

## Prescribing APIXABAN for the acute treatment and secondary prevention of Venous Thromboembolism (VTE) (Pulmonary Embolism (PE) or Deep Vein Thrombosis (DVT))

*Note: Apixaban is also licensed for the prevention of stroke in patients with non-valvular atrial fibrillation. Guidance for use for this indication can be found at: [SEL APC CVD Guidelines](#)*

Apixaban (Eliquis®) is a direct oral anticoagulant (DOAC) licensed for the acute treatment of VTE (PE or DVT) and for the secondary prevention of VTE in patients at risk of recurrent events. The National Institute for Health and Care Excellence (NICE) has approved the use of apixaban as an option for the acute management and secondary prevention of VTE.

**In South London, apixaban may be considered as an option for any patient experiencing a provoked or unprovoked DVT or PE**, except those patients in whom there is an underlying malignancy or those who are pregnant or breast-feeding where a low molecular weight heparin (LMWH) is preferred, or patients with renal impairment (creatinine clearance (CrCl) < 30ml/min) in whom warfarin is preferred (apixaban is contra-indicated when CrCl < 15ml/min).

- Patients with provoked VTE events (e.g. caused by surgery, trauma, long distance travel, immobility, pregnancy or hormone replacement therapy) usually require 3 - 6 months of apixaban therapy.
- Patients with unprovoked events or where there are on-going risk factors for recurrence may require a longer duration, as advised by the initiating clinician.

**Additional resources have been developed to support implementation including:**

- [Overview summary of VTE treatment](#)
- [Screening checklist and Notification of initiation of a DOAC for the treatment of VTE](#) This document **must be completed and sent to the General Practitioner (GP) on initiation.**
- [Transfer of prescribing responsibility to primary care for DOACs](#). This document **must be completed and sent to the GP when transferring the prescribing responsibility** in accordance to South London guidelines.

Apixaban for VTE should only be initiated by clinicians with expertise in managing anticoagulant therapy. The initiating clinician / organisation is responsible for ensuring patient follow up and providing supplies of apixaban for the first three months of treatment. During this time, efforts should be made to reinforce adherence and address any adverse effects.

### Transfer of prescribing responsibility to patients own GP

Following the initial 3 month period, patients requiring longer term anticoagulant therapy may be considered for transfer back to the patient's own GP, in line with the local transfer of care guidance. If apixaban is prescribed for non-approved / unlicensed indications, prescribing responsibility will remain with the initiating clinician / organisation.

| Contraindications (for full details – see BNF or <a href="#">SPC</a> )   | Cautions (for full details – see BNF or <a href="#">SPC</a> )   |
|--|---|
| <ul style="list-style-type: none"> <li>• Hypersensitivity to the active substance or to any of the excipients</li> <li>• Clinically significant active bleeding</li> <li>• Any lesion or condition considered a significant risk factor for major bleeding e.g. 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</li> <li>• Rare hereditary conditions such as galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption as <b>Eliquis</b> contains lactose</li> <li>• Prosthetic heart valves requiring anticoagulant treatment - the effect of apixaban has not been studied in this patient group</li> <li>• Severe hepatic impairment or hepatic disease associated with coagulopathy and clinically relevant bleeding risk</li> <li>• Established renal failure (CrCl &lt; 15 ml/min*)</li> <li>• Pregnancy and/ or breast feeding</li> <li>• For contraindications for use with other medications see overleaf</li> </ul> | <ul style="list-style-type: none"> <li>• Patients with conditions which carry a haemorrhagic risk e.g. bacterial endocarditis, thrombocytopenia, congenital or acquired coagulation disorders</li> <li>• Active cancer- efficacy and safety of apixaban in the treatment and/or prevention of VTE in patients with active cancer have not been established – LMWH preferred</li> <li>• Haemodynamically unstable PE patients or patients who require thrombolysis or pulmonary embolectomy- not recommended since the safety and efficacy of apixaban have not been established in these clinical situations</li> <li>• Low body weight &lt; 60 kg</li> <li>• Uncontrolled severe hypertension</li> <li>• Mild or moderate hepatic impairment (Child Pugh A or B)</li> <li>• Patients with elevated liver enzymes (alanine transaminase (ALT) / aspartate aminotransferase (AST)) &gt; twice the upper limit of normal (ULN) or total bilirubin ≥ 1.5 x ULN were excluded in clinical trials</li> <li>• Severe renal impairment (CrCl 15-29ml/min*)</li> <li>• For cautions for use with other medication see overleaf</li> </ul> |

**Note:** BNF=British National Formulary; SPC=Summary of Product Characteristics

**\*Estimated Glomerular Filtration Rate (eGFR) should NOT be used to guide dosing decisions. Creatinine clearance must be estimated using the [Cockcroft-Gault equation calculator](#) or refer to the South London creatinine clearance information sheet.**

***This guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.***

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Review date: June 2018

South East London Area Prescribing Committee. A partnership between NHS organisations in South East London: Bexley/ Bromley/ Greenwich/ Lambeth/ Lewisham & Southwark Clinical Commissioning Groups (CCGs) & GSTFT/KCH/SLAM/Oxleas NHS Foundation Trusts & Lewisham & Greenwich NHS Trust

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## Dosing

- **The recommended dose of apixaban for management of acute DVT or PE is 10mg TWICE daily for the first 7 days, then 5mg TWICE daily thereafter.** For patients with severe renal impairment (CrCl 15–29 ml/min), apixaban 5mg twice daily should be used with caution.
- **The recommended dose of apixaban for secondary prevention of recurrent DVT and/or PE is 2.5mg TWICE daily.** This should be initiated following completion of 6 months of acute treatment either with apixaban 5mg TWICE daily or alternative anticoagulant.
- Patients with provoked VTE events (e.g. caused by surgery, trauma, long distance travel, immobility, pregnancy or hormone replacement therapy) usually require 3 - 6 months of apixaban therapy.
- Patients with unprovoked events or where there are on-going risk factors for recurrence may require a longer duration, as advised by the initiating clinician.

*For patients identified as at risk of upper GI bleeding the co-prescription of a proton pump inhibitor (e.g. lansoprazole/omeprazole) may be considered.*

## Monitoring

International normalised ratio (INR) monitoring is not required for patients taking apixaban. However, clinical surveillance is recommended throughout the treatment period in line with good anticoagulation practice.

- All patients prescribed apixaban should be reviewed **at least annually** to assess benefits and risks of on-going therapy weighing the risk for thrombotic events against the bleeding risks.
- Patients should be monitored for signs of bleeding or anaemia; treatment should be stopped if severe bleeding occurs.
- A baseline renal function test is required and consequent re-testing should take place at least annually (frequency determined by the patient's baseline renal function as guided by the initiating clinician).
- For patients on long-term therapy clinicians will need to monitor patients and make any other dose adjustments necessary based on length of treatment completed (see dosage section above).

## Side effects (for full details see the BNF or SPC)

- As with any other forms of anticoagulation, there is a risk of bleeding during treatment with apixaban, and patients should be monitored for signs of bleeding or anaemia. Patients should be advised to seek medical advice if they experience persistent or frequent episodes of bleeding. Patients experiencing severe bleeding should seek urgent medical advice.
- Other side effects include itching and allergic reactions.

## Drug Interactions (for full details on drug interactions – see BNF or SPC)

| Drug / Drug class  | Recommendation   |
|--|--|
| Other anticoagulant agents (e.g. unfractionated heparin (UFH) or heparin derivatives, LMWHs, oral anticoagulants)                                  | Concomitant use is contraindicated due to increased risk of bleeding, except when UFH is given at doses necessary to maintain a patent catheter or if switching with other anticoagulants                      |
| Use of fibrinolytic agents for the treatment of acute ischaemic stroke   | May be considered by hyper-acute stroke units if the clinician can be certain that there is no anticoagulant effect present based on laboratory testing of clotting  |
| Aspirin and other antiplatelet agents  | Increased risk of bleeding – use with caution; should be stopped if clinically appropriate (seek advice from cardiologist); if required to continue close monitoring required and gastro-protection is advised |
| Non-steroidal anti-inflammatory drugs (NSAIDs)   | Increased risk of bleeding if used long-term. Avoid where possible; if required use at the lowest dose and for the shortest duration possible; close monitoring required and gastro-protection is advised      |
| Any other medicinal products affecting haemostasis   | May increase the risk of bleeding when used concomitantly, close monitoring required   |
| CYP3A4 or P-glycoprotein inducers - such as St. John's wort ( <i>Hypericum perforatum</i> ), rifampicin, phenobarbital, carbamazepine or phenytoin | Concomitant use will result in decreased apixaban plasma concentrations, therefore co-administration with apixaban for VTE treatment is not recommended  |
| Systemic azole-antimycotics (such as ketoconazole, voriconazole, itraconazole or posaconazole)   | Concomitant use is not recommended due to increased plasma apixaban levels   |
| HIV Protease inhibitors (e.g. lopinavir/ritonavir, indinavir)  | Concomitant use is not recommended due to increased plasma apixaban levels   |

## Roles and responsibilities

| Initiating clinician / organisation  | Patient's own GP  |
|--|---|
| <ul style="list-style-type: none"> <li>• To initiate apixaban in line with NICE and local guidance</li> <li>• To supply apixaban for the first 3 months of treatment</li> <li>• To provide counselling to improve adherence and address any early adverse effects</li> <li>• If treatment is required for longer than three months; to transfer care to the GP in line with local guidance</li> <li>• If treatment is required for longer than three months; to give clear guidance on the intended duration of</li> </ul> | <ul style="list-style-type: none"> <li>• To ensure use of apixaban is in line with the NICE and local guidance</li> <li>• To take over prescribing responsibility when the patient is stable on therapy (at least 3 months after initiation and in line with the transfer of care guidance)</li> <li>• To agree to take over prescribing earlier in patients with complex medication supply issues e.g. patients using medication compliance aids (MCA) or housebound patients</li> <li>• To emphasise the importance of adherence to apixaban</li> </ul> |

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|   |   |
|---|---|
| <p>treatment and / or further follow-up required</p> <ul style="list-style-type: none"> <li>For patients requiring long-term treatment; to arrange a follow-up at 12 months to review the ongoing need for therapy</li> </ul> | <p>therapy and address any patient concerns</p> <ul style="list-style-type: none"> <li>To ensure monitoring of renal and hepatic function is undertaken at least annually and more frequently if indicated. If results fall outside normal range then refer to contraindication, caution and dosing sections in the prescribing guidelines and/or seek specialist advice as appropriate</li> <li>To monitor ongoing risk of bleed and if appropriate, seek specialist advice</li> </ul> |
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#### Additional information

1. Patients taking apixaban should be encouraged to carry an anticoagulation card (available from initiating clinician / anticoagulation clinics) at all times or to wear a medic-alert bracelet.
2. There is no specific reversal agent should a patient experience a bleed on apixaban. In the event of a significant bleed, the patient should be referred to accident and emergency for supportive measures.
3. Other healthcare professionals should be made aware that apixaban is prescribed for any patients who are to undergo invasive treatments, including elective surgery and dental treatment.
4. Missed dose advice should be discussed at initiation: If a dose is missed, it should be taken immediately and then continue to take twice daily as before.
5. If a patient has been assessed as being appropriate for a multi-compartment compliance aid (MCA), often known as a dosette box, consideration can be given to including apixaban tablets as they do not have any special storage requirements.

#### References

1. NICE TA341: Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism. June 2015. Accessed April 2016 at <https://www.nice.org.uk/guidance/ta341/resources/apixaban-for-the-treatment-and-secondary-prevention-of-deep-vein-thrombosis-and-or-pulmonary-embolism-82602602803141>
2. SPC Eliquis. Bristol-Myers Squibb-Pfizer January 2016. Accessed April 2016 at [www.medicines.org.uk](http://www.medicines.org.uk)