

NOAC Prescribing in Patients with Non-Valvular Atrial Fibrillation: Frequently Asked Questions

*FAQ document jointly prepared by NHSGGC Haematology Service &
Medicines Information
On behalf of the Heart MCN (February 2015)*

*This document supersedes previous document entitled "Guidance on Anticoagulant Choice
in Patients with Non-Valvular Atrial Fibrillation, Version 2 August 2014"*

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Introduction

NHSGGC guidance states that patients with non-valvular atrial fibrillation (AF), who are believed to be adhering to warfarin therapy but have a poorly controlled INR, should be considered for a Novel Oral Anticoagulant (NOAC). A poorly controlled INR in this context is defined as therapeutic INR < 60% of the time. The NOACs (apixaban, dabigatran and rivaroxaban) should result in more stable anticoagulation. The Glasgow and Clyde Anticoagulation Service (GCAS) will identify such patients and contact their GPs to suggest consideration of a switch to one of the NOACs. Various factors may influence the decision to change to a NOAC and the choice between the three agents. GPs should consider these factors and patient preference before making a final decision.

The 2014 NHSGGC AF guideline also includes an option to prescribe a NOAC as a first-line anticoagulant in patients newly diagnosed with non-valvular AF requiring anticoagulation.

Section 1: Questions relating to indications/appropriateness of NOACs

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

No - NOACs are *not* indicated in patients with rheumatic mitral stenosis, mechanical prosthetic heart valve or who have had a valve repair or a tissue valve replacement.

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

A NOAC 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.

Section 2: Questions relating to choice of NOAC & dose

All 3 NOACs are indicated for AF and the dosing regimens are all different. How do I choose the most appropriate agent and dose for my patient?

The NOACs 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. All three NOACs are on the GGC Formulary for switching from warfarin due to poor INR control. Apixaban and dabigatran but not rivaroxaban are on the Formulary for newly diagnosed AF.

For patients without renal impairment (creatinine clearance [CrCl] > 50ml/min) any of the three NOACs may be used and the other factors described above will be more important in determining choice of agent and appropriate dose. [Algorithm 1](#) takes these factors into consideration and helps define the available options and doses for individual patients

In patients where there are no specific factors affecting agent or dose, the choice depends simply on licensed indications and personal preference. Prescribers may find it helpful to become familiar with one NOAC in particular.

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

All 3 NOACs may be used but the agent and dose depends on the degree of impairment:

- **Creatinine Clearance 30 – 49ml/min**
All 3 NOACs may be used in this degree of renal impairment.
Depending on other factors dose reductions may be required - use [Algorithm 2](#)
- **Creatinine Clearance 15 – 29ml/min**
Dabigatran is contraindicated.
Apixaban or rivaroxaban may be used but require dose reductions - use [Algorithm 3](#)
- **Creatinine Clearance <15ml/min**
All NOACs are contraindicated if CrCl is less than 15ml/min

Do not use eGFR to evaluate degree of renal impairment. The “Cockcroft Gault” equation can be used to estimate CrCl:

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

There is also an online Cockcroft Gault calculator which may be found [here](#). (Please note that if you are accessing from an NHS computer you will be taken directly to the calculator, **though you may have to scroll down to see it**. If you are accessing from outwith the NHS you will need to login first using an NHSScotland Athens password).

Warning: for patients with an age greater than 70 years or with an ideal weight outside of the range 45 – 90kg – the online calculator may issue a warning about validity of the result but will still generate an estimated CrCl. 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) when choosing the most appropriate dose.

Regardless of whether this calculation is done manually or using the calculator the following should be considered:

- Use 60 micromol/L if the creatinine concentration is < 60 micromol/L
- This equation may overestimate CrCl in elderly or malnourished patients
- Use ideal body weight (see below) rather than actual body weight

Ideal body weight (IBW) estimation

Height Feet/inches	Height cm	Female IBW	Male IBW
5'	152	45.5	50
5'1"	155	47.8	52.3
5'2"	157	50.1	54.6
5'3"	160	52.4	56.9
5'4"	163	54.7	59.2
5'5"	165	57	61.5
5'6"	168	59.3	63.8
5'7"	170	61.6	66.1
5'8"	173	63.9	68.4
5'9"	175	66.2	70.7
5'10"	178	68.5	73
5'11"	180	70.8	75.3
6'	183	73.1	77.6
6'1"	185	75.4	79.9
6'2"	188	77.7	82.2
6'3"	190	80	84.5
6'4"	193	82.3	86.8

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

It may not be necessary however to recalculate creatinine clearance every year if weight and eGFR are stable. Every 5 years may be sufficient. Please note however that an annual recalculation may be prudent in those patients whose creatinine clearance is borderline for dose reduction anyway. Additionally review of dosing is necessary when the patient reaches 80 years old and if they have lost weight or their eGFR has changed.

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

Any of the 3 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 as described above.

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

NOACs have fewer drug interactions than warfarin but there are some to be aware of. There are some pharmacokinetic differences between the three drugs however the available data does not currently demonstrate a clear difference in interaction profile. For patients on **verapamil** a reduced dose of dabigatran is necessary and there are a number of drugs that should not be used in combination with any of the NOACs. See table below.

Potentially interacting agents	Suggested action
Antiplatelets: Aspirin, Clopidogrel, Ticagrelor, Prasugrel, Dipyridamole (Increased bleeding risk with NOACs)	Discontinue antiplatelet unless advised otherwise (see question below)
Ketoconazole, Itraconazole, Voriconazole, Posaconazole, HIV protease inhibitors, Hepatitis C protease inhibitors, Dronedarone (Increased anticoagulant exposure)	Avoid combination with NOACs
Rifampicin, Phenytoin, Carbamazepine, Phenobarbitone, St Johns Wort (Decreased anticoagulant exposure)	Avoid combination with NOACs
Tacrolimus, Ciclosporin (No data - increased anticoagulant exposure possible on theoretical grounds)	Suggest avoid combination with NOACs

Please note

- Data are taken from published sources where possible. In some cases, due to a paucity of data, the advice is based on interpretation of known pharmacokinetics of the NOACs, specialist advice, or, where appropriate, extrapolation of published information from one of the other NOACs
- Available data is limited and may change as NOACs become more widely prescribed.
- 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 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 NOAC is started?

The co-prescription of an antiplatelet agent with a NOAC confers an additional bleeding risk. 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.

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

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 and dabigatran dosing in relation to food is unimportant.

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

There is information to suggest that either rivaroxaban or apixaban may be crushed and administered via a nasogastric tube. Dabigatran is not suitable for administration in this way.

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

Dabigatran is not suitable for inclusion in a standard compliance aid but either apixaban or rivaroxaban may be included.

Section 3: Questions relating to NOAC initiation (New patients and existing patients switching from warfarin)

I have determined that a NOAC is appropriate for my patient 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: The patient may be started on an appropriate dose of the relevant NOAC 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 NOAC
2. be asked to obtain a supply of the NOAC 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 NOAC 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 NOAC, 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 NOAC started

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

Apixaban and dabigatran may be initiated when INR is <2 and rivaroxaban when INR is <3. If it is known that this is the case then a NOAC could potentially be started immediately without a three day gap.

Section 4: Further information and advice

Is there any patient education literature available?

All 3 NOACs have a manufacturer's Patient Information Leaflet. There is some discussion going on nationally regarding the possibility of a standardised patient booklet and alert card however it may be some time before this is available. Meantime a patient information booklet adapted from the NPSA warfarin booklet and an alert card have been produced in NHSGGC. Arrangements for how these are printed, distributed and obtained locally are still subject to discussion. However the information is available in an electronic format to download [here](#).

Should the patient carry an Alert Card, and where should they get it from?

See previous question.

Who should educate the patient about starting an anticoagulant?

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

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

The marketing authorisation of any of the three available NOACs 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. The manufacturers of the other two NOACs make no specific recommendation about this however it may be good practice to take the same approach regardless of which NOAC is used. This annual check could be used as an opportunity to assess adherence and reassess whether an anticoagulant/NOAC 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).

Useful Contacts for further advice

Consultant Haematologists: For questions relating to switching from warfarin to a NOAC

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

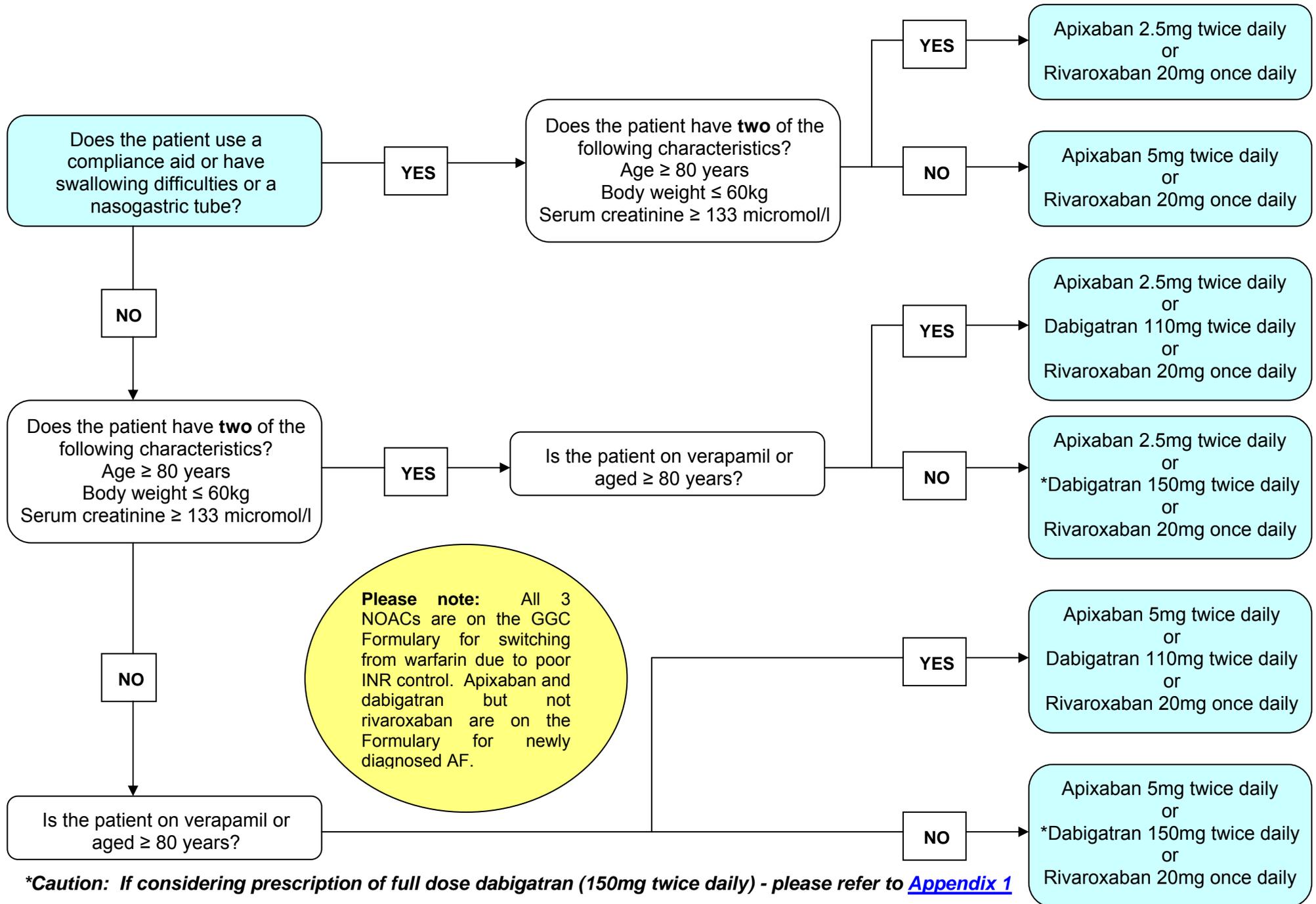
Consultant Cardiologists: For questions relating to indications for anticoagulation in patients with AF, and further investigation or treatment of AF

Joanne Lindsay	0141 211 4727	joanne.lindsay@ggc.scot.nhs.uk
Iain Findlay	0141 887 9111	iain.findlay@nhs.net
David Murdoch	0141 201 1763	david.murdoch@ggc.scot.nhs.uk

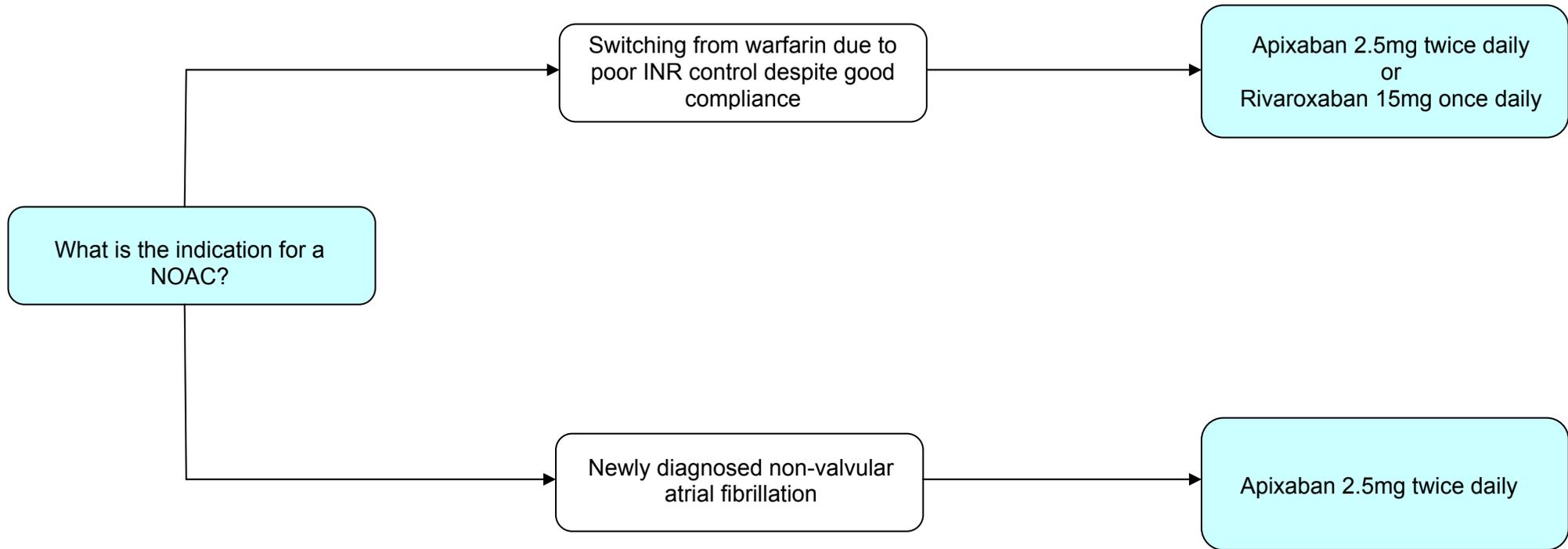
Medicines Information: For questions relating specifically to the medicines (e.g. dosing, administration, interactions etc)

Medicines Information	0141 211 4407	medinfo@ggc.scot.nhs.uk
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Decision making algorithm 1: NOAC choices in AF patients *without renal impairment (creatinine clearance > 50ml/min)*



Decision making algorithm 3: NOAC choices in AF patients *with creatinine clearance 15 - 29ml/min*



Appendix 1: Additional information

Additional prescribing notes for dabigatran

There is an option to consider dose reduction of dabigatran based on other factors. In addition to patients ≥ 80 years, 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 – 49ml/min
- Body weight of < 50kg
- Gastritis, oesophagitis or gastro-oesophageal reflux