

DOAC Prescribing in Patients with Non-Valvular AF and for the treatment and prevention of VTE

Frequently Asked Questions

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 ** NB. This FAQ supersedes Medicines Update Extra No. 5 **

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Introduction

Non-Valvular Atrial Fibrillation (AF)

A direct oral anticoagulant (DOAC) may be prescribed for patients newly diagnosed with non-valvular atrial fibrillation (AF) requiring anticoagulation. The DOACs; apixaban, dabigatran and edoxaban are included in the Formulary for this indication. Edoxaban is the preferred choice within NHSGGC.^{1,2}

A DOAC may also be considered as an alternative to warfarin for existing patients with non-valvular AF who are believed to be adhering to warfarin therapy but have a poorly controlled INR.¹ A poorly controlled INR in this context is defined as therapeutic INR < 65% of the time.^{2,3} All four DOACs; apixaban, dabigatran, edoxaban and rivaroxaban are included in the Formulary. Edoxaban is the preferred choice within NHSGGC for this indication.¹ Patients who are well controlled on warfarin should remain on warfarin therapy.¹

Treatment and prevention of venous thromboembolism (VTE)

All four DOACs; apixaban, dabigatran, edoxaban and rivaroxaban are indicated for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and prevention of recurring DVT and PE.⁴ Apixaban is the preferred DOAC within NHSGGC for this indication.¹

Section 1: Questions relating to indications/appropriateness of DOACs

My patient has AF and a mechanical prosthetic heart valve - is he eligible for a DOAC?

No - DOACs are *not* indicated in patients with a mechanical prosthetic heart valve or in patients who have moderate or severe mitral stenosis.

The DOACs are licensed for 'non-valvular' AF, however, the license doesn't specify the definition of 'non-valvular'. The European Heart Rhythm Association defines non-valvular AF as AF that occurs in the absence of mechanical prosthetic heart valves and in the absence of moderate to severe mitral stenosis (usually of rheumatic origin).³ In light of this definition, cardiologists may choose to prescribe a DOAC in patients who have tissue valves or who have undergone valve repair. If unsure of eligibility, cardiology advice should be sought for individual patients.

Given that DOACs are not licensed in patients with valvular disease - if a patient has a heart murmur and new AF should I initiate a DOAC or wait until the cause of the murmur is established?

A DOAC should be initiated immediately rather than delaying anticoagulation in a patient with AF. If valvular heart disease is later diagnosed (for example from an echocardiogram) the patient should be referred to cardiology who will review medicines as

appropriate. Edoxaban is the DOAC of choice for non-valvular AF in NHSGGC.¹

My patient has been diagnosed with a PE, can I prescribe a DOAC for the treatment of the PE and prevention of recurrence?

Yes – a DOAC can be prescribed for newly diagnosed patients with a PE.⁴ Apixaban is the preferred DOAC in NHSGGC for the treatment of PE.¹ Although the Summary of Product Characteristics (SPC) for apixaban suggests you do not have to prescribe a low molecular weight heparin (LMWH) prior to starting apixaban⁴, local guidance recommends prescribing a LMWH until diagnosis is confirmed.⁵ Once diagnosis is confirmed the LMWH should be stopped and the first dose of apixaban can be given 22-24 hours after the last dose of LMWH.⁵ If apixaban is not appropriate another oral anticoagulant may be considered. Refer to section 3 to determine LMWH requirements prior to initiating one of the other DOACs.

My patient has had recurrent DVTs on warfarin, are they eligible for a DOAC?

A DOAC may be considered for this patient if the INR has been poorly controlled despite complying with warfarin. If there are issues with compliance with warfarin, consider if a DOAC may be more suitable. If this patient has experienced recurrent DVTs despite being compliant with warfarin **and** has had a well controlled INR, particularly at the time of recurrent events, there is the possibility that a DOAC may not be effective in such a patient and a higher target INR has to be considered. A diagnosis of occult cancer should also be considered in patients with recurrent events on warfarin. Haematology advice should be sought for individual patients.

My patient has cancer and has been diagnosed with a PE. She doesn't want to receive injections, can I prescribe a DOAC?

Current GGC guidance recommends that patients with active cancer and/or receiving active treatment for cancer, who are diagnosed with a VTE, are most effectively treated with LMWH, rather than warfarin or a DOAC. DOACs have not been demonstrated to be more effective than warfarin in cancer patients.⁶ Cancer patients who receive LMWH, rather than warfarin, experience less recurrent VTE events, although rates of bleeding and mortality are unaffected.⁶ Although LMWH is the treatment of choice when a patient with cancer and/or receiving active treatment for cancer is diagnosed with a VTE, there is emerging evidence for the use of edoxaban.⁷ Note that DOACs are contraindicated in patients with malignant neoplasms at high risk of bleeding.⁴

My patient is on a DOAC for DVT and has now been diagnosed with cancer. Can he remain on the DOAC or does he have to switch to a LMWH?

The preferred option is to switch to a LMWH. The efficacy and safety of the DOACs have not been fully established for DVT/PE patients with active cancer and they are contraindicated in patients with malignant neoplasms at high risk of bleeding.⁴ However, as above there is recent evidence for the use of edoxaban.⁷ Individual cases can be discussed with the patient's oncologist or haematology.

My patient is on a DOAC for prevention of recurrent DVTs and has now been diagnosed with a further DVT, should they remain on the DOAC and if so what dose should they receive?

Firstly, check compliance with the DOAC. If the patient hasn't been taking the DOAC regularly, consider re-starting the DOAC and re-emphasise the importance of taking every day. Depending on the last time the patient took the DOAC, consider giving the initiation dose if on apixaban or rivaroxaban. Refer to BNF for dosing instructions.

If the patient has been compliant with DOAC therapy, check if the correct dose has been prescribed for age, renal function, concomitant medication etc. Amend the dose and continue the DOAC as appropriate.

If the patient has been compliant and has been taking the correct dose, warfarin therapy (with LMWH cover until INR is therapeutic) could be considered as this would enable monitoring.

Haematology advice can be sought for individual patients.

My patient is on a DOAC for AF and has just been diagnosed with a PE, should they remain on a DOAC?

As the patient has experienced a PE while on a DOAC, it may be preferable to switch to warfarin with LMWH cover until INR is therapeutic.

Haematology advice should be sought for individual patients.

My patient is on apixaban 2.5 mg twice daily to prevent recurrent DVTs, she is now in AF and the dose of apixaban for AF for this patient would be 5 mg twice daily. Should the dose be changed to this?

The dose of apixaban should be increased to 5 mg twice daily and continued indefinitely. Alternatively, the patient could be switched to edoxaban if it is felt that once daily dosing would be beneficial. Refer to the Summary of Product Characteristics (SPC) for edoxaban for dosing and switching information.⁴

What about other indications for DOACs? Can I prescribe a DOAC for orthopaedic thromboprophylaxis instead of a LMWH?

Orthopaedic thromboprophylaxis is out with the scope of this document, however, there is guidance on StaffNet on thromboprophylaxis in orthopaedic patients.⁸

Section 2: Questions relating to choice of DOAC & dose

All 4 DOACs are indicated for AF and VTE and the dosing regimens are all different. How do I choose the most appropriate agent and dose for my patient?

The DOACs all have slightly different properties and the best choice of agent and dose may be dependent on individual patient characteristics. Factors such as indication for treatment, renal function, age, body weight, ability to swallow medicines and the need for a compliance aid may be relevant.

In AF, all four DOACs are on the GGC Formulary for switching from warfarin due to poor INR control.¹ Apixaban, dabigatran and edoxaban but not rivaroxaban are on the Formulary for newly diagnosed AF.¹

Edoxaban is the preferred DOAC within NHSGGC for non-valvular AF, however, other DOACs may be prescribed if edoxaban is deemed inappropriate. Refer to Algorithm 1 (on page 8) for patients without renal impairment (creatinine clearance [CrCl] > 50ml/min) and algorithms 2 and 3 (pages 9 and 10) for patients with renal impairment.

All four DOACs are also on the GGC Formulary for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and prevention of recurring DVT and PE.¹ Apixaban is the preferred DOAC within NHSGGC for this indication, however, other DOACs may be prescribed if apixaban is deemed inappropriate. Refer to Algorithm 4 (on page 11) for patients without renal impairment (creatinine clearance [CrCl] > 50ml/min) and algorithms 5 and 6 (pages 12 and 13) for patients with renal impairment.

Is there a preferred choice of DOAC in a patient with renal impairment and is a dose reduction necessary?

All four DOACs may be used but the agent and dose depends on the degree of impairment. Calculate creatinine clearance (CrCl). See information below (do not use eGFR). Once CrCl is known, use the appropriate algorithm on pages 8-13 depending on indication for treatment. None of the DOACs are recommended if CrCl < 15ml/min and in addition, dabigatran is not recommended if CrCl < 30ml/min.⁴

How should renal function be calculated?

Do not use eGFR to evaluate the degree of renal impairment.⁴ The "Cockcroft Gault" equation can be used to **estimate** Creatinine Clearance (CrCl):

$$\text{CrCl} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{\text{serum creatinine (micromol/L)}} \times 1.23 \text{ (male) OR } \times 1.04 \text{ (female)}$$

(ml/minute)

A CrCl calculator is available within the GGC Medicines App and on [StaffNet](#). The CrCl calculator is based on the Cockcroft Gault equation using actual weight entered. If weight entered is > 20% above ideal body weight (IBW), the calculator will automatically use a weight of IBW + 20% i.e. Maximum body weight (MBW). Regardless of whether this calculation is done manually or using the calculator the following should be considered:

- Use actual body weight (ABW) or maximum body weight (MBW), whichever is lower. If the CrCl calculation is done manually, MBW will need to be calculated. Refer to the [Therapeutics Handbook](#) for a maximum body weight table. If the CrCl calculator is used, enter actual weight.
- Use 60 micromol/L if the creatinine concentration is < 60 micromol/L.
- This equation may overestimate CrCl in elderly or malnourished patients.

Warning: As described above Cockcroft Gault is used to **estimate** creatinine clearance and has some limitations. In patients where the creatinine clearance is borderline for dose reduction/contraindication it may be particularly important to consider other risk factors (see decision making algorithms on pages 8-13) when choosing the most appropriate dose.

Do I need to recalculate creatinine clearance every year as the patient's age increases?

Only the manufacturer of dabigatran state that renal function should be assessed at least once a year.⁴ Specific advice is not provided by the manufacturers of apixaban, edoxaban or rivaroxaban, however, an annual recalculation may be considered good practice and may be prudent in those patients whose creatinine clearance is borderline for dose reduction anyway. Additionally review of dosing is necessary for some DOACs when the patient reaches 80 years old and if they have lost weight or their creatinine has changed. **Please familiarise yourself with the prescribing requirements for each DOAC.**

I am commencing a DOAC in an elderly patient with low body weight. Which DOAC at what dose is best?

Any of the four agents may be used in such a patient but the threshold for dose reduction varies depending on the agent. Calculate creatinine clearance and then use the appropriate algorithm (on pages 8-13) as described above.

My patient is on a number of other medicines. Do any of the four DOACs have a more favourable interaction profile?

DOACs have fewer drug interactions than warfarin but there are some to be aware of. All four DOACs are substrates of the transport protein, P-glycoprotein (P-gp) and therefore may theoretically interact with inducers or inhibitors of P-gp.⁴ Apixaban, edoxaban and rivaroxaban are all metabolised to varying degrees by the cytochrome enzyme, CYP3A4 and therefore may theoretically interact with inducers or inhibitors of CYP3A4.⁴ It is particularly important to check for interactions with inducers or inhibitors of both CYP3A4 and P-gp.

Always check for interactions with existing medicines when prescribing any new medicine. Interactions can be checked using the BNF (access via <https://www.medicinescomplete.com/>) or the Summary of Product Characteristics (SPC) (available via <https://www.medicines.org.uk/emc/>). Medicines Information may also be contacted for further advice on interactions. See contact details in Section 4.

Please note

- Available data on interactions is limited and may change as DOACs become more widely prescribed, therefore, it is good practice to check for any changes in interaction profile.
- Some interactions may become more important in the presence of other risk factors (e.g. renal impairment).
- An awareness of potential interactions is important because of the lack of monitoring of anticoagulant effect.

My patient is on apixaban and has been prescribed clarithromycin, is there an interaction?

Clarithromycin is a potent inhibitor of CYP3A4 and also an inhibitor of P-gp and therefore may increase the levels of apixaban. The SPC for apixaban states clarithromycin (500 mg, twice a day), led to a 1.6-fold and 1.3-fold increase in mean apixaban AUC and C_{max} respectively.⁴ It is therefore preferable to prescribe an alternative antibiotic if possible. If an alternative antibiotic is not suitable, seek further advice from Pharmacy or Haematology.

I'm aware that the combination of apixaban and clarithromycin should be avoided where possible, does the same advice apply to edoxaban and clarithromycin?

Clarithromycin is a potent inhibitor of CYP3A4 and also an inhibitor of P-gp and therefore may increase the levels of edoxaban. The SPC for edoxaban does not list an interaction with clarithromycin, however, there is a documented interaction with erythromycin and therefore clarithromycin may be expected to interact similarly.⁴ Due to the clinical uncertainty of the potential interaction with clarithromycin, it is preferable to prescribe an alternative antibiotic if

possible. If an alternative antibiotic is not suitable, seek further advice from Pharmacy or Haematology.

Are there any foods that should be avoided when taking a DOAC?

No there are no known drug food interactions to be concerned about. Rivaroxaban should be taken with food to maximise bioavailability but the timing of apixaban, dabigatran and edoxaban dosing in relation to food is unimportant.⁴

My patient is already on aspirin (or clopidogrel) because of pre-existing ischaemic heart disease (or cerebrovascular disease), and now has developed AF. Should the antiplatelet agent be discontinued when the DOAC is started?

The co-prescription of an antiplatelet agent with a DOAC confers an additional bleeding risk.⁴ The antiplatelet agent should therefore be reviewed with a view to discontinuation. If there are concerns about stopping the antiplatelet then cardiology advice should be sought. Additionally if it appears from a hospital discharge letter that both are to continue this should be confirmed with a cardiologist.

My patient is on dual antiplatelet therapy (DAPT) due to recently unstable ischaemic heart disease and has now developed AF. Should dual antiplatelet therapy be discontinued when the DOAC is started?

Cardiology advice should be sought for individual patients, however, the following may be used as a guide.

The co-prescription of antiplatelet therapy with a DOAC confers an additional bleeding risk and therefore DAPT with a DOAC would confer an even greater risk. The European Society of Cardiology (ESC) has produced guidance on how to manage patients depending on their bleeding risk and whether they have a stent.⁹ Patients without a stent, with a low bleeding risk, can receive triple therapy with an oral anticoagulant (including a DOAC) and clopidogrel and aspirin for six months followed by dual therapy with an oral anticoagulant (including a DOAC) and clopidogrel or aspirin for the following six months. Patients without a stent, with a high bleeding risk, can receive triple therapy with an oral anticoagulant (including a DOAC) and clopidogrel and aspirin for one month followed by dual therapy with an oral anticoagulant (including a DOAC) and clopidogrel or aspirin for the following eleven months. Regardless of bleeding risk, the antiplatelet should then be stopped and the patient would remain on an oral anticoagulant as monotherapy.

Patients with a stent can receive triple therapy with an oral anticoagulant (including a DOAC) and clopidogrel and aspirin for one month (regardless of bleeding risk). Dual therapy with an oral anticoagulant (including a DOAC) and clopidogrel or aspirin is advised for the following five months (for

patients with a high bleeding risk) or eleven months (for patients with a low bleeding risk) and then the antiplatelet should be stopped. The patient would then remain on an oral anticoagulant as monotherapy.

My patient has a nasogastric tube. Are any of the DOACs suitable for nasogastric administration?

Apixaban and rivaroxaban may be crushed and administered via a nasogastric tube.⁴ There is also evidence to support nasogastric administration of edoxaban, however, this is currently an unlicensed method of administration.¹⁰ Dabigatran is not suitable for nasogastric administration.⁴

Are DOACs suitable for inclusion in a patient's compliance aid?

Dabigatran is not suitable for inclusion in a standard compliance aid but apixaban, edoxaban or rivaroxaban may be included.^{11,12}

Section 3: Questions relating to DOAC initiation

I have determined that a DOAC is appropriate for my patient with AF and have decided which agent and dose to use. What is the procedure for initiation?

The procedure for initiation depends on whether a patient is commencing an anticoagulant for the first time or whether they are switching from warfarin due to a poorly controlled INR:

Newly diagnosed with AF: The patient may be started on an appropriate dose of the relevant DOAC without further delay. Referral to GCAS is not necessary.

Switching from warfarin:

The patient should:

1. be given a prescription for the appropriate dose of the relevant DOAC
2. be asked to obtain a supply of the DOAC from their regular community pharmacy, **but not to start taking it** until after their next GCAS clinic visit.
3. be told to omit their warfarin for three doses (days) prior to their next anticoagulant clinic appointment
4. take their new DOAC medicine along to their next GCAS clinic visit

Assuming their INR is then at the desired level, GCAS will instruct the patient to start their DOAC, stop warfarin permanently and discharge them from further GCAS follow-up. GCAS will then write to the GP indicating that warfarin has been stopped and DOAC started.

I am switching a patient from warfarin to a DOAC and already know that their INR is currently subtherapeutic. Do I need to follow the above procedure or could I start the DOAC immediately?

Apixaban and dabigatran may be initiated when INR is <2, edoxaban when INR <2.5 and rivaroxaban when INR is ≤3 if AF indication or ≤2.5 if VTE indication.⁴ If it is known that this is the case then a DOAC could potentially be started immediately without a three day gap as described above for AF. GCAS should be informed when warfarin is stopped.

My patient has been diagnosed with a DVT, can I start a DOAC immediately or do I need to prescribe a LMWH first?

Apixaban is the preferred DOAC in NHSGGC for the treatment of DVT.¹ Although the Summary of Product Characteristics (SPC) for apixaban suggests you do not have to prescribe a low molecular weight heparin (LMWH) prior to starting apixaban⁴, local guidance recommends prescribing a LMWH until diagnosis is confirmed.⁵ Once diagnosis is confirmed the LMWH should be stopped and the first dose of apixaban can be given 22-24 hours after the last dose of LMWH.⁵ If however, apixaban is not appropriate for the patient and you wish to prescribe another DOAC, please refer to the manufacturer's dosing advice. See summary below:

- For dabigatran and edoxaban, give at least 5 days of treatment dose LMWH before starting the DOAC.⁴
- For rivaroxaban, the SPC suggests you do not have to prescribe a LMWH prior to starting rivaroxaban.⁴ However, local guidance recommends prescribing a LMWH until diagnosis is confirmed.¹³ Once diagnosis is confirmed the LMWH should be stopped and the first dose of rivaroxaban can be given 22-24 hours after the last dose of LMWH.¹³

For information on switching from a LMWH to a DOAC, refer to the Summary of Product Characteristics (SPC) for each agent. ***NB. Ensure LMWHs are not prescribed and administered concomitantly with a DOAC. LMWHs should be stopped prior to initiation of a DOAC and DOACs should not be started while a patient is currently prescribed a LMWH.***

Section 4: Further information and advice

Is there any patient education literature available?

All four DOACs have a manufacturer's Patient Information Leaflet and these are available within the medication packaging. In addition, a standard DOAC patient information booklet adapted from the NPSA warfarin booklet and an alert card have recently been developed for patients in NHSGGC. Arrangements for how these are printed, distributed and obtained locally are still under discussion, however, these are

expected to be available by Summer 2018. If you require further information on this, contact Medicines Information (see useful contacts section below).

Should the patient carry an alert card, and where should they get it from?

Yes – a manufacturer's alert card is available in each medication pack. As above, a standard DOAC alert card has also been developed for patients in NHSGGC and is expected to be available by Summer 2018. Patients should be encouraged to carry an alert card with them at all times and to show it to healthcare professionals prior to any consultation or procedure.

Who should educate the patient about starting an anticoagulant?

This should be the clinician recommending treatment with some reinforcement by the clinician prescribing the DOAC (if different).

If a DOAC is initiated in hospital, how should this be communicated to primary care?

Information on the initiation of a DOAC should be communicated in the normal manner via the discharge letter to GPs when patients are discharged from hospital. It is good practice for the prescriber to state the indication for the DOAC and any other specific instructions with regards to dose and duration of treatment. Prescribers are encouraged to specify on the discharge letter that the dose has been checked for current renal function.

Once DOAC choice and dose is determined, what monitoring/annual review is required?

The marketing authorisation of any of the four available DOACs; apixaban, dabigatran, edoxaban and rivaroxaban, does not specifically stipulate what monitoring is necessary and how frequently. The exception is that the manufacturer of dabigatran recommends that renal function should be assessed at least once a year.⁴ The manufacturers of the other three DOACs make no specific recommendation about this however it may be good practice to take the same approach regardless of which DOAC is used. This annual check could be used as an opportunity to assess adherence and reassess whether an anticoagulant/DOAC prescription is still appropriate, whether the patient has any adverse effects and whether any new interacting medicines have been commenced (e.g. over the counter).

I am worried about the risk of major bleeding. Are there any reversal agents available for the DOACs?

Idarucizumab (Praxbind®) is a specific reversal agent for dabigatran and is indicated in adult patients treated with dabigatran etexilate when rapid reversal of its anticoagulant effects is required. It binds to dabigatran with very high affinity and instantly reverses its anticoagulant effect.¹⁴ It should be considered in cases of major haemorrhage or when

surgery cannot be delayed, and should be discussed with haematology.

There are currently no specific reversal agents available for the other DOACs apixaban, edoxaban and rivaroxaban, however, other agents are in the pipeline including andexanet alfa, a factor Xa inhibitor antidote expected to be launched in 2018.¹⁵

My patient is on a DOAC and is due to have surgery, does the DOAC need to stop prior to the procedure?

There is guidance on StaffNet on how to manage patients on DOACs who are going for surgery or other invasive procedures. The guidance varies depending on the type of surgery and the DOAC prescribed.^{14,16}

I have noticed my patient is prescribed a LMWH and a DOAC on the medicine prescription form (kardex) and has been getting both. Is this correct?

No – patients should **not** be prescribed a LMWH and a DOAC at the same time. This is likely to be a

prescribing error and should be corrected immediately. The error should be reported via Datix. Healthcare professionals should ensure this combination is not prescribed or administered to a patient.

It may be good practice to endorse 'oral anticoagulant' on the kardex when prescribing a DOAC or when completing the thromboprophylaxis section at the beginning of the kardex.

My patient has been on apixaban 5 mg twice daily for AF. Compliance is an issue and she would prefer to take a once daily DOAC. How can I switch to rivaroxaban or edoxaban?

The Summary of Product Characteristics (SPC) for edoxaban state that the DOAC you want to switch from should be discontinued and edoxaban started at the time of the next scheduled dose.⁴ The SPCs for the other DOACs do not provide specific information on how to switch between DOACs, however there is information to suggest that the other DOACs can be switched in the same manner as edoxaban.³

Useful contacts for further advice

Consultant Haematologists

Campbell Tait	0141 211 5168	Campbell.tait@ggc.scot.nhs.uk
Catherine Bagot	0141 211 4671	Catherine.bagot@ggc.scot.nhs.uk

Consultant Cardiologists

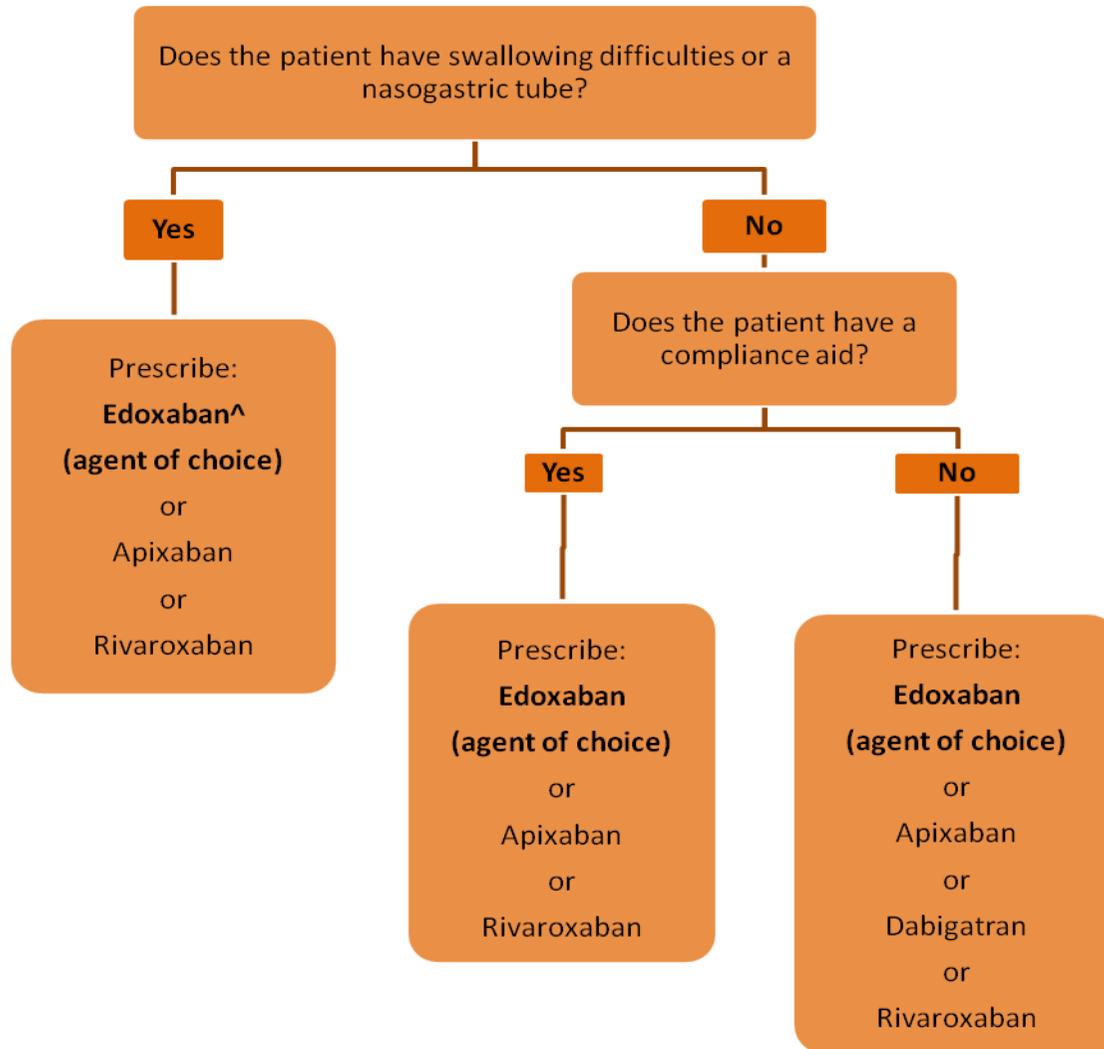
Joanne Lindsay	0141 211 4727	Joanne.lindsay@ggc.scot.nhs.uk
Iain Findlay	0141 887 9111	Iain.findlay@nhs.net
David Murdoch	0141 451 6129	David.murdoch@ggc.scot.nhs.uk

Medicines Information

0141 211 4407 medinfo@ggc.scot.nhs.uk

Decision making algorithm 1: DOAC choices in non-valvular AF patients without renal impairment (creatinine clearance > 50ml/min)

Refer to the latest version of the manufacturer's summary of product characteristics (SPC) for full prescribing advice



Dose Information

Apixaban

5 mg twice daily or 2.5 mg twice daily if at least 2 of the following:
 ≥80 years old
 ≤60 kg
 Cr ≥133 micromol/L

Dabigatran*

150 mg twice daily or
 110 mg twice daily if ≥80 years old or concomitant verapamil

***Additional prescribing notes for dabigatran**

A dose reduction to 110mg twice daily may also be considered if the patient has low thromboembolic risk combined with a high risk of bleeding and one or more of the following factors:

- Age 75 – 79 years; if standard dose is used then it should be reduced when patient reaches 80 years old
- Creatinine clearance 30 – 50ml/min
- Body weight of < 50kg
- Gastritis, oesophagitis or gastro-oesophageal reflux

Edoxaban

60 mg once daily or
 30mg once daily if ≤60kg or concomitant use of the following P-gp inhibitors: ciclosporin, dronedarone, erythromycin, ketoconazole

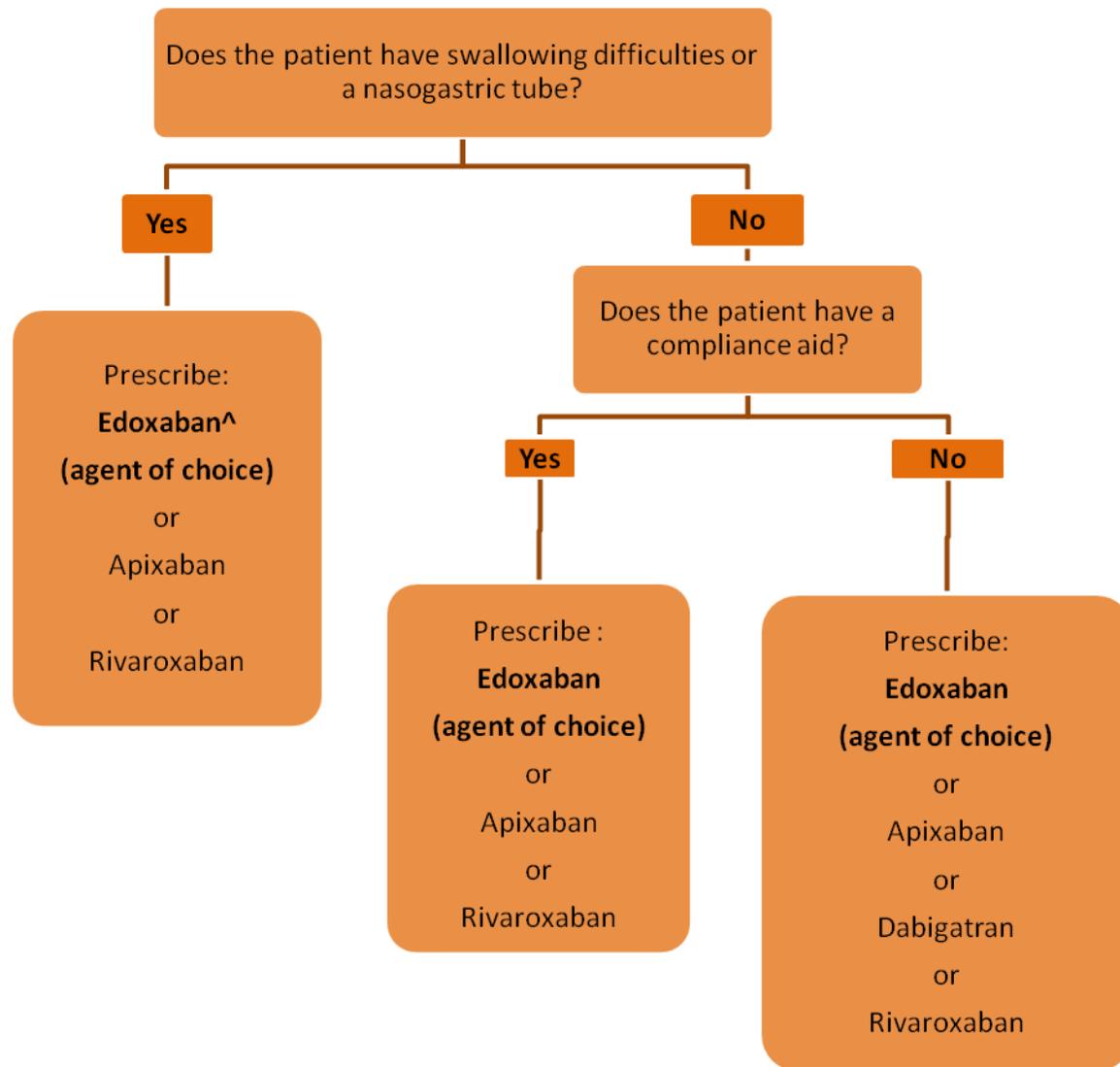
Rivaroxaban

20 mg once daily
 (NB. GGC Formulary restricts use of rivaroxaban to patients switching from warfarin, i.e not for newly diagnosed AF patients)

^Crushing edoxaban for patients with swallowing difficulties or administration via nasogastric tubes is off-label

Decision making algorithm 2: DOAC choices in non-valvular AF patients with creatinine clearance 30 - 50ml/min*

Refer to the latest version of the manufacturer's summary of product characteristics (SPC) for full prescribing advice



Dose Information

Apixaban

5 mg twice daily or 2.5 mg twice daily if at least 2 of the following:
 ≥80 years old
 ≤60 kg
 Cr ≥133 micromol/L

Dabigatran*

150 mg twice daily or 110 mg twice daily if high risk of bleeding or ≥80 years old or concomitant verapamil

***Additional prescribing notes for dabigatran**

A dose reduction to 110mg twice daily may be considered if the patient has low thromboembolic risk combined with a high risk of bleeding and one or more of the following factors:

- Age 75 – 79 years; if standard dose is used then it should be reduced when patient reaches 80 years old
- Creatinine clearance 30 – 50ml/min
- Body weight of < 50kg
- Gastritis, oesophagitis or gastro-oesophageal reflux

Edoxaban

30 mg once daily

Rivaroxaban#

If CrCl = 50ml/min: 20 mg once daily
 If CrCl 30-49ml/min: 15 mg once daily
 (NB. GGC Formulary restricts use of rivaroxaban to patients switching from warfarin, i.e not for newly diagnosed AF patients)

^Crushing edoxaban for patients with swallowing difficulties or administration via nasogastric tubes is off-label

Decision making algorithm 3: DOAC choices in non-valvular AF patients with creatinine clearance 15 - 29ml/min

Refer to the latest version of the manufacturer's summary of product characteristics (SPC) for full prescribing advice

Prescribe:
Edoxaban 30 mg once daily^
(agent of choice)
or
Apixaban 2.5 mg twice daily
or
Rivaroxaban 15 mg once daily*
(use with caution)

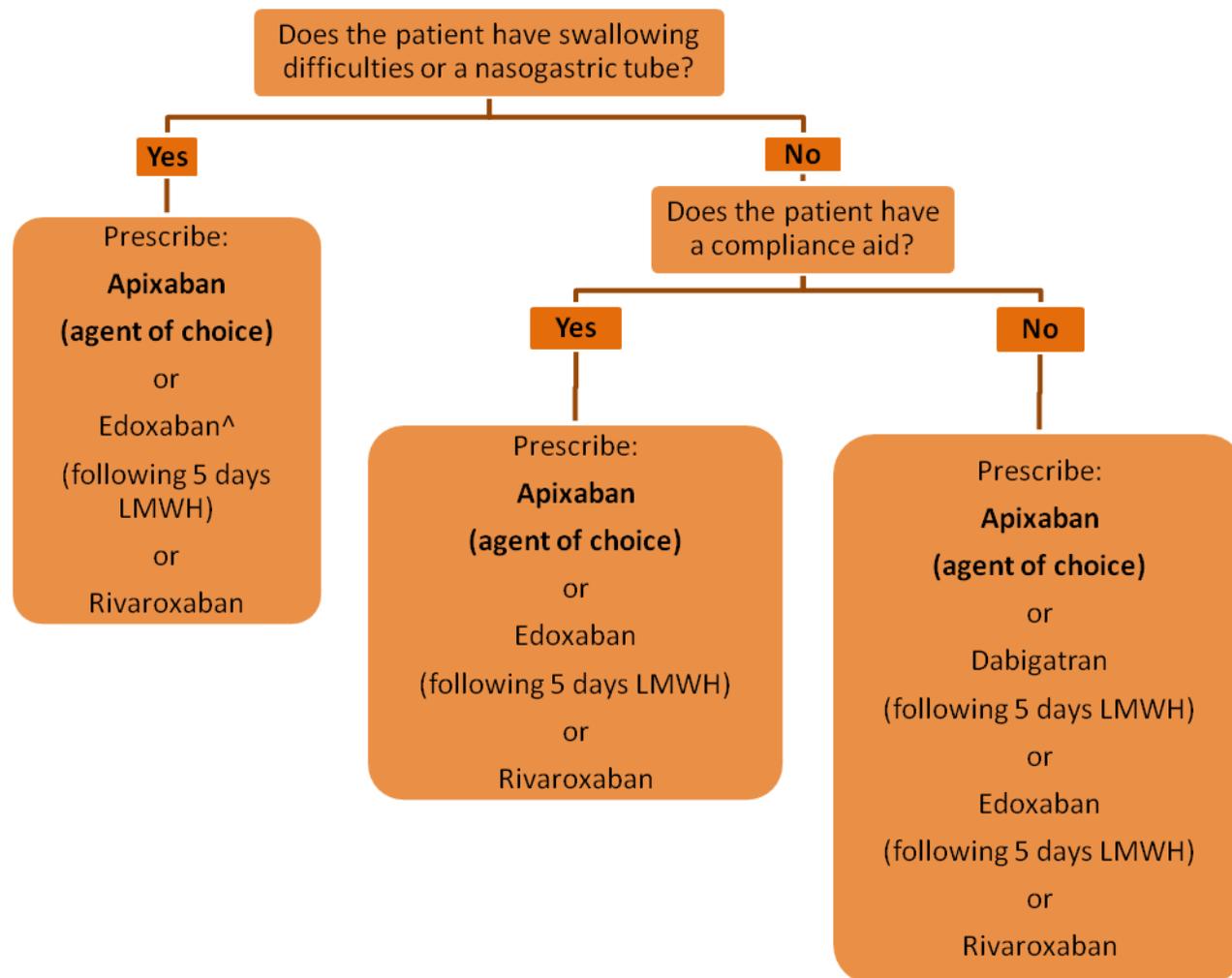
Please note

^Crushing edoxaban for patients with swallowing difficulties or administration via nasogastric tubes is off-label

**GMC Formulary restricts use of rivaroxaban to patients switching from warfarin, i.e not for newly diagnosed patients*

Decision making algorithm 4: DOAC choices in VTE patients without renal impairment (creatinine clearance > 50ml/min)

Refer to the latest version of the manufacturer's summary of product characteristics (SPC) for full prescribing advice



Dose Information

Apixaban

10 mg twice daily for 7 days then 5 mg twice daily. If long term use is indicated for prophylaxis of recurrent VTE, 2.5 mg twice daily should be prescribed after the initial 6 months treatment has been completed.

Dabigatran*

150 mg twice daily or 110 mg twice daily if ≥ 80 years old or concomitant verapamil

*Additional prescribing notes for dabigatran

A dose reduction to 110mg twice daily may be considered if the patient has low thromboembolic risk combined with a high risk of bleeding and one or more of the following factors:

- Age 75 – 79 years; if standard dose is used then it should be reduced when patient reaches 80 years old
- Creatinine clearance 30 – 50ml/min
- Body weight of < 50kg
- Gastritis, oesophagitis or gastro-oesophageal reflux

Edoxaban

60 mg once daily or 30 mg once daily if ≤ 60 kg or concomitant use of the following P-gp inhibitors: ciclosporin, dronedarone, erythromycin, ketoconazole

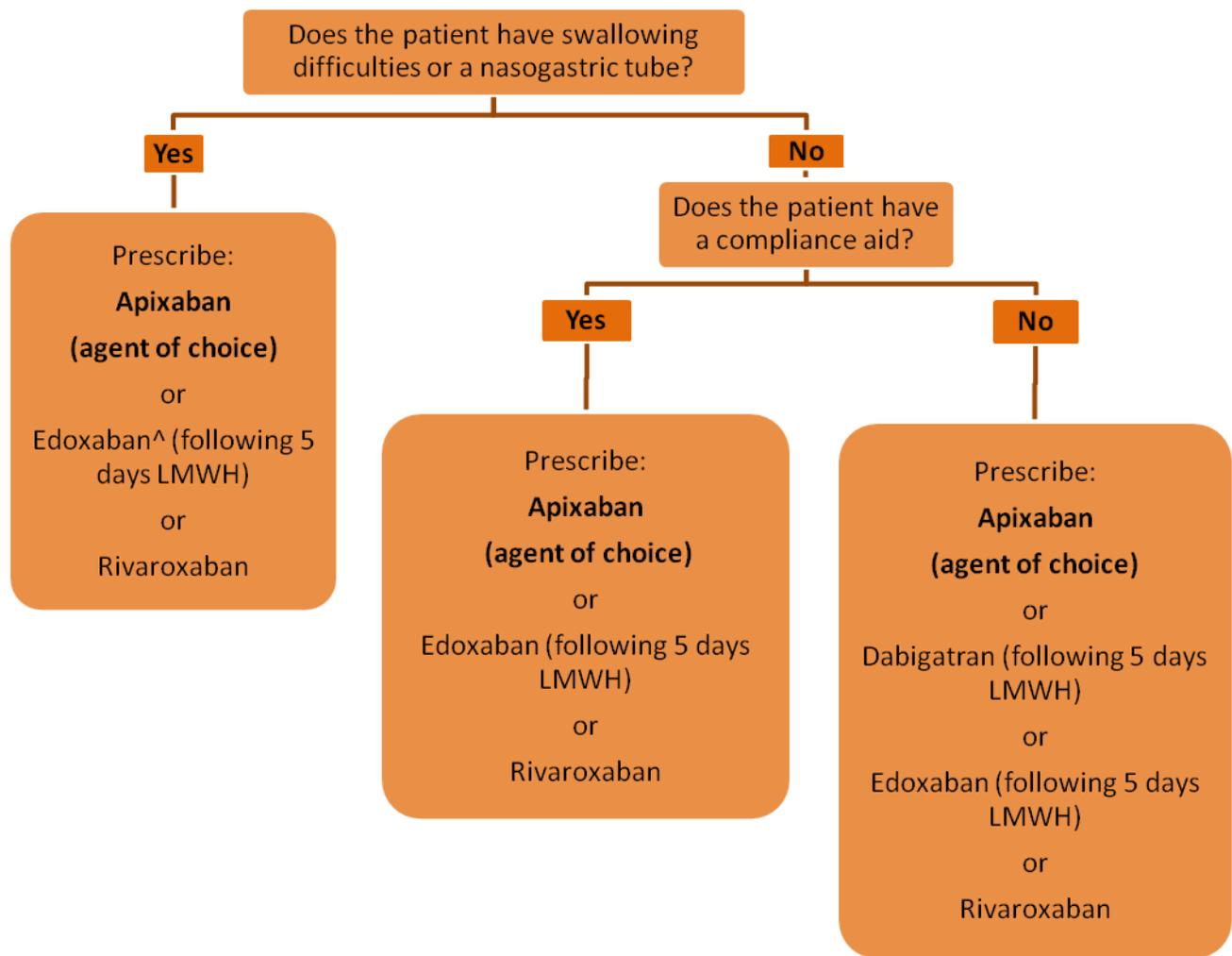
Rivaroxaban

15 mg twice daily for 3 weeks then 20 mg once daily. Refer to the SPC for dosing advice if long term use is indicated for prophylaxis of recurrent VTE after the initial 6 months treatment has been completed.

[^]Crushing edoxaban for patients with swallowing difficulties or administration via nasogastric tubes is off-label

Decision making algorithm 5: DOAC choices in VTE patients with creatinine clearance 30 - 50ml/min*

Refer to the latest version of the manufacturer's summary of product characteristics (SPC) for full prescribing advice



Dose Information

Apixaban

10 mg twice daily for 7 days then 5 mg twice daily. If long term use is indicated for prophylaxis of recurrent VTE, 2.5 mg twice daily should be prescribed after the initial 6 months treatment has been completed.

Dabigatran*

150 mg twice daily or 110 mg twice daily if ≥ 80 years old or concomitant verapamil

***Additional prescribing notes for dabigatran**

A dose reduction to 110mg twice daily may be considered if the patient has low thromboembolic risk combined with a high risk of bleeding and one or more of the following factors:

- Age 75 – 79 years; if standard dose is used then it should be reduced when patient reaches 80 years old
- Creatinine clearance 30 – 50ml/min
- Body weight of < 50kg
- Gastritis, oesophagitis or gastro-oesophageal reflux

Edoxaban

30 mg once daily

Rivaroxaban#

If CrCl = **50ml/min**: 15 mg twice daily for 3 weeks then 20 mg once daily

If CrCl **30-49ml/min**: 15 mg twice daily for 3 weeks then 20 mg once daily. If risk of bleeding outweighs the risk for recurrent DVT/PE, 15 mg twice daily for 3 weeks then 15 mg once daily.

Refer to the SPC for dosing advice if long term use is indicated for prophylaxis of recurrent VTE after the initial 6 months treatment has been completed.

^ Crushing edoxaban for patients with swallowing difficulties or administration via nasogastric tubes is off-label

Decision making algorithm 6: DOAC choices in VTE patients with creatinine clearance 15 - 29ml/min

Refer to the latest version of the manufacturer's summary of product characteristics (SPC) for full prescribing advice

Prescribe:
Apixaban (agent of choice)
(use with caution)
or
Edoxaban[^]
(following 5 days LMWH)
or
Rivaroxaban
(use with caution)

Dose Information

Apixaban

10 mg twice daily for 7 days then 5 mg twice daily.
If long term use is indicated for prophylaxis of recurrent VTE, 2.5 mg twice daily should be prescribed after the initial 6 months treatment has been completed.

Edoxaban

30 mg once daily

Rivaroxaban

15 mg twice daily for 3 weeks then 20 mg once daily. If risk of bleeding outweighs the risk for recurrent DVT/PE, 15 mg twice daily for 3 weeks then 15 mg once daily. Refer to the SPC for dosing advice if long term use is indicated for prophylaxis of recurrent VTE after the initial 6 months treatment has been completed.

[^]*Crushing edoxaban for patients with swallowing difficulties or administration via nasogastric tubes is off-label*

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Produced by NHS Greater Glasgow and Clyde Medicines Information Service ♦ Approved by the Medicines Utilisation Subcommittee of the ADTC ♦ Tel: 0141 211 4407 Email: medinfo@ggc.scot.nhs.uk

PLEASE NOTE, THE INFORMATION IN THIS BULLETIN WAS CORRECT AT THE TIME OF PUBLICATION

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