AMBER GUIDANCE FOR PRESCRIBING ANTICOAGULANTS

Recommended prescribing options

(*Please note NICE NG196 recommends that prescribers discuss the options for anticoagulation with the person and base the choice on their clinical features and preferences)*

Atrial Fibrillation			
	Recommended options		
Non-valvular AF (NVAF) SPAF Primary prevention	First-line: Apixaban (generic) Second-line: Edoxaban Third-line: Rivaroxaban Fourth-line: Dabigatran		If DOAC not appropriate: warfarin
Non-valvular AF (NVAF) SPAF secondary prevention	First-line: Apixaban (generic) Second-line: Edoxaban Third-line: Rivaroxaban Fourth-line: Dabigatran		If DOAC not appropriate: warfarin
	Recommended option		**Also approved**
Valvular AF	warfarin		*Consider patient specific need*
Heart Valve			
Prosthetic valve replacement	warfarin		Consider patient specific need *DOACs* are contraindicated*
VTE Treatment			
DVT & PE Duration as per indication	1st choice Apixaban	2nd choice LMWH plus warfarin**	rivaroxaban or long term LMWH or LMWH plus dabigatran*** or LMWH plus edoxaban***
Secondary Prevention of artherothrombotic events			
Coronary or peripheral artery disease Duration as per specialist	Rivaroxaban plus aspirin OR warfarin		
Acute coronary syndrome Review after 12 months	Rivaroxaban with aspirin 75mg OD and clopidogrel or with aspirin alone		
Orthopaedics (*2nd care only for full supply)*			
VTE Prophylaxis after orthopaedic surgery	1st choice Apixaban	2nd choice LMWH	Dabigatran or rivaroxaban
VTE Prophylaxis after Lower Limb Injury	1st choice Apixaban	2nd choice LMWH	Dabigatran or rivaroxaban
Specialist groups			
Treatment & prophylaxis in patients with active cancer	rivaroxaban or apixaban(**see guideline**) or LMWH		*Consider patient specific need.*

Medical / Surgical prophylaxis	LMWH	Fondaparinux
Administration of meds	DOACs* preferred option for patients using compliance aids. Dabigatran is not stable in multi-compartment compliance aids. Apixaban, edoxaban and rivaroxaban can be used for enteral tube administration	

LMWH of choice: Dalteparin (this might change at times of supply disruption)

*DOACs = Direct oral anticoagulants = apixaban, dabigatran, edoxaban, rivaroxaban

** for DVT/PE treatment with warfarin continue LMWH until INR in range for 2 days, minimum 5 days LMWH

***for DVT/PE treatment with dabigatran or edoxaban at least 5 days treatment with LMWH required before change to dabigatran

- **For further prescribing information see clinical information below**
- **For information on changing anticoagulants in an individual patient – refer to data sheet www.medicines.org.uk**

RECOMMENDED DOSES BY INDICATION FOR DIRECT ORAL ANTICOAGULANTS

Renal function should be monitored regularly (every 6 to 12 months, increase frequency if renal function deteriorating). See page 4 for further advice

DRUG	Stroke Prevention in Atrial Fibrillation	DVT / PE Treatment/prophylaxis	Treatment Prophylaxis Orthopaedics 2nd Care Supply
Apixaban	**Standard dose 5mg BD** **Reduce dose to 2.5mg BD** if CrCl is 15-29mls/min OR if 2 or more of the following >80 years old or a body weight of 60kg or less or renal impairment (Serum Creatinine > 133 micromol/L) **Do not use if CrCl is below 15ml/min**	**Initial dose 10mg BD for 1 week** **THEN** **Standard dose 5mg BD reduced to 2.5mg BD after 6 months (if treatment to continue)** Use with caution of CrCL is 15-29mls/min **Do not use if CrCl is below 15ml/min**	**Standard dose** 2.5mg BD Duration dependant on procedure **Do not use if CrCL is below 15 ml/min**
Dabigatran	**Standard dose 150mg BD** **Reduce dose to 110mg BD** if patients >80 years, patients taking interacting drugs (see SPC) Consider 110 mg bd when there is a low risk of thromboembolism and the bleeding risk is high (see SPC) **Do not use if CrCl is below 30ml/min**	**Following treatment with a parenteral anticoagulant for at least 5 days** **Standard dose 150mg BD** **Reduce dose to 110mg BD** if patients >80 years, patients taking interacting drugs (see SPC) Consider 110 mg bd when there is a low risk of thromboembolism and the bleeding risk is high (see SPC) **Do not use if CrCl is below 30ml/min**	*3rd line treatment in patients unsuitable for treatment with apixaban / LMWH* *See www.medicines.org.uk for dose details*
Edoxaban	**Standard Dose 60mg OD – with or without food** **Reduce dose to 30mg OD if:** CrCl is 15-49ml/min	**Following initial use of parenteral anticoagulant for at least 5 days:** **Standard Dose 60mg OD – with or without food** **Reduce dose to 30mg OD if:** CrCl is 15-49ml/min	Not licensed

	Body weight ≤ 60 kg Select P-gp inhibitors: ciclosporin, dronedarone, erythromycin, ketoconazole. **Do not use if CrCl is below 15ml/min**	Body weight ≤ 60 kg Select P-gp inhibitors: ciclosporin, dronedarone, erythromycin, ketoconazole **Do not use if CrCl is below 15ml/min**	
Rivaroxaban	**Standard dose 20mg OD** **Reduce dose to 15mg OD** if CrCl is 15-49ml/min. Extra caution is required if CrCl is 15-29mls/min due to an increased bleeding risk. **Do not use if CrCl is below 15ml/min**	**Initial dose 15mg BD for 3 weeks** **THEN** **Standard dose 20mg OD** **Reduce on-going dose to 15mg OD** if CrCL is 15-49ml/min and patient's assessed risk of bleeding outweighs risk of recurrent DVT/PE **Do not use if CrCl is below 15ml/min**	*3rd line treatment in patients unsuitable for treatment with apixaban /LMWH* *See www.medicines.org.uk for dose details*

DALTEPARIN PRESCRIBING INFORMATION FOR PRIMARY CARE

Indication	Dose of Dalteparin	Duration of Treatment
Prophylaxis of VTE *(NICE NG89)*	5000 units once daily (2500 units daily in dialysis patients)	Dependent on type of surgery and/or time taken for patient's mobility to return to normal state
Treatment of DVT / PE **See www.bnf.org.uk**	**Patient weight** — **Once daily dose** Under 46kg — 7500 units 46-56 kg — 10 000 units 57-68 kg — 12 500 units 69-82 kg — 15 000 units 83 kg and over — 18 000 units	For patients initiated on warfarin: until INR in range for 2 days (minimum 5 days of dalteparin) Where warfarin contraindicated: for 3 to 6 months Longer courses or life long treatment may be justified in patients at continued high risk of VTE
Extended treatment and prophylaxis of VTE in patients with solid tumours **See www.bnf.org.uk**	**Patient weight** — **Once daily dose** Under 46 kg — 7500 units for 6 months 46 – 56 kg — 10 000 units for 30 then 7500 units for 5 months 57 – 68 kg — 12 500 units for 30 days then 10 000 units for 5 months 69 – 82 kg — 15 000 units for 30 days then 12 500 units for 5 months 83 kg – 98 kg — 18 000 units for 30 days then 15 000 units for 5 months 99 kg and over — 18 000 units for 6 months Relevance of continuing treatment beyond this period will be evaluated according to individual risk/benefit ratio, taking into account particularly the progression of cancer. Doses may be interrupted or reduced in chemotherapy induced thrombocytopenia – as advised by haematologist / oncologist	
Further notes	• For patients with an increased risk of bleeding, an equivalent twice daily dosing may be recommended. • Monitor FBC, BCP and coagulation (PT and APTT) at baseline to check for contraindications to anticoagulation and that renal function is adequate.Monitoring with anti-Xa assay may be appropriate in pregnancy & renal failure – obtain specialist advice. • Renal failure : Dalteparin can accumulate in patients with GFR < 30 ml/min. If dalteparin treatment dose is prescribed, dose should be reduced and patient monitored closely for bleeding. • Guidelines on the diagnosis and management of heparin-induced thrombocytopenia Diagnosis and Management of Heparin Induced Thrombocytopenia: Second Edition (b-s-h.org.uk)	

Enoxaparin PRESCRIBING INFORMATION FOR PRIMARY CARE

Indication	Dose of Enoxaparin	Duration of Treatment
Prophylaxis of VTE *(NICE NG89)*	40mg once daily (20mg daily in dialysis patients)	Dependent on type of surgery and/or time taken for patient's mobility to return to normal state
Treatment of DVT / PE (uncomplicated patients with low risk of recurrence) **See www.bnf.org.uk**	**1.5mg/kg OD** **Patient weight — Once daily dose** 40-47 kg — 60mg OD 48-59 kg — 80mg OD 60-73 kg — 100mg OD 74-88kg — 120mg OD 89-109kg — 150mg OD 110-125kg — 180mg OD (can be divided as two syringes >125kg — 1.5mg/kg OD (can be divided as two syringes)	For patients initiated on warfarin: until INR in range for 2 days (minimum 5 days of dalteparin) Where warfarin contraindicated: for 3 to 6 months Longer courses or life long treatment may be justified in patients at continued high risk of VTE
Treatment of DVT/PE (patients with risk factors such as obesity, cancer, recurrent VTE)	Patients with mechanical heart valves on warfarin with sub therapeutic INR (<2) (off label) – consider risk and benefit prior to prescribing this dose Acute VTE with large clot burden i.e. massive/submassive PE/iliac vein DVT (not requiring thrombolysis) **1mg/kg BD (round to nearest syringe strength)** **Patient weight — Twice daily dose** 40-47 kg — 40mg BD 48-59 kg — 60mg BD (or 40mg OM, 60mg at tea time) 60-73 kg — 60mg BD 74-88kg — 80mg BD 89-109kg — 100mg BD 110-125kg — 120mg BD 125.1-137kg — 140mg BD (requires 1x60mg plus 1x80mg twice a day) >137kg — 1mg/kg BD (prescribed to nearest whole syringe will require multiple syringes to be injected at once)	

Extended treatment and prophylaxis of VTE in patients with solid tumours **See www.bnf.org.uk**	**The recommended dose is 100 IU/kg (1 mg/kg) administered twice daily by SC injections for 5 to 10 days, followed by a 150 IU/kg (1.5 mg/kg) once daily SC injection up to 6 months. The benefit of continuous anticoagulant therapy should be reassessed after 6 months of treatment.** Relevance of continuing treatment beyond this period will be evaluated according to individual risk/benefit ratio, taking into account particularly the progression of cancer. Doses may be interrupted or reduced in chemotherapy induced thrombocytopenia – as advised by haematologist / oncologist
Further notes	• Enoxaparin is available as both originator product (Clexane®) and multiple biosimilar products. Prescriptions should be prescribed by brand name and it is not recommended to switch between brands during treatment. The preferred brand in HUTH and NLaG is Inhixa®. • For patients with an increased risk of bleeding, an equivalent twice daily dosing may be recommended. • Monitor FBC, BCP and coagulation (PT and APTT) at baseline to check for contraindications to anticoagulation and that renal function is adequate. Monitoring with anti-Xa assay may be appropriate in pregnancy & renal failure – obtain specialist advice. • Renal impairment: For treatment dose and extended prophylaxis when CrCL<30ml/min use 1mg/kg OD (round to nearest syringe) • Guidelines on the diagnosis and management of heparin-induced thrombocytopenia Diagnosis and Management of Heparin Induced Thrombocytopenia: Second Edition (b-s-h.org.uk)

Additional notes

CrCl vs eGFR: whilst SPCs state dose adjustments in relation to a patient's CrCl, eGFR is used in practice. eGFR is normalised to a standard body surface area of 1.73 m2 so is less reliable at extremes of body weight. **For prescribing of DOACs it is recommended to adjust dose according to calculated creatinine clearance[4].**

In certain patient groups e.g. people of African-Caribbean / African family origin, people with extremes of muscle mass e.g. bodybuilders, amputees or those with muscle wasting disorders, interpret eGFR with caution. Reduced muscle mass will lead to overestimation of actual GFR and increased muscle mass to underestimation of actual GFR. For more information see BNF "Principles of dose adjustment in renal impairment" https://www.evidence.nhs.uk/formulary/bnf/current/guidance-on-prescribing/prescribing-in-renal-impairment/principles-of-dose-adjustment-in-renal-impairment

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Guidance on switching between anticoagulants

To	Warfarin	From Parenteral or SC (UFH or LMWH or Fondaparinux)	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Warfarin **See links below**	***In patients with renal impairment, higher than therapeutic plasma concentrations are expected and a longer interval may be required.**	**Treatment of DVT/PE**; stop warfarin and initiate treatment dose LMWH when INR <2.0. **Prevention of stroke and systemic embolism**; review thrombotic risk on a case-by-case basis and consider initiating	Discontinue warfarin and commence apixaban as soon as INR is <2.0.	Discontinue warfarin and commence dabigatran as soon as INR is <2.0.	Discontinue warfarin and commence edoxaban as soon as INR is <2.5.	**DVT, PE and prevention of recurrence**; stop warfarin and initiate rivaroxaban once INR is ≤2.5. **Prevention of stroke and systemic embolism**; stop warfarin and initiate rivaroxaban once INR ≤3.0.
From Parenteral (UHF) or SC (LMWH or Fondaparinux)	Commence warfarin in combination with LMWH, and monitor INR. Discontinue LMWH once INR in therapeutic range for 2 consecutive days.	Stop UFH. Start LMWH or Fondaparinux within 1 hour. Stop LMWH or Fondaparinux. Start UFH at next scheduled LMWH dose.	Discontinue LMWH or Fondaparinux and commence apixaban at the time of the next scheduled dose. These medicinal products should not be administered simultaneously.	Discontinue LMWH or Fondaparinux and commence dabigatran 0-2 hours before the time that the next scheduled dose of LMWH would be due. For UFH, start dabigatran at time of stopping UFH.	Discontinue LMWH or Fondaparinux and commence edoxaban at the time of the next scheduled. For UFH: discontinue the infusion and start edoxaban 4 hours later.	Discontinue LMWH and commence rivaroxaban 0-2 hours before the time that the next scheduled dose of LMWH would be due. For UFH, start rivaroxaban at time of stopping UFH.
Apixaban	Commence warfarin in combination with apixaban. Apixaban should be discontinued when INR is ≥ 2.0. Measure INR prior to each dose of apixaban.	Discontinue apixaban and commence LMWH at the time that the next scheduled dose of apixaban would be due.		Discontinue apixaban and commence dabigatran at the time that the next scheduled dose of apixaban would be due*.	Discontinue apixaban and commence edoxaban at the time that the next scheduled dose of apixaban would be due*.	Discontinue apixaban and commence rivaroxaban at the time that the next scheduled dose of apixaban would be due*.

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Dabigatran	**Conversion protocol depends on renal function.** For **CrCl ≥ 50ml/minute**, commence warfarin 3 days prior to discontinuing dabigatran. For **CrCl 30-50ml/minute**, commence warfarin 2 days prior to discontinuing dabigatran.	Discontinue dabigatran and commence LMWH 12-hours after the last dose of dabigatran was administered (for orthopaedic prophylaxis: wait 24 hours from last dabigatran dose).	Discontinue dabigatran and commence apixaban at the time that the next scheduled dose of dabigatran would be due*.		Discontinue dabigatran and commence edoxaban at the time that the next scheduled dose of dabigatran would be due*.	Discontinue dabigatran and commence rivaroxaban at the time that the next scheduled dose of dabigatran would be due*.
Edoxaban	**Oral option**: For patients taking 60 mg of edoxaban, reduce the dose to 30 mg and begin warfarin concomitantly. For patients receiving 30 mg of edoxaban, reduce the edoxaban dose to 15 mg and begin warfarin concomitantly. INR must be measured at least weekly and just prior to the daily dose of edoxaban to minimize the influence of edoxaban on INR measurements. Once a stable INR ≥2.0 is achieved, edoxaban should be discontinued and the warfarin continued. **Parenteral option**: Discontinue edoxaban and administer a parenteral anticoagulant and warfarin at the time of the next scheduled edoxaban dose. Once a stable INR ≥2.0 is achieved, the parenteral anticoagulant should be discontinued and the warfarin continued.	Discontinue edoxaban and start the parenteral anticoagulant at the time the next dose of edoxaban was due.	Wait 24 hours after last dose of edoxaban to initiate apixaban.	Wait 24 hours after last dose of edoxaban to initiate dabigatran.		Wait 24 hours after last dose of edoxaban to initiate rivaroxaban.
Rivaroxaban	Commence warfarin in combination with rivaroxaban. Rivaroxaban should be discontinued when INR is in therapeutic range. Measure INR prior to each dose of rivaroxaban being administered.	Discontinue rivaroxaban and commence LMWH at the time that the next scheduled dose of rivaroxaban would be due.	Discontinue rivaroxaban and commence apixaban at the time that the next scheduled dose of rivaroxaban would be due*.	Discontinue rivaroxaban and commence dabigatran at the time that the next scheduled dose of rivaroxaban would be due*.	Discontinue rivaroxaban and commence edoxaban at the time that the next scheduled dose of rivaroxaban would be due*.	

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Document and version control	**This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.**		
	Version number:		1
	Date approved by Guidelines and SCF Group:		Jan 2024
	Date approved by APC:		Feb 2024
	Review date:		Feb 2027
Version number	Author	Job title	Revision description:
1	Jane Morgan	Principal Pharmacist	New document adapted from HERPC and NLAG documents