NHS
Kent and Medway
Clinical Commissioning Group

Guidance for Switching from Warfarin to Direct-acting Oral Anticoagulants (DOACs) for patients with Non-Valvular - Atrial Fibrillation (NVAF) or Venous Thromboembolism (VTE) (DVT /PE) during the COVID-19 Pandemic

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Please Note:
Every effort is made to ensure that the information contained in this guidance is up to date at the time of publication. Please be aware that information about medicines and therapeutics will change over time, and that information may not be current after the initial date of publication. Please take note of the publication date and seek further advice if in any doubt about the accuracy of the information

Scope for use:

This approach is for the duration of the COVID-19 pandemic. The national guidance which has been endorsed by the Royal College of General Practitioners and the British Haematology Society may be accessed via the link Guidance on safe switching of warfarin to DOAC COVID-19

This information is to support GPs or experienced independent prescribers (IP) who are switching patients from warfarin to a DOAC. The information should be used in conjunction with the NHS guidance on anticoagulant services during the coronavirus pandemic [(1)], relevant Summaries of Product Characteristics (SPCs)[(2)] and the local formulary.

Rationale:

INR monitoring is an essential service which must continue despite the scale of the COVID-19 outbreak (RCGP guidance). In order to relieve the burden of INR testing both on patients and practices at this time it may be appropriate to consider switching patients, where appropriate to a DOAC, INR self-testing or even low molecular weight heparin (LMWH). Consideration should be given to the implications for both the patient and for NHS staff workload.

Whilst DOACs require blood tests to assess renal function throughout treatment – the monitoring is predictable, less rigorous than INR testing with warfarin. Switching from warfarin to a DOAC must be done with careful consideration as not all patients are suitable for a switch to DOAC, and in some cases, specialist advice may be required.

Which groups of patients should be switched?

Consider prioritising patients with *poor control of INR* as this cohort will require the most frequent INR checks and address non-adherence if there is an underlying reason for poor INR control.

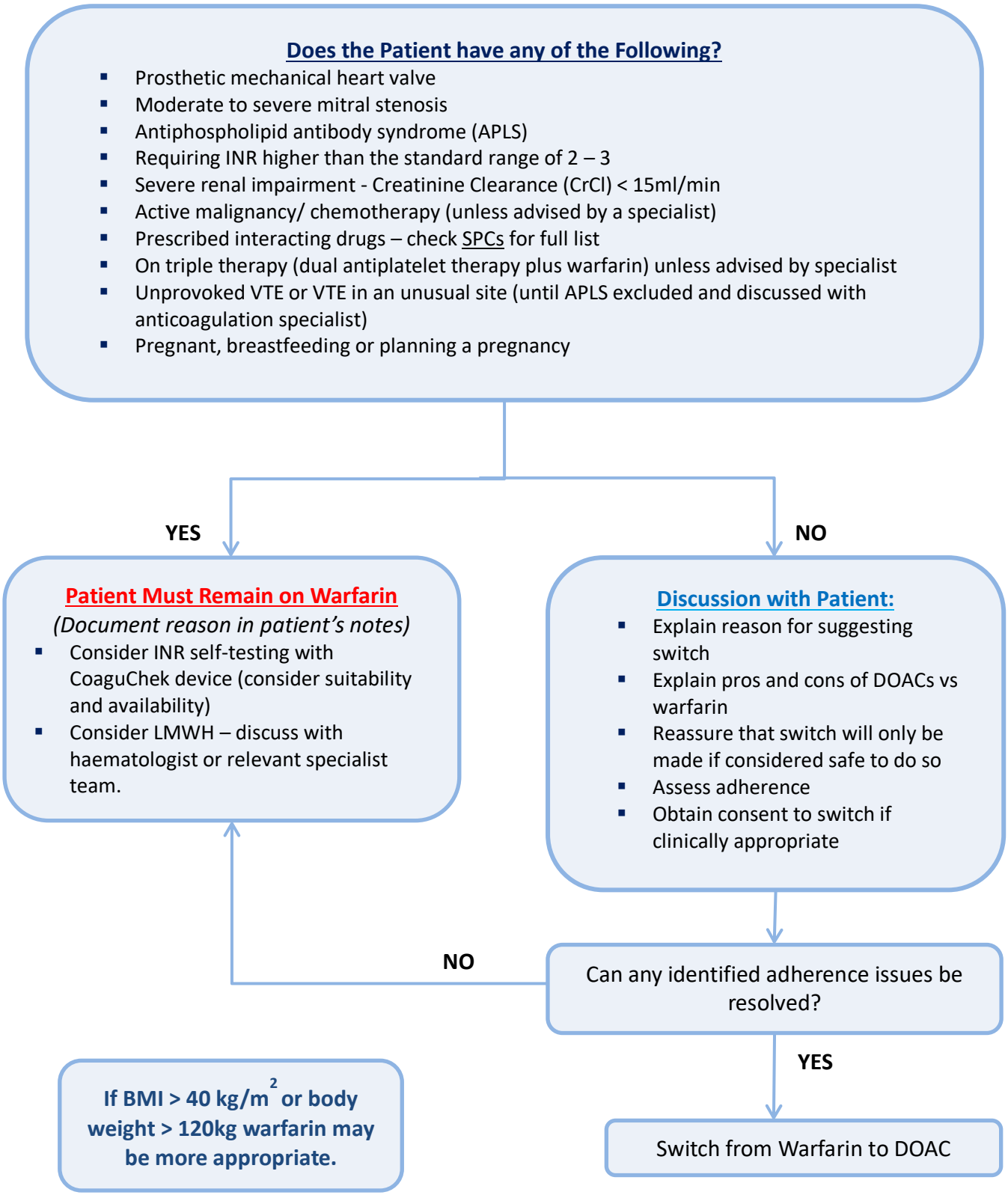
Prioritisation for switching is recommended to be given to

1. Housebound patients with NVAF
2. Housebound patients with provoked VTE
3. Time in therapeutic range (TTR) under 65% in NVAF
4. TTR under 65% in provoked VTE
5. Other NVAF who wish to transfer over to DOACs.
6. VTEs which are unprovoked after excluding antiphospholipid syndrome (APLS) (This service may not be available during Covid19)
7. Patient's choice

Patients should only be switched from warfarin to a DOAC following a shared decision with the patient or patient representative.

To protect the supply chain for all patients – take a phased approach over the 12-week cycle of INR monitoring.

Assess Suitability of DOAC Therapy



Management of Switch from Warfarin to DOAC

The European Heart Rhythm Association (EHRA) guidance provides pragmatic advice on switching from warfarin to DOACs reducing the need for repeated INR checks.

If INR ≤ 2	Stop warfarin and start DOAC on the same day
If INR between 2 and 2.5	Stop warfarin and start DOAC on the next day (ideally) or on the same day
If INR between 2.5 and 3.0	Withhold warfarin for 24-48 hours and then initiate DOAC

INR targets may differ depending on the indication. Choose DOAC drug and dose according to the therapeutic indication, patient age, actual bodyweight, renal function – calculated Creatinine Clearance (CrCl), drug interactions and patient preference/lifestyle. Specific guidance on switching between anticoagulants is provided in the SPCs [(2)] for individual DOACs as follows:

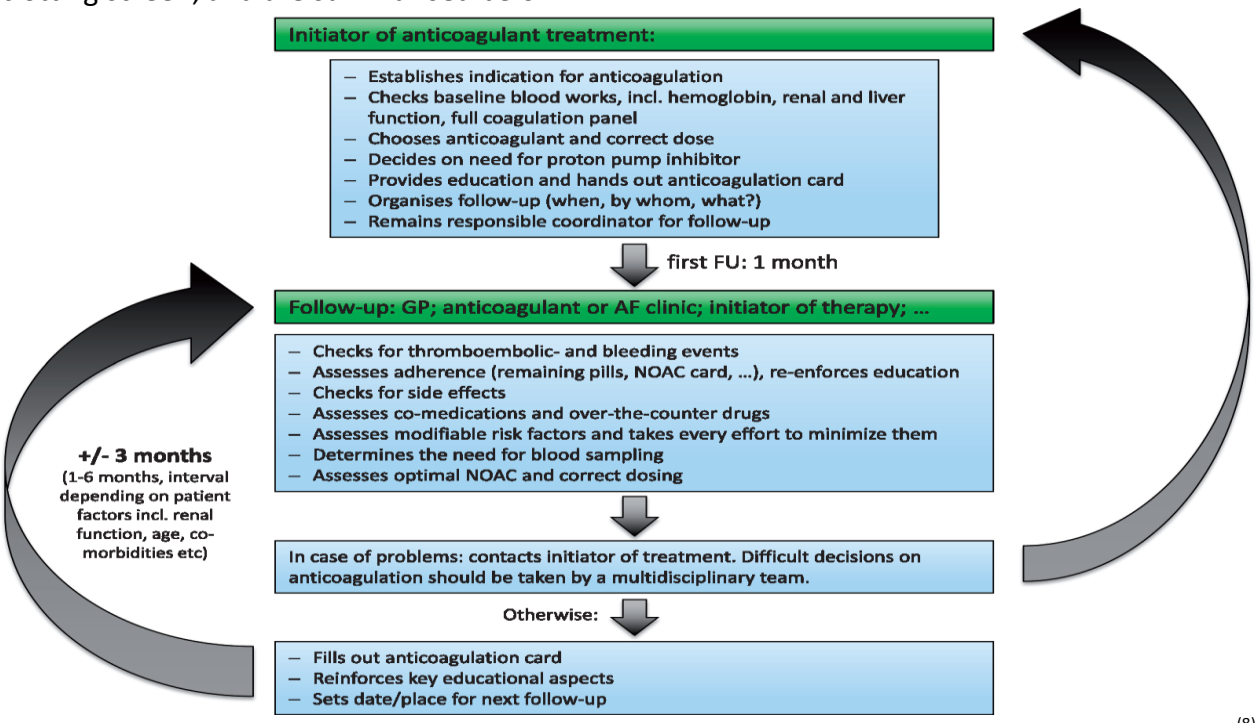
Edoxaban	Stop warfarin and start edoxaban when INR ≤ 2.5
Dabigatran	Stop warfarin and start dabigatran when INR < 2
Apixaban	Stop warfarin and start apixaban when INR < 2
Rivaroxaban	Stop warfarin and start rivaroxaban when INR ≤ 3

Suggested process for safe switching from warfarin to a DOAC *(Undertake steps remotely where possible).*

1. **Check clinical system for recent U&Es, LFTs and FBC (within last 3 months).**
2. **At next INR visit– check INR, record weight, take bloods if not already available or are unstable.**
3. Calculate creatinine clearance (CrCl). (Template Cockroft available on EMIS for working out the creatinine clearance).
4. Prescribe DOAC at appropriate dose and advise patient to obtain supplies.
5. Advise patient when to stop warfarin in relation to starting DOAC. INR should be < 2.5 when DOAC is started. (EHRA guidance, 2018).
6. Provide written instructions and involve family members / carers where possible to minimise the risk of patients taking both warfarin and the DOAC concurrently. Particular care should be taken where patients are using medication compliance aids to minimise the risk of incorrect dosing.
7. Provide an up-to-date Anticoagulant Alert card. (Dispensing pharmacy to supply with medicine).
8. Where the switch to a DOAC is undertaken outside the GP practice, provide accurate information relating to indication, baseline tests and monitoring requirements to allow primary care to safely take over prescribing responsibility.
9. Inform community nursing teams and anticoagulation service if they have been monitoring INR or administering warfarin.

DOAC Review

The European Heart Rhythm Association (EHRA)[3] makes recommendations for baseline screening and follow-up on initiating DOAC therapy. These have been adopted by NICE[4] with the addition of a baseline clotting screen, and are summarised below.



EHRA 2018[8]

Renal and liver function should be monitored at least 6-monthly in patients aged ≥ 75 years and/or those with frailty. Monitoring should be more frequent in the case where factors, e.g. intercurrent illness, may affect renal or liver function.[3] Hospital admission should specifically act as a trigger for review. Renal function may need to be monitored more frequently.

At each DOAC review a check of the following should be made[3][4] and the patient's anticoagulant alert card updated.

Adherence

- Reinforce regular dosing advice and to take rivaroxaban with food

Bleeding

- Advise on management
- Reduce modifiable risk factors
- Review DOAC dose as appropriate

Other Adverse Effects

- Provide reassurance/monitor as appropriate
- Consider switching to alternative anticoagulant

Assess for Thromboembolic Events

- Stroke, TIA, peripheral thromboembolism
- Pulmonary embolism

Other medication, including OTC Medicines

Monitoring:

At least annual review of renal profile if CrCl > 60ml/min with FBC and LFTs

- 6 monthly review if CrCl 30-60ml/min and/or aged >75 years and/or frail
- 3 monthly review of renal profile if CrCl 15-30ml/min

Check for side effects/bleeding issues and patient adherence to therapy at each routine appointment.

Guidance on DOAC Prescribing for Non-Valvular AF and DVT/PE

DOAC	Apixaban	Edoxaban	Rivaroxaban	Dabigatran
How to change from Warfarin	**Stop warfarin**. Start DOAC when **INR ≤2.5** - *See additional guidance overleaf,* from EHRA guidance https://academic.oup.com/eurheartj/article/39/16/1330/4942493?guestAccessKey=e7e62356-8aa6-472a-aeb1-eb5b58315d49)			
Baseline checks	Renal function (CrCl)- serum creatinine (Cr) and bodyweight, full blood count (FBC), liver function tests (LFTs). Use results from last 3 months if stable. If for AF: CHA_2DS_2VASC and HASBLED scores.			
Dosing in Non-valvular AF *(lifelong unless risk: benefit of anticoagulation therapy changes)*	**Prescribe Apixaban 5mg twice daily** Reduce dose to 2.5mg twice daily If: at least two of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 133 micromol/l or if exclusive criteria of CrCl 15 - 29ml/min.	**Prescribe Edoxaban 60mg once daily** Reduce dose to 30mg once daily If: Body weight <61kg, or CrCl< 50ml/min, or co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole.	**Prescribe Rivaroxaban 20mg once daily** Reduce dose to 15mg once daily If: CrCl< 50mL/min in NVAF patients only.	**Prescribe Dabigatran 150mg twice daily** If: aged <75 years, CrCl> 50mL/min, low risk of bleeding (weight <50kg with close clinical surveillance) Reduce dose to 110mg twice daily If: aged >80 years or prescribed verapamil consider 110mg twice daily based on individual assessment of thrombotic risk and risk of bleeding in patients aged 75-80 years or with CrCl <50mL/min or with increased risk of bleeding (including gastritis, oesophagitis, gastro-oesophageal reflux).
Dosing in patients with DVT / PE *(loading doses are not required if patient has been stabilised on warfarin)*	Dose is 5mg twice daily (use with caution if CrCl <30ml/min). Check intended duration of therapy. For long term prevention 2.5mg twice daily (after 6 months' treatment dose).	Dosing as above. Check intended duration of therapy.	Dose is 20mg daily (consider 15mg dose if CrCl<50ml/min and bleeding risk outweighs VTE risk). Check intended duration of therapy. For long term prevention 10mg daily to be considered.	Dosing as above. Check intended duration of therapy.
Duration of therapy for DVT/PE	For a provoked DVT/PE: 3 months treatment if provoking factors have been addressed. For unprovoked DVT/PE or recurrent DVT/PE: At least 6 months treatment dose followed by prophylaxis dosing as indicated/advised.			
Contraindications	CrCl <15ml/min	CrCl <15ml/min	CrCl <15ml/min	CrCl <30ml/min
Cautions See also individual SPC		CrCl >95ml/min	CrCl <30ml/min. Take with or after food (15mg and 20mg doses).	Do not use in a standard medication compliance aids (MCA)
Interactions Check BNF: www.bnf.org Check SPC: www.medicines.org.uk	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir - not recommended. Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – use with caution. Do not use apixaban with patients on strong enzyme inducers for acute VTE treatment	Rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort – use with caution Ciclosporin, dronedarone, erythromycin, ketoconazole – reduce dose as above.	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir, dronedarone – not recommended. Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – Should be avoided.	Ketoconazole, ciclosporin, itraconazole, tacrolimus, dronedarone – contraindicated. Rifampicin, St John's Wort, carbamazepine, phenytoin –should be avoided. Amiodarone, quinidine, ticagrelor, posaconazole – use with caution. Verapamil (use reduced dose). Antidepressants: SSRIs and SNRIs- increased bleeding risk

Acknowledgements

Adapted from Surrey Heartlands MMT Guidelines: Support for Switching from Warfarin to Direct-acting Oral Anticoagulants for patients with Non-Valvular -Atrial Fibrillation or Venous Thromboembolism during the COVID-19 Pandemic. 15th April 2020.

References

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