that patients understand apixaban treatment and monitoring (e.g. renal function) or follow up that is required (using advocacy if appropriate).
3. Ensure baseline investigations are normal before commencing treatment. Give the patient a patient held anticoagulant card.
4. Initiate treatment and prescribe until the GP formally agrees to shared care. Supply the first month of treatment
5. Send a letter to the GP requesting shared care for the patient following completing the prior approval form and receiving agreement from the Central Eastern Commissioning Support Unit Medicines Management Team.
6. Send a letter/results notification to the GP after the clinic meeting confirming the current dose and most recent blood results.
7. Evaluation of any reported adverse effects by GP or patient.
8. Advise GP on review, duration or discontinuation of treatment where necessary.
9. Ensure that backup advice is available at all times.

**General Practitioner**

1. Reinforce the patient's understanding of the nature, effect and potential side effects of apixaban before prescribing it as part of the shared care programme and contact the specialist for clarification where appropriate. Monitor patient's overall health and well-being.
2. Report any adverse events to the consultant, where appropriate.
3. Report any adverse events to the CSM, where appropriate.
4. Help in monitoring the progression of disease.
5. Prescribe the drug treatment as described.
6. Undertake monitoring outlined in monitoring section once shared care agreed.

**CCG**

1. To provide feedback to trusts via Trust Medicines Committee.
2. To support GPs in decision making and facilitate appropriate use and monitoring of apixaban.
3. To support trusts in resolving issues that may arise as a result of shared care.

**Patient/ Carer**

1. Report any adverse effects to their GP and/or specialist.
2. Ensure they have a clear understanding of their treatment (apixaban).
3. Report any changes in disease symptoms to GP and/or specialist.
4. Alert GP and/or specialist of any changes of circumstance which could affect management of disease.
5. Take/ administer apixaban as prescribed.

**Contact details**

Initial contact should be made with the initiating consultant. Contact consultant haematologist if haematologist is the initiating consultant or on the advise of the initiating consultant.

| | |
|---|---|
| Initiating consultant at BTUH<br><br>Name (please print): | Please insert:<br><br>Contact details: |

**Acknowledgement:** These shared care guidelines are based on information contained in the shared care guidelines by NHS North East London Cardiovascular and Stroke Network

## Appendix I

Approval Form for Dabigatran, Rivaroxaban and Apixaban Usage in Atrial Fibrillation

Patient name: DOB:

Patient Hospital no: NHS no:

This form is for completion by **haematology, stroke and cardiac consultants ONLY**. Forms filled in by any other grade or speciality will be declined. Only patients meeting the agreed criteria will be supplied with NOACs (a prescription is also required).

The agreed criteria for NOACS usage in SW Essex are:

**Patient must have a CHADS2 score of 2 or more**

| | | | | | |
|---|---|---|---|---|---|
| Congestive heart failure | 1 | Hypertension >140/90 | 1 | Age >75yrs | 1 |
| Diabetes Mellitus | 1 | Previous Stroke or Previous TIA | | | 2 |

**Please circle the relevant risk factors*

Plus the patient should have **one** of the following
**Please circle which apply*

**Clinical contraindications to warfarin** causing drug discontinuation

| | | |
|---|---|---|
| Yes | No | The CIs are: |

**Allergy to warfarin**

| | | |
|---|---|---|
| Yes | No | The allergy is: |

**Experience of substantial side effects with warfarin causing drug discontinuation**

| | | |
|---|---|---|
| Yes | No | The SEs are: |

**A further embolic event whilst on warfarin if eligible for 150 mg dabigatran**

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|---|---|
| Yes | No |

**Time in therapeutic range for warfarin of less than 60% for 4 months i.e. poor control (Note: concordance issues must be fully explored and resolved before looking at poor control)**

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|---|---|
| Yes | No |

**Patient requiring domiciliary phlebotomy**

| | |
|---|---|
| Yes | No |

**Please send completed form with the prescription to Fatemeh Leedham, pharmacy department**

Consultant name: Signature: Date …../…../……

CSU advisor name: Signature Date …../…../……

Treatment approved:
Treatment rejected:

Drug choice: Please choose strength

| Dabigatran 110mg or 150 mg | Rivaroxaban 20mg | Apixaban 2.5mg or 5mg |
|---|---|---|
| | | |

**Please only dispense when approval is received from CSU.**

NOACs: New Oral Anticoagulants CSU: Commissioning Support Unit

Date approved: October 2013
Approved by: Medicines Management Committee
Review date: October 2014, or earlier as appropriate

Appendix II

**Shared care agreement letter**

Name of Trust: Basildon and Thurrock University Hospital NHS FT
Apixaban (Eliquis®)
Prevention of stroke and embolism in adult patients with non-valvular atrial fibrillation

Name of GP …… Address ……
……..……..……
……..

Dear GP

Re: Patient's Name……
Date of Birth……
NHS Number……..
Hospital Number……..……

Indication for oral apixaban 2.5mg / 5 mg (delete as appropriate) twice daily for prevention of stoke and embolism in adult patients with non-valvular atrial fibrillation.

Enclosed is a copy of the shared care guidelines for apixaban to be retained in the patient's notes.
Should you agree to shared care, we will send a letter containing the details of the patient's treatment plan, the dose to be prescribed and all relevant blood results.

Please sign below and return this letter to the Hospital Specialist if you agree to the shared care arrangements for this patient.

Many thanks

| | |
|---|---|
| Hospital Specialist | GP |
| Signature……... | Signature……... |
| Name ……..……... | Name ……... |
| Date……... | Date……..…..……... |

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If you are not taking on shared care for this patient please state the reason why and return this letter to the Hospital Specialist.
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