NHS
Surrey Heartlands
Clinical Commissioning Group

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

Applies to:

This information is to support GPs or experienced independent prescribers (IP) who are switching patients from warfarin to a DOAC within Surrey Heartlands CCG.

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)[2-5], and locally approved guidance available on the PAD.[6]

Rationale:

During COVID-19, INR monitoring is a service which GPs should aim to continue regardless of the scale of the virus outbreak (RCGP guidance) however it may be appropriate to consider switching to a DOAC, INR self-testing or even low molecular weight heparin (LMWH) in appropriate patients. Consideration should be given to the implications for both the patient and for NHS staff workload.

Prioritisation for switching is recommended to be given to

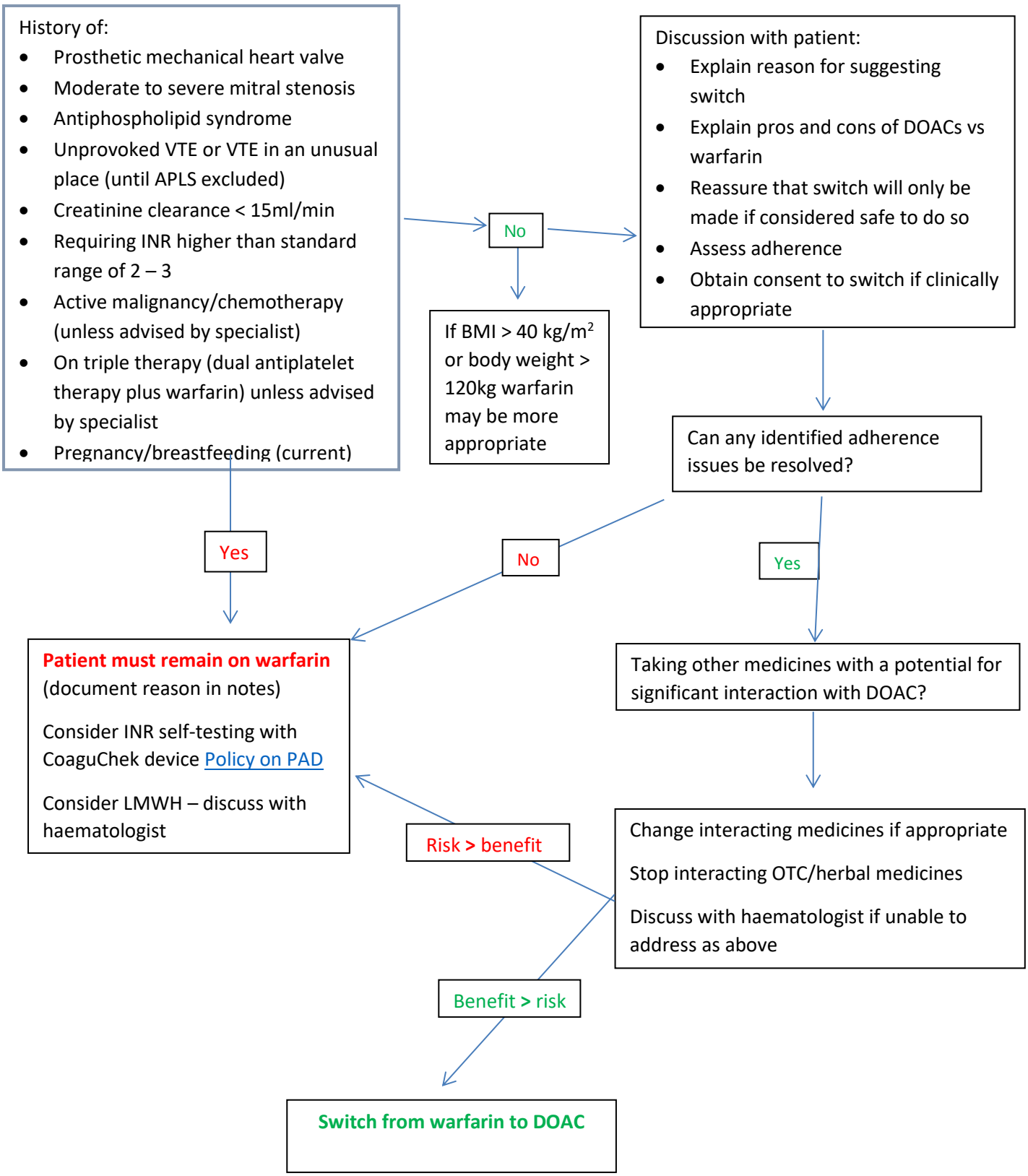
1. Housebound patients with NVAF
2. Housebound patients with provoked VTE (unprovoked VTE - exclude antiphospholipid syndrome (APLS))
3. Time in therapeutic range (TTR) under 65% in NVAF
4. TTR under 65% in provoked VTE
5. Other NVAF who wish to transfer over to DOACs.
6. VTEs which are unprovoked after excluding APLS (NB: testing suspended during Covid19)

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

This approach has been adopted throughout Surrey for the duration of the COVID-19 pandemic. The full document 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)

Note: This information was accurate at the time of writing and we will endeavour to update as soon as possible if new information becomes available.

Assess suitability of DOAC therapy



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Considerations in selecting DOAC treatment [2-5][7]

DOAC	Edoxaban	Dabigatran	Apixaban	Rivaroxaban
Medication Compliance Aid (MCA)	Suitable	Not suitable for standard MCA due to hygroscopic nature of the drug and resulting loss of stability if removed from original packaging	Suitable	Suitable
Food	With or without food	With or without food	With or without food	15mg and 20mg doses must be taken with a meal
Crushing and administration via enteral feeding tubes	May be crushed and mixed with 15-30ml of water or apple puree (unlicensed) Tablets may be crushed and mixed with water for administration via enteral feeding tubes (unlicensed)	Capsules may not be opened and contents must not be crushed before administration as this may lead to a significant increase in oral bioavailability and increased bleeding risk	May be crushed and mixed with 15-60ml of water, apple juice or apple puree (licensed). Tablets may be crushed and suspended in 60 ml of water immediately prior to administration via a nasogastric tube (licensed)	May be crushed and mixed with water or apple puree. Immediately follow 15mg or 20mg dose with food (licensed) Tablets may be crushed and administered in a small amount of water via a gastric tube. Flush tube with water after dose. Immediately follow 15mg or 20mg dose with enteral feed
Drug interactions Check SPC https://www.medicines.org.uk and BNF https://bnf.nice.org.uk/ for full list and details	Avoid HIV protease inhibitors (no data) Use with caution Carbamazepine Clarithromycin Phenobarbital Phenytoin Rifampicin St. John's Wort Reduce dose Ciclosporin Dronedarone Erythromycin Ketoconazole	Avoid Carbamazepine Ciclosporin Dronedarone Itraconazole Ketoconazole Phenytoin Rifampicin St. John's Wort Tacrolimus HIV protease inhibitors (no data) Use with caution Amiodarone Posaconazole Quinidine Ticagrelor Reduce dose Verapamil	Avoid Itraconazole Ketoconazole Posaconazole Voriconazole HIV protease inhibitors Use with caution (but **avoid** with VTE treatment) Carbamazepine Phenobarbital Phenytoin Rifampicin St John's Wort	Avoid Carbamazepine Dronedarone Itraconazole Ketoconazole Posaconazole Rifampicin Phenobarbital Phenytoin St. John's Wort Voriconazole HIV protease inhibitors
	Increased risk of bleeding Antiplatelets / NSAIDs / SSRIs / SNRIs			

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DOAC dosing in non-valvular AF [2-5] see local DOAC selection tool for drug choice

DOAC	Edoxaban*	Dabigatran*	Apixaban*	Rivaroxaban*
Dose	60mg od Reduce dose to 30mg od if one or more of: • CrCl 15-50ml/min • Body weight ≤ 60 kg • Concomitant use of ciclosporin, dronedarone, erythromycin, or ketoconazole	150mg bd Reduce dose to 110mg bd if: • Age > 80 yrs • On verapamil Consider reducing dose to 110mg bd if: • Age 75-80 yrs • CrCl 30-50ml/min • Increased bleeding risk, including gastritis, GORD, oesophagitis	5mg bd Reduce dose to 2.5mg bd if two or more of: • Age ≥ 80 years, • Body weight ≤ 60 kg, • or serum creatinine ≥ 133 micromol/l or if CrCl 15-29ml/min regardless of the above	20mg od Reduce dose to 15mg od if CrCl < 15-50ml/min

***Locally preferred DOAC**

***Second line if high risk factors for GI bleeding**

***Can be prescribed if edoxaban or dabigatran are not clinically appropriate**

DOAC dosing in VTE [2-5]

Before switching, check intended duration of therapy and consider whether treatment may be stopped.

Loading doses are not needed if patient is established on warfarin treatment.

DOAC	Edoxaban	Dabigatran	Apixaban	Rivaroxaban
Dose	60 mg od	150 mg bd	Treatment: 5 mg bd Prevention of recurrence following 6 months treatment: 2.5 mg bd	Treatment: 20mg od Prevention of recurrence following 6 months treatment: 10mg od
	Reduce dose to 30mg od if one or more of: • CrCl 15-50ml/min • Body weight ≤ 60 kg • Concomitant use of ciclosporin, dronedarone, erythromycin, or ketoconazole	Reduce dose to 110mg bd if: • Age > 80 yrs • On verapamil Consider reducing dose to 110mg bd if: • Age 75-80 yrs • CrCl 30-50ml/min • Increased bleeding risk, including gastritis, oesophagitis, GORD	Use with caution if CrCl 15-29ml/min	Consider reducing treatment dose to 15mg od* if CrCl 15-49ml/min and bleeding risk exceeds risk of recurrent VTE Consider 20mg od to prevent recurrence in patients with high risk of recurrence or those who have developed recurrent VTE on secondary prevention dose of 10mg od (but consider reducing to 15mg od* if CrCl 15-49ml/min and bleeding risk exceeds risk of recurrent VTE)

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Management of switch from warfarin to DOAC

EHRA guidance provides pragmatic advice on switching from warfarin to DOACs reducing the need for repeated INR checks.

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

Specific guidance on switching between anticoagulants is provided in the SPCs [2-5] 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

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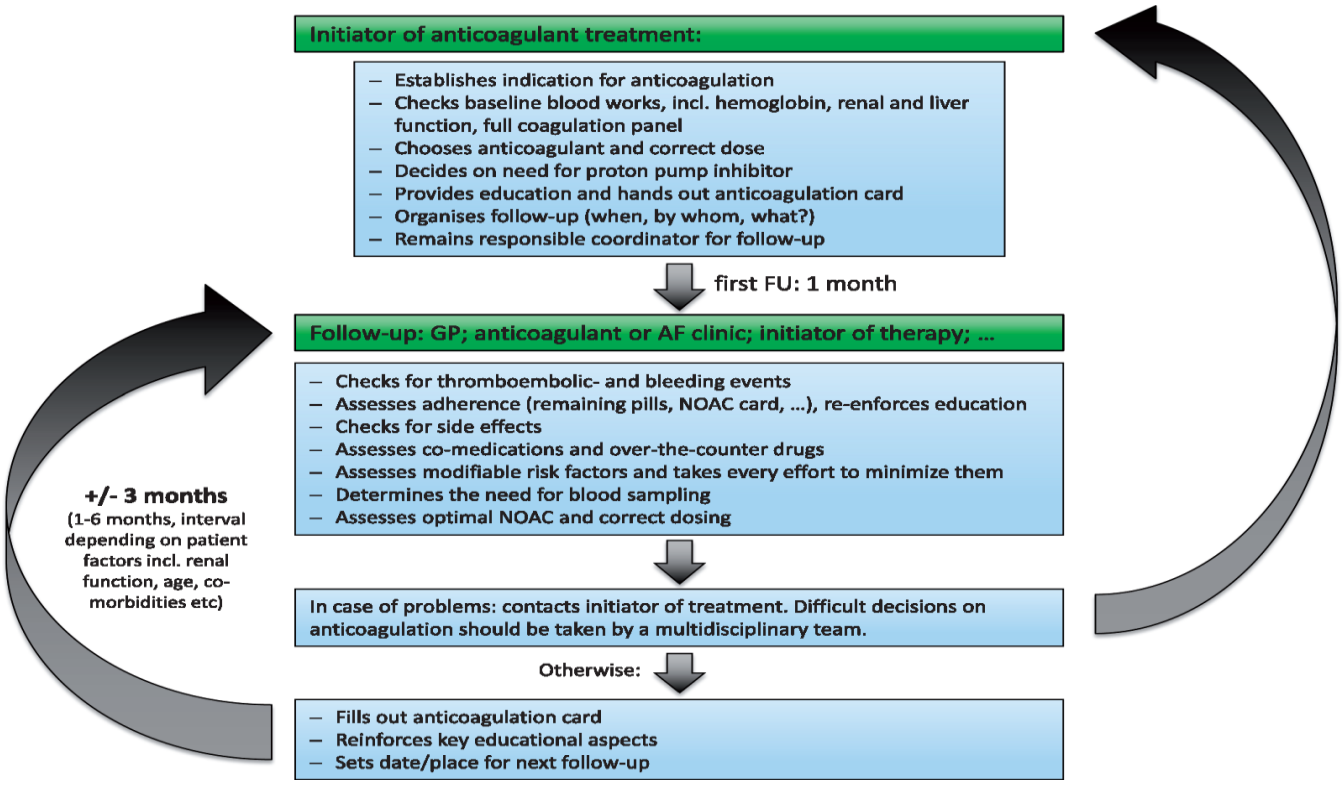
DOAC review

The European Heart Rhythm Association (EHRA)[8] makes recommendations for baseline screening and follow-up on initiating DOAC therapy. These have been adopted by NICE[9] 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.[8] 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[8][9] 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

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Acknowledgements

Adapted from Central Surrey Health's Policy for Switching from Warfarin to Direct-Acting Oral Anticoagulants (DOACs) during COVID-19 by Carolyn Adamson.

References

1. National Health Service. (2020). Clinical guide for the management of anticoagulant services during the coronavirus pandemic. Available: https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/C0077-Specialty-guide_Anticoagulant-services-and-coronavirus-v1-31-March.pdf. Accessed 6th April 2020
2. Edoxaban (Lixiana®). https://www.medicines.org.uk/emc/product/6905/smpc. Accessed 6th April 2020
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6. Surrey & North West Sussex Area Prescribing Committee. (2020). Guidelines : Atrial fibrillation. Available: https://surreyccg.res-systems.net/PAD/Guidelines/Detail/4387. Accessed 6th April 2020.
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8. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, Haeusler KG, Oldgren J, Reinecke H, Roldan-Schilling V, Rowell N, Sinnaeve P, Collins R, Camm AJ, and Heidbuchel H. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. European Heart Journal 2018; 39: 1330–1393
9. National Institute for Health and Care Excellence Clinical Knowledge Summary (Jan 2020). Anticoagulation – Oral

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