

Specialty guides for patient management during the coronavirus pandemic

Clinical guide for the management of anticoagulant services during the coronavirus pandemic

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As healthcare professionals we all have general responsibilities in relation to coronavirus and for these we should seek and act on national and local guidelines. We also have a specific responsibility to ensure that anticoagulant care continues with the minimum burden on the NHS. We must engage with management and clinical teams planning the local response in our hospitals and across primary care.

Anticoagulant services may not seem to be in the frontline with coronavirus but we do have a key role in continuing to keep patients on anticoagulants as safe as possible; this must be planned. In response to pressures on the NHS, the way we deliver anticoagulants may need to change. We should seek the best local solutions to continue the safe management of patients on anticoagulation while protecting resources for the response to coronavirus.

Categories of patients to consider:

- **Obligatory inpatients:** a small proportion of patients on anticoagulation will need acute inpatient care, eg due to major bleeding or stroke.
- **Patients requiring initiation of oral anticoagulation.**
- **Patients already receiving warfarin** who are not self-managing and are currently being managed in outpatient or community settings: aim to minimise attendances, where possible.
- **Patients already receiving direct oral anticoagulants (DOACs)** who should have appropriate primary care-based monitoring in place.

When planning your local response, please consider the following:

Obligatory inpatients

- Anticoagulant specialist support will be required for patients experiencing a major bleed during therapy or a stroke while on anticoagulant therapy.
- Haematologist support may be needed for patients with COVID-19 who develop coagulopathies.
- Specialist anticoagulant staff should be available to address anticoagulant-related queries from secondary and primary care.
- It can be very stressful during a crisis. Support each other and share the workload. Do not expect the clinical director to do all the co-ordination!

Patients requiring initiation of oral anticoagulation

- Anticoagulation should only be initiated by clinicians in primary or secondary care with experience in managing anticoagulation.
- DOACs should be initiated, if possible, instead of warfarin to minimise the monitoring burden and need for regular INR (International Normalised Ratio) monitoring.
- In line with NICE guidance, where more than one product is available for the indication, the product with the lowest acquisition cost should be used.
- Patients with mechanical heart valves should be initiated on warfarin. However, when monitoring is not possible, then a brief period of low molecular weight heparin (LMWH) could be considered if the patient can be taught to self-inject or a family member living with them can administer the injection.
- For other patients in whom DOACs are not an option, consider a LMWH if the patient can be taught to self-inject or a family member living with them can administer the injection.
- **In view of recognised supply issues with LMWH, these should only be used if there are no other appropriate options.**
- If a patient must have warfarin, can they or a family member living with them be taught to self-test their INR using a CoaguChek machine (providing this can be secured), and then phone in the results for dose adjustment?
- Where possible, move to remote consultations to initiate anticoagulant therapy and provide follow-up by telephone.
- Provide patients with written information to support any discussions.
- Ensure systems are in place for provision of medicines in a timely manner.
- Provide accurate information to primary care concerning indication, INR range if applicable, baseline tests and monitoring requirements, to allow its safe takeover of prescribing responsibility.

- Issue 28-day quantities and, where possible, use repeat electronic prescribing.
- Do not provide larger quantities as these may compromise the supply chain.
- Hospitals should work to provide prescriptions directly to community pharmacies.

Patients receiving warfarin requiring management in outpatient or community settings

- 400,000 people have been prescribed warfarin in the past nine months.
- Dosing for patients on warfarin is often done remotely.
- Patients prescribed warfarin require regular blood tests for INR monitoring – at least every 12 weeks if their INR is stable and more frequently if not.
- Monitoring may be carried out in general practices, hospitals or other community-based settings, such as clinical hubs, community pharmacies and in patients' own homes.

Issues

- General workload related to INR monitoring in the current context of COVID-19.
- Risks to patients and staff from attending anticoagulant hubs for INR monitoring.
- Increasing numbers of patients infected with COVID-19, self-isolating with their household or socially distancing could pass the burden of INR testing to community nursing teams who will not have the capacity to respond.
- Infection with COVID-19 is likely to have a detrimental effect on warfarin control.
- Increased number of calls to anticoagulation clinics may mean that some patients' queries are not answered in a timely manner.

Anticoagulation service provision should consider the following:

1. Is warfarin still required?

This is an opportunity to review if long-term warfarin therapy is still indicated, eg in patients with prior deep vein thrombosis (DVT) or pulmonary embolism (PE) for whom the risk of recurrence is now considered low.

2. Can patients on warfarin be switched to an alternative oral anticoagulant, such as a DOAC?

While DOACs do require blood tests to assess renal function throughout treatment, the monitoring is predictable, less rigorous than INR testing with warfarin and routinely carried out in primary care.

Patients should only be switched from warfarin to a DOAC by clinicians in primary or secondary care with experience in managing anticoagulation.

To protect the supply chain for all patients – take a phased approach over the 12-week cycle of INR monitoring. Consider prioritising patients with poor control of INR as this cohort will need the most frequent INR checks. Address non-adherence if this an underlying reason for poor INR control.

All DOACs are licensed for the prevention of:

- atrial fibrillation (AF)-related stroke in people with non-valvular AF
- treatment and secondary prevention of DVT/PE
- prevention of DVT/PE post-hip and knee surgery.

Low-dose rivaroxaban is also licensed for:

- acute coronary syndrome
- stable coronary artery disease
- symptomatic peripheral arterial disease.

In line with NICE guidance, where more than one product is available for the indication, the product with the lowest acquisition cost should be used.

A switch from warfarin to a DOAC **should not** be considered for patients:

- with a prosthetic mechanical valve
- with moderate-to-severe mitral stenosis
- with antiphospholipid antibodies
- who are pregnant, breastfeeding or planning a pregnancy
- requiring a higher than standard INR range of 2.0–3.0
- with severe renal impairment (creatinine clearance (CrCl) <15mL/min)
- with active malignancy/chemotherapy (unless advised by a specialist)
- prescribed some HIV antiretrovirals and hepatitis antivirals – check the HIV drug interactions website (<https://www.hiv-druginteractions.org/>)
- on phenytoin, carbamazepine, phenobarbitone or rifampicin; these patients are likely to have low DOAC levels so should be discussed with an anticoagulation specialist
- there is little data on DOACs for patients with venous thrombosis at unusual sites and they should be discussed with an anticoagulation specialist
- on triple therapy (dual antiplatelet plus warfarin); switching these patients should be discussed with an anticoagulation specialist or cardiologist.

Recommendations for switching to a DOAC are given in Appendix 1.

3. Could patients be trained to self-test INR in their own homes?

NICE guidance recommends self-testing of INR using CoaguChek self-testing meters for patients with prosthetic mechanical valves and for those with AF.

<https://www.nice.org.uk/guidance/dg14>.

Roche Diagnostics reports that supplies of CoaguChek monitors are currently low due to increased demand in the past two to four weeks. It is working to increase availability in the UK as soon as possible. When devices are available, these should be prioritised for patients at highest risk of COVID-19 infection.

While a move towards patient self-testing will present challenges in terms of purchasing equipment, provision of test strips, training patients and undertaking quality assurance checks, self-testing should be considered for patients/carers capable of doing this to minimise INR monitoring workload across the system.

Patients or carers need to be carefully selected for use of CoaguChek, taking into account their manual dexterity, cognitive function, vision and ability to use technology.

Dosing recommendations should be provided by the patient's current anticoagulation service by phone or electronically. Digital solutions to facilitate the electronic transfer of data are available through, for example, LumiraDX, InHealthcare and INR Star Engage Platform.

Processes covering what to do when results are out of range should be in place locally to support patients who are self-testing their INR.

Ensure systems are in place for timely provision of CoaguChek test strips.

4. Have blood testing facilities been optimised to reduce risk of infection?

- Could the frequency of INR monitoring be reduced for stable patients on warfarin? Keep to a maximum of 12 weeks between INR checks. For those who cancel their 12-week check due to symptoms of coronavirus, extend the interval to 14 weeks if safe to do so.
- Have patients been advised to avoid public transport where possible? Can transport by taxi be offered to these patients?
- Could a drive-through INR testing model be employed to minimise exposure?
- Are facilities for handwashing available? If not, is alcohol hand sanitizer available?
- Have appointments been spaced out as far as possible? Take a 'one in one out' approach, group low-risk patients together and respect social distancing advice.

- Are waiting rooms set up to reduce risk of infection (eg space between chairs, regular cleaning, etc).
- Can patients write the result and dose in their own yellow book?
- Have patients at most risk been advised to attend at a quieter time?
- Has enough personal protective equipment (PPE) been supplied to staff members working in anticoagulation/blood testing services?

5. Strategies to minimise the impact on community nursing services over the next weeks/months

Local community nursing teams are unlikely to have the capacity to take on INR monitoring for large numbers of patients who become housebound through COVID-19 infection, self-isolation of the household or social distancing strategies.

- Would provision of healthcare professional CoaguChek machines to community nursing services, to facilitate point of care testing, reduce their workload (eg by reducing the need to transport blood samples to laboratories)?
- Could small community INR testing hubs be set up, eg within primary care networks (PCNs) or in local community pharmacies? Note: these strategies still carry infection risk but do reduce the need for hospital/GP practice attendance.
- Could other teams be deployed in the community to take blood samples for patients at home?
- Could anticoagulation service staff support INR testing in patients' own homes?

6. Suspend warfarin treatment temporarily in selected patients (in whom DOACs and LMWH are not suitable)

As a last resort, for individual patients for whom INR testing is not possible and therefore warfarin cannot be dosed safely, warfarin therapy could be temporarily stopped after weighing the benefit and risk and discussion with the patient. Regular review should be undertaken with a view to restarting warfarin therapy as soon as it is safe to do so.

Patients with mechanical valves in situ must continue on warfarin at all times – seek advice from a cardiologist.

Patients receiving DOACs should have appropriate primary care-based prescribing and monitoring in place

- Telephone triage, instead of face-to-face consultations, should be in place to support patients, eg for those experiencing bleeding symptoms in primary care.

- Standard renal monitoring should be undertaken at least annually, and more regularly in people with renal dysfunction, over the age of 75 years or who are frail.
- Specialist support for primary care prescribers should be available should issues arise during DOAC treatment.

Information and support for patients

- Anticoagulation UK: <https://www.anticoagulationuk.org/>
- Atrial Fibrillation Association: <https://www.heartrhythmalliance.org/afa/uk/>
- British Heart Foundation: <https://www.bhf.org.uk/>

Appendix 1: Guidance for the safe switching of warfarin to direct oral anticoagulants (DOACs) for patients with non-valvular AF and venous thromboembolism (DVT/PE) during the coronavirus pandemic

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<https://www.rpharms.com/development/coronavirus-cpd-resources#warfarindoac>

Switching appropriate patients from warfarin to a DOAC may be considered to avoid regular blood tests for INR monitoring. Whilst DOACs require blood tests to assess renal function throughout treatment– the monitoring is predictable, less rigorous than INR testing with warfarin and is routinely carried out in primary care. 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.

Patients should only be switched from warfarin to a DOAC by clinicians in primary or secondary care with experience in managing anticoagulation.

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

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

All DOACs are licensed for the prevention of atrial fibrillation (AF)-related stroke in people with non-valvular AF and for the treatment and secondary prevention of deep vein thrombosis (DVT) and pulmonary embolism (PE).

Is anticoagulation still required?

For example, can anticoagulant therapy be stopped in patients with prior DVT / PE, where the risk of recurrence is now considered low – seek specialist advice if necessary

Is a switch to a DOAC appropriate?

A switch from warfarin to a DOAC **should not** be considered for patients:

- With a prosthetic mechanical valve
- With moderate to severe mitral stenosis
- With antiphospholipid antibody syndrome (APLS)
- Who are pregnant, breastfeeding or planning a pregnancy
- Requiring a higher INR than the standard INR range of 2.0 – 3.0
- With severe renal impairment - Creatinine Clearance (CrCl) < 15ml/min
- With active malignancy/ chemotherapy (unless advised by a specialist)
- Prescribed interacting drugs – check SPCs (links below) for full list
 - Some HIV antiretrovirals and hepatitis antivirals - check with HIV drug interactions website at <https://www.hiv-druginteractions.org/>
 - Some antiepileptics – phenytoin, carbamazepine, phenobarbitone or rifampicin are likely to reduce DOAC levels so should be discussed with an anticoagulation specialist
- On triple therapy (dual antiplatelet therapy plus warfarin) without discussing with an anticoagulant specialist or cardiologist
- There is little data on DOACs for patients with venous thrombosis at unusual sites (e.g. portal vein thrombosis) and these patients should be discussed with an anticoagulation specialist.

When switching to a DOAC, care should be taken to follow the recommendations in the relevant SPC:

- Apixaban (Eliquis®) <https://www.medicines.org.uk/emc/product/2878/smpc>
- Dabigatran (Pradaxa®) <https://www.medicines.org.uk/emc/product/4703/smpc>
- Edoxaban (Lixiana®) <https://www.medicines.org.uk/emc/product/6905/smpc>
- Rivaroxaban (Xarelto®) <https://www.medicines.org.uk/emc/product/2793/smpc>

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 (see table below).

Guidance on DOAC prescribing for non-valvular AF and DVT/PE

DOAC	Apixaban	Edoxaban	Rivaroxaban	Dabigatran
How to change from warfarin	<p>Stop warfarin. Start DOAC when INR ≤ 2.5 - See additional guidance overleaf</p> <p>(from EHRA guidance: https://academic.oup.com/eurheartj/article/39/16/1330/4942493?guestAccessKey=e7e62356-8aa6-472a-aeb1-eb5b58315d49)</p>			
Baseline checks	<p>Renal function (CrCl)- serum creatinine (Cr) and bodyweight, full blood count (FBC), liver function tests (LFTs). Use results from last 3 months if stable.</p> <p>If for AF: CHA₂DS₂VASC and HASBLED scores.</p>			
Dosing in Non-valvular AF <i>(lifelong unless risk:benefit of anticoagulation therapy changes)</i>	<p>Prescribe Apixaban 5mg twice daily</p> <p><u>Reduce dose to 2.5mg twice daily</u> 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 - 29 ml/min.</p>	<p>Prescribe Edoxaban 60mg once daily</p> <p><u>Reduce dose to 30mg once daily</u> if: Body weight <61kg, or CrCl < 50ml/min, or co-prescribed with ciclosporin, dronedarone, erythromycin or ketoconazole.</p>	<p>Prescribe Rivaroxaban 20mg once daily</p> <p><u>Reduce dose to 15mg once daily</u> if CrCl < 50ml/min in NVAF patients only.</p>	<p>Prescribe Dabigatran 150mg twice daily if aged <75 years, CrCl > 50ml/min, low risk of bleeding (weight <50kg with close clinical surveillance)</p> <p><u>Reduce dose to 110mg twice daily</u> if aged > 80 years or prescribed verapamil. Consider 110mg twice daily based on individual assessment of thrombotic risk and the risk of bleeding in patients aged between 75 and 80 years or with CrCl <50ml/min or with increased risk of bleeding (including gastritis, oesophagitis, gastro-oesophageal reflux).</p>
Dosing in patients with DVT / PE <i>(loading doses are not required if patient has been stabilised on warfarin)</i>	<p>Dose is 5mg twice daily (use with caution if CrCl <30ml/min). Check intended duration of therapy. For long term prevention of recurrence 2.5mg twice daily (after 6 months' treatment dose).</p>	<p>Dosing as above. Check intended duration of therapy.</p>	<p>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 of recurrence 10mg daily could be considered.</p>	<p>Dosing as above. Check intended duration of therapy.</p>
Duration of therapy for DVT/PE	<p>For a provoked DVT/PE: 3 months treatment if provoking factors have been addressed.</p> <p>For unprovoked DVT/PE or recurrent DVT/PE: At least 6 months treatment dose followed by prophylaxis dosing as indicated/advised.</p>			
Contraindications	CrCl <15 ml/min	CrCl <15 ml/min	CrCl <15 ml/min	CrCl <30 ml/min

Cautions See also individual SPCSs		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 SPC: www.medicines.org.uk	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir - not recommended (See SPC for full details) 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. (See BNF and SPC for information)	Ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir, dronedarone – not recommended (See SPC for full details) Rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort – Should be avoided.	Ketoconazole, ciclosporin, itraconazole, tacrolimus, dronedarone - contraindicated (See SPC for full details) 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

Pragmatic Approach to Stopping Warfarin and Starting DOAC in relation to the INR

SPCs recommend different INRs at which to initiate DOACs after stopping warfarin:

- Apixaban and Dabigatran: Start when INR < 2
- Edoxaban: Start when INR < 2.5
- Rivaroxaban: Start when INR < 3

This approach would require repeat INR checks daily until the required INR is achieved.

EHRA guidance gives pragmatic guidance on when to start DOACs after stopping warfarin:

- If INR < 2: Commence DOAC that day
- If INR between 2 and 2.5: Commence DOAC the next day (ideally) or the same day
- If INR between 2.5 and 3: Withhold warfarin for 24-48 hours and then initiate DOAC

<https://academic.oup.com/eurheartj/article/39/16/1330/4942493?guestAccessKey=e7e62356-8aa6-472a-aeb1-eb5b58315d49>

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)
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)
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
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 if they have been monitoring INR or administering warfarin

Ensure local community pharmacies are made aware of the likely increase in the usage of DOACs locally

Counselling: See attached checklist

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.

For patients in whom DOACs are not suitable – is low molecular weight heparin (LMWH) an option?

- Whenever possible, patients with mechanical heart valves should remain on warfarin, however if monitoring is impossible then a brief period of LMWH could be considered if the patient can be taught to self-inject or a family member that lives with them can administer the injection.
- For other patients in whom DOACs are not an option, consider a LMWH if the patient can be taught to self-inject or a family member that lives with them can administer the injection.

In view of recognised supply issues with LMWH, these should only be used if there are no other appropriate options

For patients continuing warfarin therapy - is self-testing of INR with a CoaguChek self-testing meter a possibility?

There are limited supplies of CoaguChek self-testing meters available in the UK but, where available, these should be used for appropriate patients continuing warfarin therapy. Dosing recommendations should be provided by the patient's current anticoagulation service provider by phone or electronically. See <https://www.nice.org.uk/guidance/dg14>

DOAC Counselling Checklist

Apixaban (Eliquis®), Dabigatran (Pradaxa®), Edoxaban (Lixiana®), Rivaroxaban (Xarelto®)

DOAC Agent Counselling:

Counselling points	Sign
Explanation of an anticoagulant (increases clotting time and reduces risk of clot formation) and explanation of indication for therapy (AF and stroke risk reduction/DVT/PE)	
Differences between DOAC and warfarin (if applicable for patients converting from warfarin to DOAC therapy <u>or</u> offering choice of anticoagulation agent) <ul style="list-style-type: none"> No routine INR monitoring Fixed dosing No dietary restrictions and alcohol intake permitted (within national guidelines) Fewer drug interactions 	
Name of drug: generic & brand name	
Explanation of dose: strength & frequency	
Duration of therapy: lifelong for AF or explain course length for DVT / PE treatment or prevention	
To take with food (dabigatran and rivaroxaban). Not required for apixaban or edoxaban	
Missed doses: <ul style="list-style-type: none"> Apixaban and dabigatran can be taken within 6 hours of missed dose, otherwise omit the missed dose Edoxaban and rivaroxaban can be taken within 12 hours of missed dose, otherwise omit the missed dose 	
Extra doses taken: obtain advice immediately from pharmacist/GP/NHS Direct (111)	
Importance of adherence: short half-life and associated risk of stroke and/or thrombosis if non-compliant	
Common and serious side-effects and who/when to refer: symptoms of bleeding/unexplained bruising. Avoidance of contact sports. <ul style="list-style-type: none"> Single/self-terminating bleeding episode – routine appointment with GP/pharmacist Prolonged/recurrent/severe bleeding/head injury – A&E Major bleeds managed/reversed by supportive measures, Prothrombin Complex Concentrate (PCC), and availability of antidote	
Drug interactions and concomitant medication: avoid NSAID's. Always check with a pharmacist regarding OTC/herbal/complimentary medicines	
Inform all healthcare professionals of DOAC therapy: GP, nurse, dentist, pharmacist i.e. prior to surgery	
Pregnancy and breastfeeding: potential risk to foetus – obtain medical advice as soon as possible if pregnant/considering pregnancy. Avoid in breastfeeding	
Storage: dabigatran <u>must</u> be kept in original packaging – moisture sensitive. All other DOAC are suitable for standard medication compliance aids/ dosette boxes if required	
Follow-up appointments, blood tests, and repeat prescriptions: where and when	
Issue relevant patient information AF booklet/leaflet and anticoagulant patient alert card	
Give patient opportunity to ask questions and encourage follow up with community pharmacist (NMS – New Medicine Service)	