Southern Health and Social Care Trust

CLINICAL GUIDELINES ID TAG	
Title:	**Anticoagulation- Guideline on the Safe Prescribing of Direct Oral Anticoagulants; Apixaban, Dabigatran, Edoxaban, Rivaroxaban**
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Guideline on the Safe Prescribing of Direct Oral Anticoagulants; Rivaroxaban, Apixaban, Dabigatran, Edoxaban

1. Licensed indications and NICE Approval:

	Therapeutic indications
Apixaban	• Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); age≥ 75 years; hypertension; diabetes mellitus; symptomatic heart failure (NYHA Class ≥ II). **NICE approved (TA 275) Feb 2013** • Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults **NICE approved (TA 341) June 2015** • Prophylaxis of venous thromboembolism in adults after hip or knee replacement surgery. **NICE approved (TA 245) Jan 2012**
Dabigatran	• Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) with one or more risk factors, such as prior stroke or transient ischemic attack (TIA); age ≥ 75 years; heart failure (NYHA Class ≥ II); diabetes mellitus; hypertension. **NICE approved (TA 249) March 2012** • Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults **NICE approved (TA 327) Dec 2014** • Prophylaxis of venous thromboembolism in adults after hip or knee replacement surgery. **NICE approved (TA 157) Sept 2008**
Rivaroxaban	• Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack. **NICE approved (TA 256) May 2012** • Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults. **NICE approved DVT (TA 261) July 2012 & PE (TA 287) June 2013** • Prophylaxis of venous thromboembolism in adults after hip or knee replacement surgery. **NICE approved (TA 170) April 2009** • Prevention of adverse outcomes after acute management of acute coronary symptom. **NICE approved (TA 335) March 2015** • Prevention of artherothrombotic events in adults with coronary artery disease or peripheral artery disease at high risk of ischaemic events **NICE approved (TA 607) October 2019**
Edoxaban	• Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack (TIA). **NICE approved (TA 355) Sept 2015** • Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults. **NICE approved (TA 354) Aug 2015**

2. Key points to consider when choosing a Direct Oral Anticoagulant:

- Licensed indication
- Renal function (calculated ideally by Cockcroft Gault method using patient's actual body weight)
  - **If CrCl < 30 ml/min**; **Do not start dabigatran** as it is contraindicated in severe renal impairment.
  -Limited clinical data for patients with severe renal impairment (CrCL 15 – 29ml/min) indicate that plasma concentrations are increased which may lead to an increased bleeding risk. Apixaban, edoxaban and rivaroxaban should be used with caution in these patients. Use is not recommended in patients with CrCL <15ml/min.
- Age
- Weight (<50kg or >120kg) – lack of clinical data in patients at extremes of weight
- Contraindications
- Drug interactions
- History of gastritis
- History of bleeding
- Female of child-bearing age – Safety and efficacy of DOACs have not been established in pregnant women
- Compliance issues
- Need for medidose – Dabigatran is not suitable for a medidose, must remain in original packaging
- Patient choice: once or twice daily dosing; lack of antidote as yet for edoxaban.
- Antidote- lack of antidote as yet for edoxaban

3. Remember to take baseline bloods (Any blood results obtained in the previous month are not necessary again)

- U+E
- LFTs
- FBP
- Coagulation Screen
- Group + Hold (if not on labs)
- Pregnancy Test (women of child-bearing age)
- Weight – Calculate CrCl

4. Use starter pack to inform patient about the treatment. This includes;
   - SHSCT patient counselling checklist specific for each DOAC (one for patient + one for patient notes)
   - Manufacturer's booklet
   - Patient Alert Card

5. Dosing of DOACs

- **APIXABAN**

APIXABAN FOR AF

The usual dose of apixaban for stroke prevention in AF is **5mg BD**.

Reduce to 2.5mg BD if either:

- 2 of following 3 risk factors present [age ≥80 years, weight ≤60kg, creatinine ≥133umol/L]
- **OR** CrCl <30ml/min

APIXABAN FOR VTE

VTE treatment

The usual dose of apixaban for VTE treatment is **10mg BD for 7 days**, then **5mg BD for at least 3 months**

VTE prevention

The dose for the prevention of recurrent DVT and/or PE in adults following completion of 6 months of treatment with Apixaban 5mg BD or with another anticoagulant: **Apixaban 2.5mg BD**

- **DABIGATRAN**

DABIGATRAN FOR AF

The usual dose of dabigatran for stroke prevention in AF is **150mg BD**.

Consider reducing to 110mg BD if: 75-80 years and increased bleeding risk, CrCl 30-50 ml/min, gastritis/GORD, other patients at increased risk of bleeding (e.g. HASBLED ≥3, history of GI bleed, etc.)

Always reduce to 110mg BD if ≥80 years or if taking verapamil

If CrCl <30 ml/min – stop and consider switching to alternative anticoagulant

DABIGATRAN FOR VTE

The usual dose of dabigatran for treatment of DVT/PE or prevention of recurrent DVT and PE is **150mg BD**, **following initial treatment with a parenteral anticoagulant for at least 5 days**.

Consider reducing to 110mg BD if: 75-80 years and increased bleeding risk, CrCl 30-50 ml/min, gastritis/GORD, other patients at increased risk of bleeding (e.g. HASBLED ≥3, history of GI bleed, etc.)

Always reduce to 110mg BD if ≥80 years or if taking verapamil

If CrCl <30 ml/min – stop and consider switching to alternative anticoagulant

- **EDOXABAN**

EDOXABAN FOR AF

The usual dose of edoxaban for stroke prevention in AF is **60mg OD**.

Reduce to 30mg OD if either:

- Moderate or severe renal impairment (CrCl <50ml/min)
- Low body weight ≤60kg
- Concomitant use of ciclosporin, dronedarone, erythromycin or ketoconazole

EDOXABAN FOR VTE

The usual dose of edoxaban for treatment of DVT/PE and prevention of recurrent DVT/PE is **60mg OD following initial treatment with a parenteral anticoagulant for at least 5 days.**

Reduce to 30mg OD if either:

- Moderate or severe renal impairment (CrCl <50ml/min)
- Low body weight ≤60kg
- Concomitant use of ciclosporin, dronedarone, erythromycin or ketoconazole

- **RIVAROXABAN**

RIVAROXABAN FOR AF

The usual dose of rivaroxaban for stroke prevention in AF is 20mg OD.

If CrCl <50 ml/min – reduce to 15mg OD in AF only

RIVAROXABAN FOR VTE TREATMENT + PREVENTION

The recommended dose for the initial treatment of acute DVT or PE is 15 mg twice daily for the first three weeks followed by 20 mg once daily for the continued treatment and prevention of recurrent DVT and PE, as indicated in the table below.

		Dosing schedule	Maximum dose
Treatment and prevention of recurrent DVT and PE	Day 1 – 21	**15mg twice daily**	30mg
	Day 22 and onwards	**20mg once daily**	20mg
Prevention of recurrent DVT and PE	Following completion of at least 6 months therapy for DVT or PE	**10mg once daily or** **20mg once daily**	10mg or 20mg

* If CrCl <50 ml/min – after the initial three weeks, a reduction of the dose from 20mg once daily to 15mg once daily should be considered if the patient's assessed risk for bleeding outweighs the risk for recurrent DVT and PE

*The recommendation for the use of 15 mg is based on PK modelling and has not been studied in this clinical setting.

6. Information for **primary care** needs to be communicated either via the discharge letter or clinic letter. This includes;

Indication:
Length of treatment:
Written + verbal counselling provided and by whom:
Patient Weight:
CrCl (ideally by Cockcroft Gault method): Date:

Recommended blood monitoring: Hb, U&E, LFTs at least annually or more frequently according to clinical concern (NB check every 6 months if CrCl 30-60 ml/min, >75 years or fragile OR every 3 months if CrCl 15-30 ml/min).

Dabigatran is contraindicated if CrCL < 30ml/min.
Limited clinical data for patients with severe renal impairment (CrCL 15 – 29ml/min) indicate that plasma concentrations are increased which may lead to an increased bleeding risk. Apixaban, edoxaban and rivaroxaban should be used with caution in these patients. Use is not recommended in patients with CrCL <15ml/min.

7. When an outpatient in ED has been diagnosed with a VTE, follow the VTE pathway for treatment plan and use the Apixaban starter pack to educate patient and provide information to GP.

8. For patients with AF (seen at Outpatient Clinics), refer to Trust guidance and the drug SPC to decide on appropriate DOAC for the patient. Then:
    - Give patient prescription for hospital pharmacy to dispense a 28 day supply for the new agent so that it can be started immediately.
    - Ask patient to read the product information and carry the alert card.
    - Educate patient using the starter pack on Sharepoint for whichever DOAC chosen.
    - Inform GP of medication prescribed using the clinic letter from the starter pack.

9. Refer to Trust guidance on preparation for emergency and elective procedures, management of haemorrhage, management of overdose, or how to start a specific DOAC when a patient is on LMWH or warfarin (this information is located in the Anticoagulant section of Sharepoint).

10. Monitoring of DOACs in Primary Care

    All patients on long-term anticoagulants require a general review at least once a year.

    - Assessment of stroke/VTE and bleeding risk
        - Enquire about the presence of bleeding
        - Identify and minimise any modifiable risk factors
        - Confirm anticoagulation is still appropriate
    - Assess adherence
        - Ensure being taken correctly, any missed doses?
        - Identify any side effects, especially those that may be impacting on compliance
    - Co-medications
        - Review other medications (including OTC and herbal medication) for drug interactions
    - Blood sampling and weight
        - Yearly: Hgb, renal and liver function
        - If ≥ 75 years, CrCL 30 – 60ml/min or frail: 6 monthly renal function
        - If CrCL 15 – 30ml/min: 3 monthly renal function
        - If intercurrent condition that may have impact: renal and/or liver function.

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