Prescribing criteria for direct-acting oral anticoagulants (DOACs) in the treatment of venous thromboembolism (VTE) e.g. deep vein thrombosis (DVT) &pulmonary embolism (PE) and prevention of recurrent DVT and PE in adults.

Apixaban is the <u>first line</u> cost-effective formulary choices DOAC for DVT or PE management, provided there are no contraindications and clinically appropriate.
Rivaroxaban can be considered as a <u>second line</u> option if intolerant to apixaban or where once daily dosage regimen is deemed to be beneficial.

Edoxaban and **Dabigatran** are also licensed for the treatment of VTE but require initial 5 days treatment with Low Molecular Weight Heparin (LMWH) before commencing. This complicates the treatment pathway and hence not included as one of the BSW formulary's preference choices for DVT or PE treatment.

Local hospital treatment pathways found via links below advise primary care how to deal with suspected VTE according to which hospital trust the patient is to be sent to for further investigation. The treatment pathways should be used in conjunction with our other DOAC documents found on BSW formulary/MedsOp website. Also see generic contact emails for queries.

Royal United Hospital RUH Bath ruh-tr.AnticoagulationTeam@nhs.net

BEMS DVT service - Referral criteria and pathway – BEMS - DVT Referral Information

- Information for Clinicians: DVT and PE: http://nww.ruh-bath.nhs.uk/For_Clinicians/clinical_guidelines/documents/medicine/ACUTE-086_Deep_Vein_Thrombosis_and_Pulmonary_Embolism.pdf

Salisbury Foundation Trust (SFT) Wiltshire sft.anticoagulation.service@nhs.net

- Anticoagulation: Oral Anticoagulation - drugs not needing active monitoring (microguide.global)
- Suspected DVT pathway: Suspected DVT (microguide.global)
- Superficial vein thrombosis: Ultrasound proven superficial vein thrombosis of lower limb (microguide.global)

Great Western Hospital (GWH) Swindon gwh.anticoag.clinic@nhs.net

- Microguide full section on anticoagulation Anticoagulation (microguide.global)
- Microguide Medicines guidance for DVT Deep Vein Thrombosis (microguide.global)
- Microguide Medicines guide for PE Pulmonary Embolism (microguide.global)

NICE recommends all of the DOACs as possible treatments for adults with PE and to prevent further DVT or PE as follows:

- Rivaroxaban (2013): http://www.nice.org.uk/guidance/ta287
- Dabigatran (2014): http://www.nice.org.uk/guidance/ta327
- Apixaban (2015): https://www.nice.org.uk/guidance/ta341
- Edoxaban 2015: https://www.nice.org.uk/guidance/ta354

And see individual medicine SPC for dosage details:

- Rivaroxaban (Xarelto®): https://www.medicines.org.uk/emc/search?q=rivaroxaban
- Dabigatran (Pradaxa®): https://www.medicines.org.uk/emc/search?q=dabigatran
- Apixaban (Eliquis®/generic): https://www.medicines.org.uk/emc/search?q=apixaban
- Edoxaban (Lixiana®): https://www.medicines.org.uk/emc/search?q=edoxaban

Considerations when choosing the right anticoagulant to use

Refer to your local acute trust's diagnostic work up guidelines to ensure the correct samples are done before initiating anticoagulation. Ensure baseline U&Es & FBC are done.

Should I admit or not?

- Do you have reason to suspect serious renal failure? *Patient not suitable for ambulatory treatment, refer for hospital assessment*
- Do you suspect serious (pelvic) DVT or PE? *Medical assessment in hospital required +/- consideration of catheter directed thrombolysis etc.*
- Does the patient have ongoing bleeding or serious anaemia? *Seek specialist advice*

Will a DOAC be okay for this patient?

- Is the patient already on DOACs/LMWHs or warfarin for other conditions and a new VTE is suspected? *Contact specialist team for advice.*
- Is there a chance the patient is pregnant? Or is the patient breastfeeding? *DOAC not suitable. Use LMWH &/or seek specialist advice.*
- Do you suspect the patient has active cancer? *Use a LMWH until the situation is clear.*
- Does the patient have an extreme body weight? *Due to limited evidence for the use of DOACs in patients with extreme body weight < 60kg or > 150kg. Contact hematology or anticoagulation service for advice.*
- Does the patient have significant mucosal bleeding? (e.g., Heavy periods, frequent rectal bleeding / haematuria) *If DOAC is indicated, Apixaban is first line and the preferred choice.*
- Does the patient already suffer with dizziness / hypotension / troublesome headaches? *If DOAC is indicated, Apixaban is first line and the preferred choice.*
- Is the patient on any medications which might alter DOAC effectiveness (eg. Anti-epileptics, dronedarone)? *Commence LMWH and seek specialist advice.*
- Consider history of allergies and previous adverse reactions. *See SPCs &/or seek specialist advice*.

Once diagnosis is confirmed:

- Dose of DOACs – see appendix summary table and BNF for full prescribing information.
- Duration of treatment for confirmed DVT varies depending on clinical presentation. A shorter duration of therapy (at least 3 months) should be based on transient risk factors (e.g. recent surgery, trauma, immobilisation) and longer durations should be based on permanent risk factors or idiopathic DVT or PE. If unprovoked, review at 3 months and consider lifelong anticoagulation.
- All patients who need to be considered for lifelong anticoagulation should be referred to / discussed with a haematologist.

Ensure patient knows to ask their community pharmacist for an anticoagulant patient alert card.

Appendix 1: Prescribing Information for Direct Oral Anticoagulants (DOACs) for DVT or PE

Medicine	**Apixaban** - **BSW Formulary's preferred first line cost-effective DOAC choice**.			**Rivaroxaban** - **considered as a second line option if intolerant to apixaban or where once daily dosage regimen is deemed to be beneficial.**	
Licensed indication	Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults. Not recommended in PE patients who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy.				
Standard dosing for PE and DVT	**Treatment**	**Day 1 to7**	**10 mg BD**	**Day 1 to 21**	**15 mg BD**
		Day 8 and after	**5mg BD**	**Day 22 and after**	**20 mg OD**
	Treatment Duration	• 3 months anticoagulation treatment and then stop. If there is uncertainty regarding the significance of a provoking factor refer to the Haematology Thrombosis Clinic. • Patient with cancer require at least 6 months anticoagulation and should be referred to the cancer associated thrombosis clinic for follow up.			
	Prophylaxis	**For those requiring long-term prophylaxis as directed by specialists**	**2.5mg BD** **NB: 5mg BD is not a licensed long-term dose for DVT/PE. Continuing at the higher dose may be reasonable in certain situations on the advice of haematology or anticoagulation specialist.**	**For those requiring long-term prophylaxis as directed by specialists**	**10 mg OD,** **20 mg OD if risk of recurrent DVT or PE is high**
Use in Renal impairment	• DOACs can be used in patients with renal impairment in line with the SPC of the specific agent (as below). • If acute renal failure CrCL< 15ml/min is suspected, advise patient to discontinue DOAC and seek specialist advice. • Always use creatinine clearance for direct-acting oral anticoagulants (DOAC) dose calculations and NOT eGFR as recommended by the MHRA and SPCs for relevant DOACs. Use of eGFR for dosing of DOACs is known to increase risk of bleeding events as a consequence of overestimating renal function. See BSW local guidance: here				
CrCL 30-50 mL/min	No dosage adjustment			Consider **reducing to 15mg once daily if CrCl 15-49 mL/min** and the risk of bleeding outweighs the risk of recurrent DVT or PE.	
CrCL 15-30 mL/min	Use with caution				
CrCL <15 mL/min	**Avoid** in CrCl < 15mL/min			**Avoid** in CrCl < 15mL/min	
Use in Hepatic Impairment	Caution in mild to moderate impairment (or if hepatic transaminases greater than 2 times the upper limit of normal, or if bilirubin is equal or greater than 1.5 times the upper limit of normal); avoid in severe impairment or impairment associated with coagulopathy and clinically relevant bleeding risk.				

Consult product's SmPC and BNF for full details of contraindications, drug interactions and prescribing caution information.

Seek advice from your local Anticoagulant Specialist in the event of any uncertainty on DVT or PE management. Specialist Anticoagulant advice can be obtained from our local hospitals:

- GWH: gwh.anticoag.clinic@nhs.net or sarah.bond6@nhs.net Tel: 01793 60434
- RUH: ruh-tr.AnticoagulationTeam@nhs.net or nathan.hutchinson-jones@nhs.net or via Cinapsis
- SFT: nicolamcquaid@nhs.net or sft.anticoagulation.service@nhs.net