

Transfer of Care:

Apixaban (Eliquis®) for the treatment of acute venous thromboembolism and prevention of recurrent venous thromboembolism

Purpose and scope

This transfer of care document is written for all health care professionals involved in the prescribing, dispensing or administration of anticoagulation and aims to provide sufficient information to ensure that it is continued safely and appropriately in primary care.

Indication

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Initiation would be by secondary care only and in accordance with its licensed indication and NICE guidelines.

Dosing

Apixaban film coated tablets are available in two strengths: 2.5mg and 5mg. The dose is dependent on creatinine clearance (CrCl) as outlined in table below

Treatment for acute DVT/PE:

	Renal function*		
	CrCl ≥30ml/min	CrCl: 15 to 29ml/min	CrCl <15ml/min
First 7 days	10mg twice daily	10mg** twice daily	Contraindicated
Day 8 onwards	5mg twice daily	5mg** twice daily	

Prevention of recurrent DVT/PE following completion of at least 6 months of treatment dose:

	Renal function*		
	CrCl ≥30ml/min	CrCl: 15 to 29ml/min	CrCl <15ml/min
Dose	2.5mg twice daily	2.5mg** twice daily	Contraindicated

*Cockcroft and Gault formula to calculate CrCl (ml/min):

$$\frac{k (1.23 \text{ in males and } 1.04 \text{ in females}) \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine } (\mu\text{mol/L})}$$

**No dose reduction of apixaban is advised, however apixaban is to be used with caution due to increased risk of bleeding based on limited clinical data in this population.

Dose alterations:

Patients with an increased bleeding risk, oesophagitis, or gastroesophageal reflux should be closely monitored and apixaban should be used cautiously. Ongoing treatment should be decided at the discretion of the physician, following assessment of the potential benefit and risk to an individual patient.

If clinically relevant bleeding occurs, treatment should be interrupted and reviewed prior to re-initiation.

Surgery and invasive procedures:

Patients on apixaban who undergo surgery or invasive procedures are at increased risk of bleeding. Therefore surgical interventions may require temporary discontinuation of apixaban. If an invasive procedure or surgical intervention is required, apixaban should be stopped at least 24-48 hours before the intervention, depending on the risk of bleeding associated with the procedure - see apixaban Summary of Product Characteristics (SPC) for further details. If surgery cannot be delayed the case should be discussed with haematology for advice on reversal if required.

Apixaban should be restarted after the invasive procedure or surgical intervention as soon as possible provided the clinical situation allows and adequate haemostasis has been established.

Contraindications and cautions

Hypersensitivity to the active substance or to any of the excipients. Active bleeding; significant risk of major bleeding (e.g. recent gastro-intestinal ulcer, oesophageal varices, recent brain, spine, or ophthalmic surgery, recent intracranial haemorrhage, malignant neoplasms, vascular aneurysm, major intraspinal or intracerebral vascular abnormalities, arteriovenous malformations).

Apixaban is contraindicated in severe liver disease and should be used with caution in patients with elevated hepatic enzymes.

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

Please refer to apixaban SPC for comprehensive information on cautions, contraindications and interactions.

Patient pathway

Clinical Speciality	Prescribing Initiated by	Prescribing Reviewed by	Prescribing Continued and Monitored by	Duration of treatment
Haematology	Secondary care prescriber	Hospital after 1 - 4 weeks of initiation	GP after 8 weeks	Individualised for each patients. All VTE patients will be seen by haematologist within 6 months of initiation to confirm duration of treatment.

Patients are to be initiated in the first instance by a clinician in secondary care. If apixaban is suitable, 8 weeks supply will be issued alongside the anticoagulation alert card and patient booklet.

The patient will be reviewed by the anticoagulation clinic after the initial 1 week to ensure adequate follow up during the initiation phase providing adherence counselling and addressing any concerns regarding therapy. If the patient has concerns prior to commencing continuation with the GP they should contact the hospital anticoagulant team. The patient

will be advised to contact their GP within 7 weeks of initiation. A NOAC initiation letter will be given to the patient and will also be forwarded to the GP confirming transfer of care.

Duration of treatment will be advised initially by the anticoagulation team. A follow up within 3 to 6 months would then be carried out by a haematologist to assess the patient and extend the duration of treatment, if needed. Long-term treatment should be reviewed at least annually by GP and an assessment made for new contraindications to ongoing anticoagulation with apixaban (e.g. temporary discontinuation for surgery, marked decline in renal function and increased bleeding risk - see below for further advice on bleeding risk). Where new contraindications are found, treatment is to be reviewed and anticoagulation therapy withdrawn if risks are deemed to outweigh benefits. Ongoing adherence should be reviewed on a regular basis, the duration and method of adherence assessment should be determined by the GP, taking into account individual patient circumstances and factors. The GP is to re-educate the patient each time for the need to stop their apixaban and seeing any doctor as soon as possible in case of significant bleeding.

Monitoring

All patients on long-term anticoagulants require a general review at least once a year in order to re-assess optimal NOAC and correct dosing. The following should be reviewed:

Assess adherence

- Re-educate on importance of strict intake schedule
- Identify any side effects, especially those that may be impacting on compliance
- If adherence is low, consider alternative anticoagulation that can be monitored, i.e. warfarin

Co-medications

- Review other medications (inclusive of over the counter and herbal medication) for drug interactions

Blood sampling and weight as outlined in table below.

Patient group	U&Es	Weight	CrCl	FBC	LFTs
CrCl* > 60mL/min	Annually	Annually	Annually	Annually	Annually
CrCl* ≤ 60mL/min	CrCl/10** = minimum recheck interval in months	CrCl/10** = minimum recheck interval in months	CrCl/10** = minimum recheck interval in months	Annually	Annually
Age ≥ 75 years or frail***	4 monthly	4 monthly	4 monthly	Annually	Annually
Concurrent conditions that may impact renal or liver function (e.g. infection, NSAID use, dehydration, hypovolemia)	If needed	If needed	If needed	If needed	If needed

**Using Cockcroft and Gault equation*

***For example: if CrCl is 52ml/min then recheck interval would be every 5 months*

****Defined as ≥ 3 of the following criteria: unintentional weight loss, self-reported exhaustion, weakness assessed by handgrip test, slow walking speed/gait apraxia, low physical activity*

Routine clotting tests (PT and APTT) are not very reliable indicators of the level of apixaban and should not be used for monitoring purposes. If measurement of a apixaban level is required it should be with an anti-Xa assay following discussion with the haematology.

Adverse effects and actions

This lists the key adverse drug reactions, for comprehensive information please refer to the current British National Formulary and SPC. GP's are not expected to initiate reversal agents.

Adverse effect	Symptoms/signs	Actions
Minor Bleeding	Scratches, cuts.	Self-terminating, monitor at home.
	Nose bleeds.	Advise to plug, pinch nose, use of cold pack, remain still and calm, investigation of underlying causes by referring to ENT.
	Gum bleeding.	Ensure dental health is sufficient.
		If numerous episodes of minor bleeding are observed, patient at high risk of bleed, patient/physician concerned, then contact local haematology department for advice.
Significant bleeding	The degree of bleeding will dictate the action. Bleeding that does not stop with appropriate first aid, should be referred to local A&E. If in doubt contact local haematology department for advice.	The degree of bleeding will dictate the action. If bleeding stops spontaneously consider omitting a dose. For bleeding that does not stop with intervention, send patient to local A&E.
Gastrointestinal	Dyspepsia.	Consider gastro protection in accordance with local guidance. If no further improvement, consider alternatives or referral to specialist.
Bruising	Severe and unexplained spontaneous bruising.	Refer to local A&E due to risk of internal bleeding.

Transfer of care

This document 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 transfer of care should be explained to the patient. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. 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/Anticoagulant team

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) and follow up that is required (using advocacy if appropriate).
3. Ensure baseline investigations are satisfactory before commencing treatment. Give the patient an anticoagulant alert card patient booklet.
4. Counsel the patient on the risks and benefits of treatment with apixaban as well as importance of adherence to treatment.
5. Initiate treatment, prescribe and monitor for the first 8 weeks.
6. Send a NOAC initiation letter to the GP.
7. Clear documentation should be made as to reason for dose reduction.
8. Report any abnormal blood results to the GP where appropriate.
9. Evaluation of any reported adverse effects by GP or patient.
10. Advise GP on review, duration or discontinuation of treatment where necessary.
11. Ensure a 3 to 6 months follow up is arranged with haematologist. Duration of treatment and stop dates will be clearly communicated to the GP in writing.
12. Ensure that backup advice is available at all times.
13. Inform the patient to make a GP appointment within 7 weeks of initiation for further supplies.

General Practitioner

1. Reinforce the patient understands the nature, effect and potential side effects of apixaban before prescribing and contact the specialist for clarification where appropriate.
2. Monitor patient's overall health and well-being.
3. Report any adverse events to the consultant, where appropriate.
4. Report any adverse events to the MHRA yellow card scheme, where appropriate.
5. Help in monitoring the progression of disease.
6. Prescribe and monitor the drug treatment as described and stop the drug at the specified time. Consider managing the drug as an acute prescription as oppose to a repeat.

Clinical Commissioning Group

1. To provide feedback to Trust via Barts Health Drugs and Therapeutic Committee.
2. To support GPs to prescribe apixaban safely and effectively.
3. To support trusts in resolving issues that may arise as a result of transferred 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. Carry an anticoagulation card with them at all times.
4. Report any changes in disease symptoms to GP and/or specialist.
5. Alert GP and/or specialist of any changes of circumstance which could affect management of disease.
6. Administer apixaban as prescribed and attend hospital/GP for assessment and monitoring as required.

Contacts

Contact	Telephone number / bleep
Barts Health NHS Trust Consultant Haematologists	Telephone (via switchboard) 0203 416 5000 and ask for site & department OR Via advice and guidance
Royal London and St Bartholomew's	
Haematology SpR	Telephone 0203 416 5000 Bleep 1155 or via switchboard out of hours
Anticoagulation clinic (For Postcodes: E1, E2, E3, E14, EC1, EC2, EC3, EC4, WC1V, WC2A, N1)	020 3594 1885 OR Email: theanti.coagteam@nhs.net
Pharmacist	020 324 60140
Newham University Hospital	
Haematology SpR	Telephone (via switchboard) bleep 4130/4247
Anticoagulation clinic (For Postcodes: E6, E7, E12, E13, E15, E16, E20)	020 7363 8730 OR Email: newhamanticoagteam@nhs.net/ BHNT.Newhamanticoagteam@nhs.net
Whipps Cross University Hospital	
Haematology SpR	Telephone (via switchboard) Bleep 2075/2076
Anticoagulation clinic (For Postcodes: E4, E10, E11, (parts of E6, E7, E12), E17, E18, IG1-10)	020 8535 4538 OR Email: wxanticoadmin@bartshealth.nhs.uk
Clinical Commissioning Group Medicines Optimisation Team	
Newham CCG	Telephone: 0203 688 2654 NEWCCG.medicinesmanagement@nhs.net
Tower Hamlets CCG	Telephone: 020 36882556 THCCG.medicinesoptimisation@nhs.net
Waltham Forest CCG	Telephone: 0203 688 2654 WFCCG.MedicinesOptimisation@nhs.net

References

Steffel, J., Collins, R., Antz, M., Cornu, P., Desteghe, L., Haeusler, K.G., Oldgren, J., Reinecke, H., Roldan-Schilling, V., Rowell, N., Sinnaeve, P., Vanassche, T., Potpara, T., Camm, A.J., Heidbüchel, H., Lip, G.Y.H., Deneke, T., Dagres, N., Boriani, G. and Chao, T.-F. (2021). 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation. *EP Europace*.

Eliquis 5 mg film-coated tablets - Summary of Product Characteristics (2021) - (emc). [online] Available at: <https://www.medicines.org.uk/emc/product/2878/smpc#gref>. Accessed 10/10/2021.