NHS Grampian

Direct Oral Anticoagulant (DOAC) Prescribing Guidance For The Prevention Of Stroke And Systemic Embolism In Adult Patients With Non-Valvular Atrial Fibrillation (NVAF)

Co-ordinators:		**Approver:**
Clinical Pharmacist Cardiology		Medicine Guidelines and Policies Group

Signature:		**Signature:**
		

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Executive Sign-Off

This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature: _____

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Responsibilities for implementation:

Organisational: Chief Executive and Management Teams
Corporate: Senior Managers
Departmental: Heads of Service/Clinical Leads
Area: Line Managers
Hospital/Interface services: Assistant General Managers and Group Clinical Directors
Operational Management Unit: Unit Operational Managers

Policy statement: It is the responsibility of all staff to ensure that they are working to the most up to date and relevant policies, protocols procedures.

Review: This policy will be reviewed in three years or sooner if current treatment recommendations change.

Responsibilities for review of this document:	Medicines Management Team
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Revision History:

Revision Date	Previous Revision Date	Summary of Changes (Descriptive summary of the changes made)	Changes Marked* (Identify page numbers and section heading)
March 2023	April 2021	Addition of information regarding weight influencing choice of DOAC or warfarin.	P1/P2 - notes section weight
March 2023	April 2021	Addition of information re ORBIT bleeding risk score.	P2 - Flow charts and baseline monitoring section
March 2023	April 2021	Removal of link to Scientific and Standardisation Committee – International Society on Thrombosis and Haemostasis.	P2 – Apixaban Prescribing Information
March 2023	April 2021	Addition of statement (may be appropriate if warfarin unsuitable).	Apixaban cautions P5/P7
March 2023	April 2021	Warfarin to rivaroxaban switching information addition of ‘re-check INR in 3 days if >3’.	Rivaroxaban Prescribing Information - Switching Warfarin to Rivaroxaban P7
March 2023	April 2021	Updated consultation group.	P9
March 2023	April 2021	Updated references.	P9

* Changes marked should detail the section(s) of the document that have been amended, i.e. page number and section heading.

Direct Oral Anticoagulant (DOAC) Prescribing Guidance For The Prevention Of Stroke And Systemic Embolism In Adult Patients With Non-Valvular Atrial Fibrillation (NVAF)

- **Apixaban is the first line choice of DOAC for NVAF in NHS Grampian.**
- **Rivaroxaban is the second line choice of DOAC and should be considered where apixaban is not suitable.**
- **Warfarin may still be the most appropriate anticoagulant for some patients.**

Notes:

Definition of Non-Valvular Atrial Fibrillation (NVAF)

The term “Valvular AF" refers to patients with mitral stenosis (moderate or severe) or mechanical heart valves and such patients should be considered **only** for warfarin therapy for stroke prevention. The term “Non-Valvular AF” therefore encompasses cases of AF in the absence of the above.

Biological valve replacements, or other valvular heart conditions, such as mitral regurgitation, aortic stenosis and aortic regurgitation, do not tend to result in conditions of low flow in the left atrium and therefore are not thought to further increase the risk of thromboembolism brought by AF. This group of patients, when it comes to choice of oral anticoagulation, can also be included under the term Non-Valvular AF and the choice of anticoagulant could include either warfarin or a DOAC.

Renal Monitoring for DOACs

All DOACs are renally excreted and may require dose adjustment according to renal function. It is important to note that the choice of dosage is based on a calculation of creatinine clearance (CrCl) using the Cockcroft-Gault equation (Box A).

Creatinine clearance using the Cockcroft-Gault equation is not the same as the estimated glomerular filtration rate (eGFR). If the eGFR is used this may overestimate renal clearance particularly in elderly patients with low body weight/body mass index.

When calculating CrCl, it is recommended to use adjusted body weight in overweight patients BMI ≥25.

GP clinical systems have built in tools to calculate CrCl, when using these tools it is necessary to ensure up to date clinical parameters particularly weight and renal function. Up to date clinical parameters and ensuring the correct BMI has been selected will enable the calculator to use actual, ideal or adjusted body weight as appropriate (this is essential when BMI ≥25 where adjusted body weight should be used in the calculations).

Not using the Cockcroft-Gault equation to calculate CrCl may result in prescribing the incorrect DOAC dose. This may put patients at increased risk of embolic events/preventable strokes if a lower dose is prescribed or at increased risk of bleeding if a higher than indicated dose is prescribed.

Body Weight – Influencing choice of Warfarin or DOAC

Warfarin remains the first line choice, for the treatment of NVAF, in patients with increased body weight (BMI >40 or >120kg). However, there is some evidence that apixaban and rivaroxaban may also be suitable options for these patients. This is based on the International Society on Thrombosis and Haemostatis (ISTH) sub-committee communication regarding DOAC use in patients, above these weights, in the treatment and prevention of venous thromboembolism. This evidence is limited in patients with BMI >50, however it may still be acceptable to use following appropriate risk assessment.

If a patient is deemed unsuitable for warfarin therapy, if the risk/benefit of using warfarin therapy is negative, or it they are unable to hold an adequate time in the therapeutic range for their target INR, then either apixaban or rivaroxaban may be considered as alternative treatment.

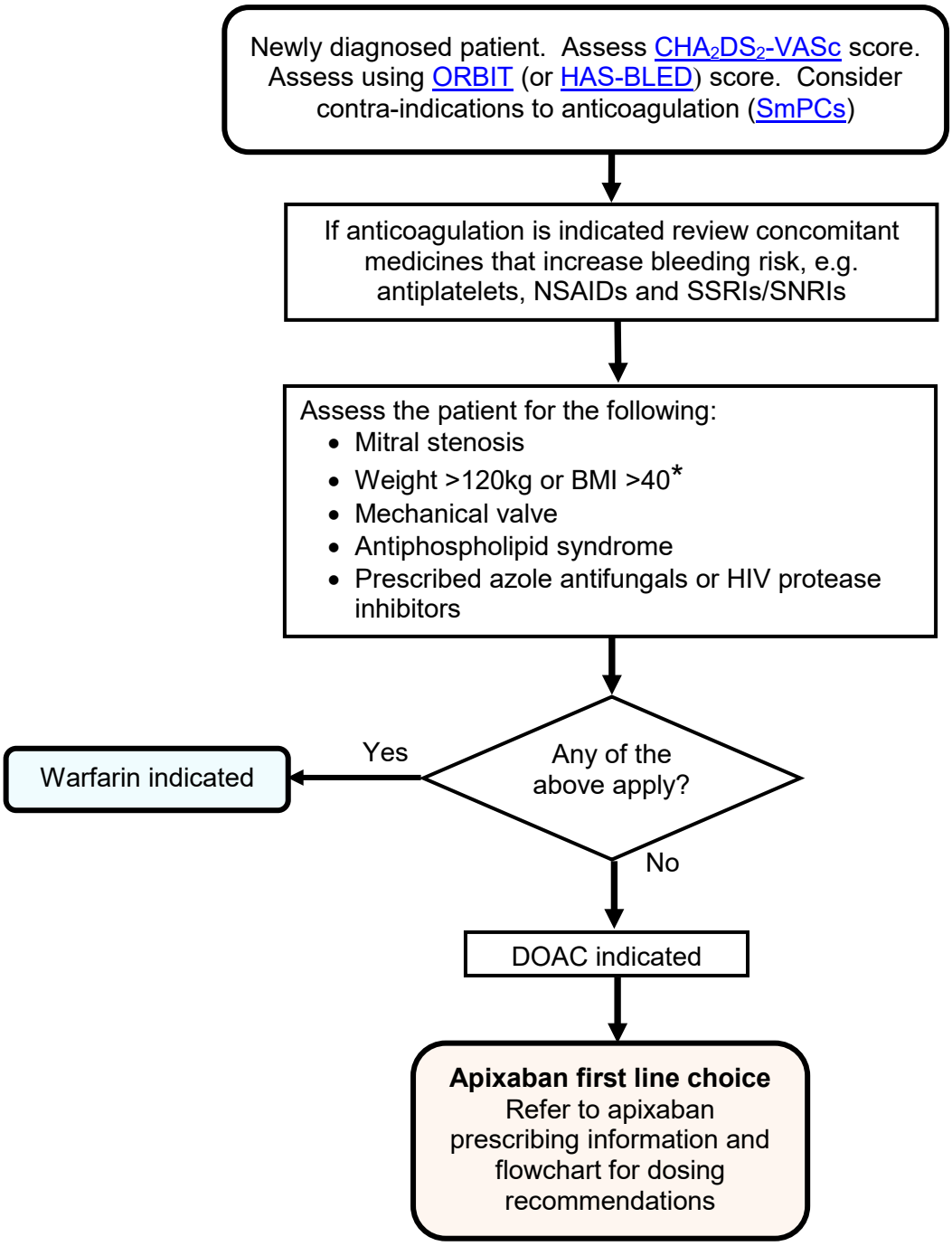
Low body weight ≤60kg is considered a risk factor that may necessitate a dose reduction of apixaban to 2.5mg twice daily. Review of all risks (age, renal function, creatinine and weight) is required to determine the appropriate dose.

Bleeding Risk Score – ORBIT or HAS-BLED

NICE guideline (NG196) Atrial Fibrillation: Diagnosis and management states that the ORBIT bleeding risk score is preferred. Evidence shows that it has a higher accuracy in predicting absolute bleeding risk than other bleeding risk tools. Accurate knowledge of bleeding risk supports shared decision making and has practical benefits, for example, increasing patient confidence and willingness to accept treatment when risk is low and prompting discussion of risk reduction when risk is high. Although ORBIT is the best tool for this purpose, other bleeding risk tools (such as HAS-BLED) may need to be used until ORBIT is embedded in clinical pathways and electronic systems.

Calculations of risk score on any system will only be accurate when coding is up to date, clinical history should be confirmed with the patient.

DOAC/Anticoagulation Initiation Guidance (Non-Valvular Atrial Fibrillation)



Box A - Cockcroft-Gault

CrCl mL/min = ((140 - age) x (actual weight (kg)) x (constant^)
Cr (µmol/L)

^constant = 1.23 men/1.04 woman

Note: Need to use adjusted body weight (ABW) if overweight, BMI ≥25

ABW = Ideal Body Weight (IBW) + 0.4 (Actual Body Weight – IBW)

IBW (men) = 50kg + 2.3kg (height [inches] **–** 60 [inches])

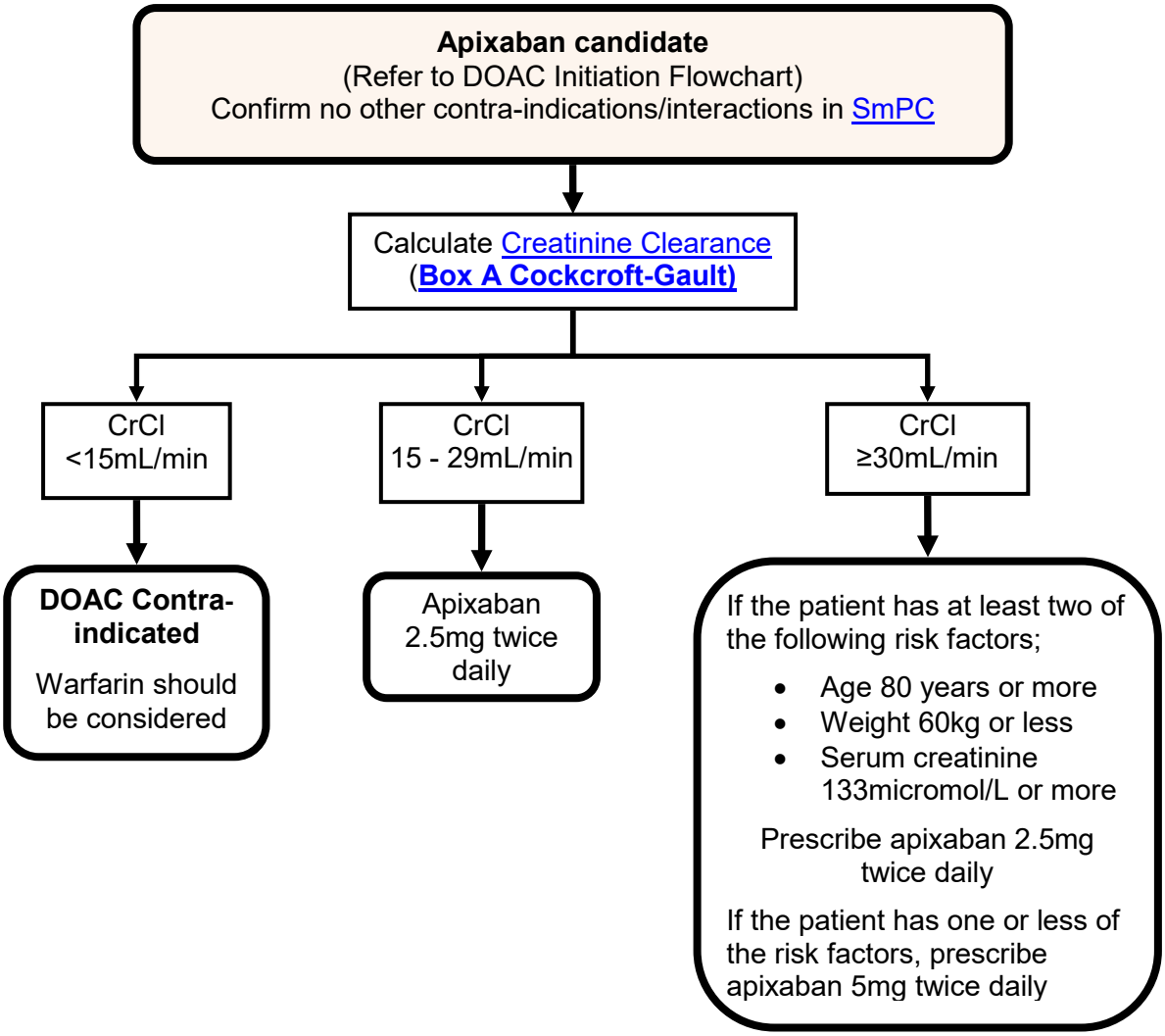
IBW (women) = 45.5kg + 2.3kg (height [inches] **–** 60 [inches])

If using Creatinine Clearance calculator refer to *Creatinine Clearance Modified for Overweight Patients* result.

**See section on body weight for more information (page 2)*

Apixaban Prescribing Information

Apixaban is the first line choice of DOAC.



Contra-indications – Apixaban is NOT recommended in the following situations:

- Concomitant treatment with any other anticoagulant except when switching therapy or under specialist supervision.
- Allergy or hypersensitivity to active ingredient or excipients.
- Active bleeding/major bleeding risks – unless under specialist recommendation and review.
- CrCl <15mL/min, or on dialysis.
- Severe liver impairment.
- Pregnancy/breastfeeding.
- Uncontrolled severe hypertension.
- Concomitant treatment with HIV protease inhibitors, azole antifungals.
- Conditions where warfarin is preferred, i.e. mitral stenosis, mechanical valve.
- Treatment failure while on apixaban (e.g. ischaemic stroke/systemic embolism while on treatment) further discussion with haematology advised.

Apixaban Prescribing Information

Additional Cautions

- Weight >120kg or BMI >40 (may be appropriate if warfarin not suitable). See section on body weight for more information (page 2).
- Surgery please refer to EHRA guidance 'Practical Guide on the use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation' (section 12).
- Drug therapy (this list is not exhaustive – refer to individual SmPC)
  - CYP3A4 and P-gp inducers (e.g. rifampicin, St John's Wort, carbamazepine, phenytoin, phenobarbital) – can reduce effect of apixaban, caution advised.
  - CYP3A4 inhibitors (e.g. amiodarone) – can ↑ effect of apixaban, no dose adjustments necessary however ensure appropriate counselling.
  - Antibiotics – avoid erythromycin/clarithromycin. Consider appropriate alternatives e.g. doxycycline.
  - Clopidogrel – only if following specialist cardiology advice.

Dosage – As per flow chart above, dependant on risk factors either apixaban 2.5mg or 5mg twice daily.

Monitoring Requirements

BASELINE	U+Es (inc CrCl – calculate using Cockcroft-gault calculator/Box A), LFTs, FBC, ORBIT (or HAS-BLED) score, CHA_2DS_2-VASc score.
ONGOING	- Review treatment annually as a minimum – include compliance assessment, side-effects, Over the Counter (OTC) medicines, risk factors (age, weight). - Review full bloods (U+Es, CrCl, LFTs + FBC, serum creatinine) annually. *(Note it is recommended if CrCl<60mL/min monitoring is more frequent than annually – EHRA guidance recommends monitoring CrCl/10 (in months) e.g. CrCl 50mL/min recommended monitoring every 5 months).* - If CrCl <15mL/min apixaban is no longer recommended, a review is required and consider switch to warfarin. - If CrCl 15-29mL/min ensure appropriate apixaban dose is prescribed, 2.5mg twice daily. - If two or more risk factors (≥80years, ≤60kg, serum creatinine ≥133micromol/L) ensure appropriate apixaban dose is prescribed, 2.5mg twice daily.

Switching

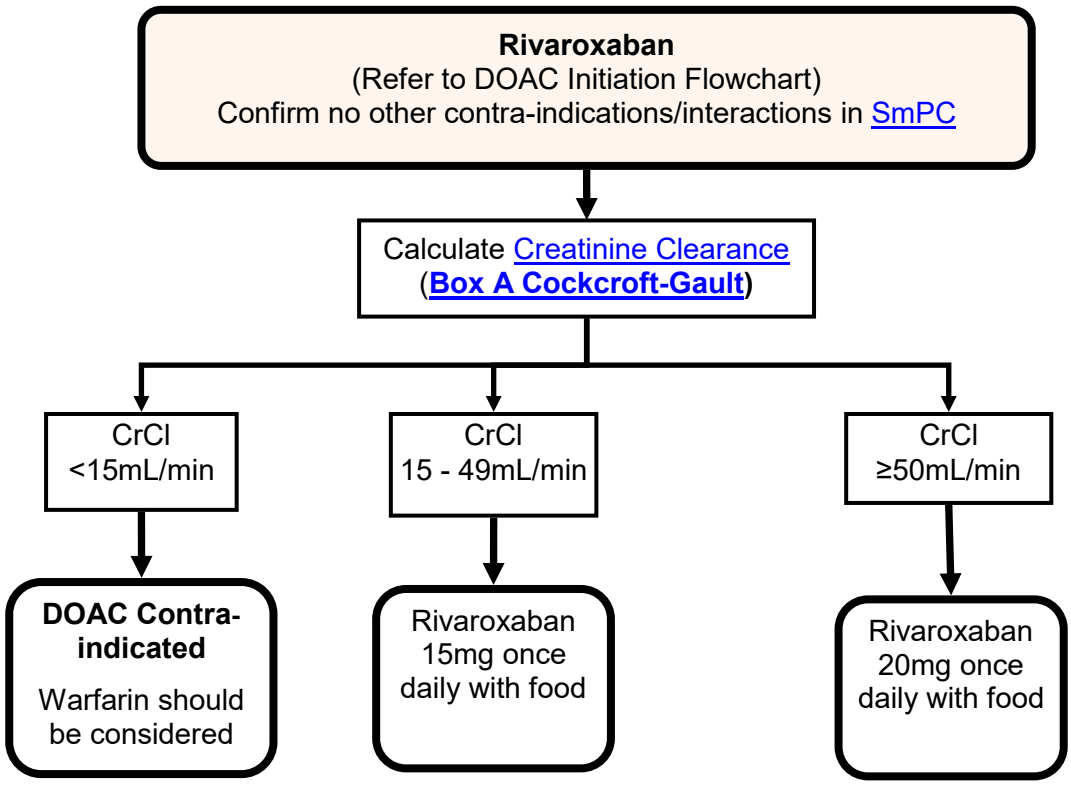
Warfarin → Apixaban	**DOAC → Alternative DOAC (e.g. edoxaban to apixaban)**
Check baseline INR. Discontinue warfarin and re-check INR in 3 days if >2; Start apixaban when INR <2. **Ensure very careful and robust counselling advice to ensure a safe switch.**	Agree designated switch day to allow the patient to use up supplies of current DOAC. The designated switch day should be the day following completion of the current DOAC supplies and the new DOAC should be taken when the next dose of the previous DOAC was due. Ensure the patient is aware of the dosing schedule for the new DOAC, i.e. apixaban twice daily.

Apixaban Prescribing Information

Counselling Points

- ✓ Advise patient to carry alert card at all times.
- ✓ This is lifelong treatment with regular monitoring required *(as outlined above).*
- ✓ Take as directed, regularly, do not stop without speaking to a healthcare professional.
- ✓ Ensure patient aware of signs of bleeding and what action to take.
- ✓ Ensure patient aware of what to do if a dose is missed.
- ✓ Inform all healthcare professionals (including dentist, pharmacist) of DOAC treatment.
- ✓ Advise patient must check with a pharmacist before taking any new medicine (including over the counter medicines and supplements) to ensure it is suitable to take alongside their DOAC.
- ✓ Suitable to go in a compliance aid (ensure communication with community pharmacy).
- ✓ Link to DOAC video for patients.
- ✓ Additional patient support materials can be found here.

In circumstances where apixaban is not suitable, rivaroxaban is the second line DOAC.



Contra-indications – Rivaroxaban is NOT recommended in the following situations:

- Concomitant treatment with any other anticoagulant except when switching therapy or under specialist supervision.
- Allergy or hypersensitivity to active ingredient or excipients.
- Active bleeding/major bleeding risks – unless under specialist recommendation and review.
- CrCl <15mL/min, or on dialysis.
- Severe liver impairment.
- Pregnancy/breastfeeding.
- Uncontrolled severe hypertension.
- Concomitant treatment with HIV protease inhibitors, azole antifungals, dronedarone.
- Conditions where warfarin is preferred, i.e. mitral stenosis, mechanical valve.
- Treatment failure while on rivaroxaban (e.g. ischaemic stroke/systemic embolism while on treatment) further discussion with haematology advised.

Additional Cautions

- Weight >120kg or BMI >40 (may be appropriate if warfarin not suitable). See section on body weight for more information (page 2).
- Surgery please refer to EHRA guidance 'Practical Guide on the use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation' (section 12).
- Drug therapy (this list is not exhaustive – refer to individual SmPC)
  - CYP3A4 and P-gp inducers (e.g. rifampicin, St John's Wort, carbamazepine, phenytoin, phenobarbital) – can reduce effect of rivaroxaban caution advised
  - CYP3A4 inhibitors (e.g. amiodarone) – can ↑ effect of rivaroxaban, no dose adjustments necessary however ensure appropriate counselling
  - Antibiotics – avoid erythromycin/clarithromycin. Consider appropriate alternatives e.g. doxycycline
  - Clopidogrel – only if following specialist cardiology advice.

Dosage – As per flow chart above, dependant on renal function, either 15mg or 20mg once daily with food.

To note, other doses are not licensed for the prevention of stroke and systemic embolism in NVAF.

Monitoring Requirements

BASELINE	U+Es (inc CrCl – calculate using Cockcroft-gault calculator/Box A), LFTs, FBC, ORBIT (or HAS-BLED) score, CHA_2DS_2-VASc score
ONGOING	- Review treatment annually as a minimum – include compliance assessment, side-effects, Over the Counter (OTC) medicines, risk factors (age, weight). - Review full bloods (U+Es, CrCl, LFTs + FBC, serum creatinine) annually. *(Note it is recommended if CrCl<60mL/min monitoring is more frequent than annually – EHRA guidance recommends monitoring CrCl/10 (in months) e.g. CrCl 50mL/min recommended monitoring every 5 months).* - If CrCl <15mL/min rivaroxaban is no longer recommended, a review is required and consider switch to warfarin. - If CrCl 15-49mL/min ensure appropriate rivaroxaban dose is prescribed, 15mg once daily.

Switching

Warfarin → Rivaroxaban	**DOAC → Alternative DOAC (e.g. edoxaban to rivaroxaban)**
Check baseline INR. Discontinue Warfarin and recheck INR in 3 days if >3; Start rivaroxaban when INR ≤3. **Ensure very careful and robust counselling advice to ensure a safe switch.**	Agree designated switch day to allow the patient to use up supplies of current DOAC. The designated switch day should be the day following completion of the current DOAC supplies and the new DOAC should be taken when the next dose of the previous DOAC was due. Ensure the patient is aware of the dosing schedule for the new DOAC and requirement to take with food.

Counselling Points

- ✓ Advise patient to carry alert card at all times.
- ✓ This is lifelong treatment with regular monitoring required *(as outlined above).*
- ✓ Take as directed, regularly, do not stop without speaking to a healthcare professional.
- ✓ Take with food.
- ✓ Ensure patient aware of signs of bleeding and what action to take.
- ✓ Ensure patient aware of what to do if a dose is missed.
- ✓ Inform all healthcare professionals (including dentist, pharmacist) of DOAC treatment.
- ✓ Advise patient must check with a pharmacist before taking any new medicine (including over the counter medicines and supplements) to ensure it is suitable to take alongside their DOAC.
- ✓ Suitable to go in a compliance aid (ensure communication with community pharmacy).
- ✓ Link to DOAC video for patients.
- ✓ Additional patient support materials can be found here.

Consultation Group (March 2023)

Name	Title
Rebecca Anderson	Lead Pharmacist NHS Grampian Medicines Information Centre
Dr Jonathan Affolter	Consultant Cardiologist
Lesley Coyle	Associate Director of Pharmacy, Grampian Medicines Management Team
Lynne Davidson	Clinical Pharmacist, Cardiology
Claire Douglas	Primary Care Pharmacist/Team Lead Aberdeen City HSCP
Dr Mohammed Khan	Consultant Haematologist
Karen Mckessack	Clinical Pharmacist ARI, Medical Team Lead
Dr Karen Simpson	GP, Cluster Lead, Garioch Cluster

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