NHS
Nottingham and Nottinghamshire

Procedure for switching to rivaroxaban for existing patients with non-valvular atrial fibrillation (NVAF) on edoxaban

This resource has been developed to facilitate the safe and effective switch from edoxaban to rivaroxaban, using current accessible references and is correct at the time of approval.

Clinicians using this resource must refer to local guidelines, use their own clinical judgement and take responsibility for their prescribing decisions.

Nottingham and Nottinghamshire ICB (N&N ICB) Medicines Optimisation Team only have oversight for the management of errors occurring within their own organisation. Each organisation is therefore responsible for any prescribing errors or omissions that may occur within their organisation because of using this resource and must follow their own safety governance process.

Organisations must inform N&N ICB Medicines Optimisation team should they become aware of any errors or updates required within this document.

Adapted from the Welsh Medicines Advice Service guidance for switching to apixaban. With thanks and acknowledgement to Derby & Derbyshire ICB Medicines Optimisation Team.

1. Contents

2. Introduction

There are currently four direct oral anticoagulants (DOACs) available and licensed in the UK for stroke prevention in non-valvular atrial fibrillation (NVAF); apixaban, dabigatran, edoxaban, and rivaroxaban. Apixaban and rivaroxaban are now available as a generic preparation, making them the most cost-effective DOACs.

This document gives guidance on switching from edoxaban to rivaroxaban (both once daily DOACs).

3. Non-valvular atrial fibrillation

Non-valvular atrial fibrillation refers to atrial fibrillation in the **absence of a mechanical prosthetic heart valve or moderate-to-severe mitral stenosis** (usually of rheumatic origin), where the choice of oral anticoagulant could include either warfarin or a DOAC.

4. Comparative efficacy

The evidence indicates that rivaroxaban is as effective as warfarin and other DOACs. Rivaroxaban is licensed for NVAF and has been recommended by NICE.

5. Scope

The procedure supports prescribers and pharmacists to:

- **switch individuals aged 18 years and over established on edoxaban, to rivaroxaban for stroke prevention in NVAF, where clinically appropriate** as part of shared decision making.
- **review the DOAC and dosing appropriateness prior to switching to ensure rivaroxaban is prescribed safely and only where appropriate.**

This procedure does not include advice on switching patients from warfarin to rivaroxaban, this is outside of the scope of this procedure.

This procedure does not include advice on switching patients from apixaban or dabigatran to rivaroxaban, this is outside of the scope of this procedure.

Changes should only be made AFTER consultation with the individual.

6. Individuals EXCLUDED from edoxaban to rivaroxaban switch

Individuals should not be switched to rivaroxaban if:

- They do not provide consent.
- They are less than 18 years of age.
- They have an indication other than NVAF (see section 6).
- They would not be able to consistently take rivaroxaban with a meal as this can significantly affect absorption and subsequent drug levels. This should be considered carefully in elderly and frail patients.
- They require drug administration via NJ/PEJ/PEGJ tube, as rivaroxaban should not be administered distal to the stomach – see Summary of Product Characteristics (SmPC) for details.
- They have a known hypersensitivity to rivaroxaban or any of the excipients.
- Their creatinine clearance is less than 15 mL/min, or they are undergoing dialysis (warfarin is recommended).
- No recent (within the last 6 months) recommended monitoring has occurred.
- They have metallic heart valves (warfarin is recommended).
- They have AF requiring intervention for acute coronary syndrome or planned cardioversion.
- They have severe hepatic impairment or hepatic disease with coagulopathy and clinically relevant bleeding risk.
- They have antiphospholipid syndrome.
- They are pregnant or breastfeeding.
- They have uncontrolled severe hypertension (systolic BP ≥170 mmHg and/or diastolic BP ≥100 mmHg).
- They have a major bleeding risk (e.g., current or recent gastrointestinal ulcer; oesophageal varices; recent brain/ spinal injury; recent brain, spine, or ophthalmic surgery; recent intracranial haemorrhage; malignant neoplasm at high risk of bleeding; vascular aneurysm; active bleeding; arteriovenous malformations; major intraspinal or intracerebral vascular abnormalities).
- They are taking the following medicines:
    - other anticoagulants
    - chronic NSAIDs use

Please refer to the APC Anticoagulants in AF document and to the SmPC for Rivaroxaban for information on interactions.

Please check the SmPC for the full list of contraindications and cautions to consider when switching to rivaroxaban. Patient preference is also an important factor to consider.

7. Patients prescribed DOACs for multiple indications

There are several reasons why patients may be taking a DOAC either for a fixed period or for the long-term. All DOACs are licensed and approved by NICE for prevention of stroke in NVAF and for the treatment/prophylaxis of thrombosis (DVT/PE). Some DOACs are also used for thromboprophylaxis following joint replacement. This procedure is for **patients receiving a DOAC for stroke prevention in NVAF**. If a patient is on a long-term DOAC for another indication, this is outside of the scope of this procedure.

8. Switching to rivaroxaban

- When individuals on edoxaban for NVAF present for a medication review or DOAC monitoring is due the prescriber should consider switching the DOAC to rivaroxaban as part of shared decision making.
- A search can be run to identify suitable individuals:
    - adults aged 18 years and over who are currently receiving prescriptions for edoxaban and have NVAF with no valid exclusion criteria as outlined above (section 5).
    - A data collection form (Appendix 2) can be used to identify suitable patients. Use medical records to populate relevant information as per the data collection form.
- Refer to the SmPC for rivaroxaban for detailed information of cautions and contraindications that may need to be considered before proceeding with the switch.
- Use recent (within the last 6 months) weight and creatinine values to calculate creatinine clearance (CrCl). Individuals without documented results of the recommended monitoring will need the necessary tests completing before considering a switch.
- The appropriate dosing of rivaroxaban should be considered (see section 8 below).
- All consultations for changes must take place with direct patient contact. This may be via a face-to-face or telephone consultation. In addition, a leaflet should also be issued for patients suitable for the switch in a format that is clear and accessible for the patient and/or their representative. This can be found in Appendix 3.
- Individuals should be advised to use up their supply of edoxaban before starting the newly prescribed rivaroxaban to prevent any wastage.
- After finishing their supply of edoxaban, start rivaroxaban at the time the next dose of edoxaban would have been due. NB: see below.
- Advise the individual that the new DOAC, rivaroxaban, needs to be taken **once a day with a main meal.** Patients may need to change the time of day that they usually take their dose to ensure they can take it with a meal.
- Add rivaroxaban to repeat medications and remove edoxaban from repeats.
- Ensure repeat issues are only authorised until next blood test or as per practice protocol.
- Ensure ongoing review / recall dates are in place as per the patient's original monitoring schedule and in line with the APC Anticoagulants in AF document.
- Practices may wish to consider contacting patients after the switch to check that patients are taking rivaroxaban correctly and not experiencing any problems.

9. Rivaroxaban dosing

The standard recommended dose for stroke prevention in AF is rivaroxaban **20mg once daily**. However, consideration must be given to renal function.

Prescribe a reduced dose rivaroxaban **15mg once daily** for individuals with severe renal impairment (**creatinine clearance 15-49 mL/min**).

In patients with **creatinine clearance below 15 mL/min**, or in patients undergoing dialysis, there is no clinical experience therefore rivaroxaban is **not recommended**.

Calculating renal function
Use of the Cockcroft-Gault equation is recommended to calculate creatinine clearance (CrCl), as this equation accounts for body weight, accurately reflecting renal function. Cockcroft-Gault calculators can be accessed within the GP clinical system tools and on the MDcalc website.

https://www.mdcalc.com/calc/43/creatinine-clearance-cockcroft-gault-equation

The most up to date values for the patient's actual body weight and height will have to be inserted. It should be remembered that all values are estimates of renal function.

Patient actual bodyweight should be used in the calculation because actual body weight was used in the clinical trials. However, use adjusted bodyweight if patients > 120kg / BMI > 40.

SystmOne CrCl calculator uses:	EMIS CrCl calculator uses:
SystmOne renal calculator highlights the dates for when the weight and the creatinine value were last recorded and gives three values for the CrCl using: ideal, actual, and adjusted body weight.	Actual body weight for CrCl calculation for patients taking apixaban, edoxaban or rivaroxaban - and ideal body weight for dabigatran. There is text information added to advise whether actual or IBW has been used each time a calculation is made.

10. Body weight

Initial clinical trials only included patients between 50kg and 120kg, but there is increasing evidence that these medications can safely be used up to 150kg (see APC Anticoagulants in AF guideline).

The local consensus from specialists is to use any of the DOACs in patients under 150kg (except edoxaban – not used in patients over 120kg) irrespective of indication for anticoagulation. Rivaroxaban or apixaban can be used in patients above 150kg who have had DVT or PE only (i.e. not in context of AF).

For an individual with extremes of body weight (less than 50kg or over 150kg), warfarin is the preferred anticoagulant for NVAF. These individuals require a careful risk/benefit discussion about their anticoagulant choice.

11. Liver disease

All DOACs are contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk and are not recommended in patients with severe hepatic impairment.

The manufacturer does not make any specific recommendations around the use in patients with mild to moderate hepatic impairment.

Liver function tests are therefore recommended prior to treatment, and rivaroxaban should be used with caution in such patients. Regular monitoring of liver function is recommended.

12. Drug Interactions

Please refer to the APC Anticoagulants in AF document and to the SmPC for Rivaroxaban for information on interactions.

13. Patient education/discussion

Arrange a consultation to discuss anticoagulation options and establish whether the individual is suitable for a switch to rivaroxaban. When discussing the benefits and risks of anticoagulation, use clinical risk profiles and personal preferences to guide treatment choices. Practical considerations may include, but are not limited to, the ability to reliably take with food, and the use of NJ/PEJ/PEGJ tubes.

When discussing the anticoagulation treatment options advise the individual of the risks and benefits of the different DOACs. Explain the need for cost-effective prescribing to make the best use of NHS resources. Explain that rivaroxaban is as effective as other DOACs.

If suitable to switch, advise the individual:

- rivaroxaban must be taken **once a day with a main meal.**
- to use up the supply of their existing DOAC before switching to the rivaroxaban.
- to switch to rivaroxaban the **day after** using up their existing DOAC supply.
- to update their DOAC alert card

Refer to appendix 1 and appendix 3 to aid discussion with the patient.

14. Patient compliance

- Ensure the patient is aware that rivaroxaban needs to be taken **ONCE A DAY, WITH A MEAL**. If there are any concerns regarding compliance with taking with a meal, the patient should not be switched to rivaroxaban.
- There are no known issues with using rivaroxaban in compliance devices, however, repackaging medication outside of the manufacturers original packaging involves risks and is often unlicensed. The community pharmacist should be made aware of the change to avoid dispensing/supply error/duplication of script.
- The tablets can be swallowed whole or crushed and mixed with water or apple puree. If crushing the tablets, this should be done immediately before taking the dose. The crushed tablet may also be given through gastric tubes. This is a **licensed** use – see SmPC for details.

15. Monitoring renal function and weight

- At initiation of rivaroxaban treatment (new or switching), renal function should have been confirmed within the last 6 months and weight in the last 12 months.
- If renal function decreases during treatment, the rivaroxaban dose may need to be reviewed.
- Alternatively, if a reduced dose of rivaroxaban has been initiated during an episode of impairment of renal function, then the dose will need to be reviewed if renal function subsequently improves.
- Weight should then be checked annually once the patient has been reviewed and confirmed to be on an appropriate dose of rivaroxaban. Renal function should be checked at least annually and more frequently for patients with impaired renal function or additional risk factors including frailty, multiple co-morbidities, or age ≥ 75 years. See APC Anticoagulation in AF guidance for monitoring schedule.

Version Control – **Procedure for switching to rivaroxaban for existing patients with non-valvular atrial fibrillation (NVAF) on edoxaban**			
Version	Author(s)	Date	Changes
1.0	Sue Haria, ICB Medicines Optimisation Pharmacist	26/09/2024	New document

16. Appendix 1 – Rivaroxaban switch algorithm

Switching from edoxaban to rivaroxaban in adult individuals with non-valvular AF

Use this support tool alongside the APC Anticoagulation in AF guidance.

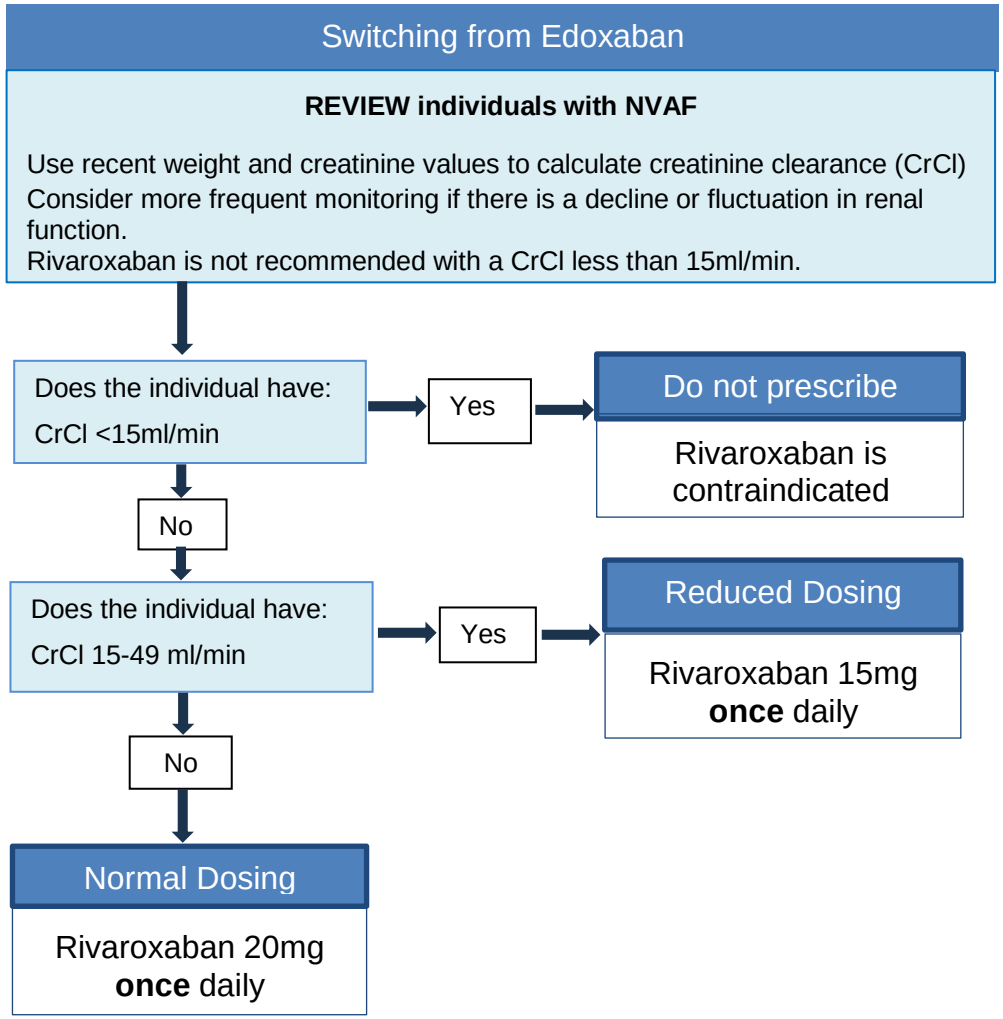
This tool does not replicate complete source information or consider all individual patient circumstances. Avoid using it for the sole basis of decisions or a substitute for a clinical conversation with a healthcare professional.

Do not switch individuals who:

- Are on a DOAC other than rivaroxaban for NVAF for a clinical reason (e.g., potential drug interactions)
- Have previously been switched from rivaroxaban to an alternative DOAC for a clinical reason.

Counselling points

- Take the first rivaroxaban dose when the next dose of edoxaban would have been due.
- Rivaroxaban must be taken once a day.
- Rivaroxaban tablets must be taken with a meal.
- **Individuals must NOT be on more than one DOAC at the same time.**
- Supply a patient information leaflet and counsel the patient and update DOAC alert card.



Consult rivaroxaban summary of product characteristics (SmPC) before prescribing. https://www.medicines.org.uk/emc

17. Appendix 2 – Data collection form

Patient ID	Age (18 years or over)	Current Edoxaban dose	Diagnosis of NVAF and no other DOAC indication (Y/N)	Serum creatinine in last 6 months	Weight in last 12 months	Creatinine Clearance	Proposed rivaroxaban dose	C/I or exclusion to rivaroxaban switch? (Y/N)	Switch agreed (Y/N)

18. Appendix 3 – Patient Information Leaflet

Important Changes to your medication: Edoxaban

Switching to Rivaroxaban

Information for patients

You have received this leaflet because you are taking a blood thinning medicine, Edoxaban (Lixiana ®)

Rivaroxaban is another blood thinning medicine. It is as effective as the other blood thinning medicines. Until recently only one manufacturer made rivaroxaban. As it is no longer covered by a patent, rivaroxaban is now available from other manufacturers. This drives the price of rivaroxaban down, making it more cost effective for the NHS.

Soon, you will receive prescriptions for rivaroxaban **instead of** edoxaban.

How the switch will happen

Your GP practice will discuss with you about switching to rivaroxaban and provide more information.

How to take rivaroxaban

- Use up your current supply of edoxaban **before** starting the rivaroxaban.
- Start the rivaroxaban the day after you finish your edoxaban.
- Take your first dose of rivaroxaban at the time you would normally take the next dose of edoxaban. **Please note that it is very important that you take rivaroxaban with a main meal, so this might mean that you need to change the time of day that you take it.**
- Take the rivaroxaban **once a day, with a meal.**
- If you find the tablets hard to swallow, it may help to crush them and mix them with water, apple juice or apple puree immediately before taking them.

If you forget to take rivaroxaban

Take the tablet as soon as you remember unless it's nearly time for your next dose. In this case, skip the missed dose and take your next dose at the usual time. Do not take more than 1 dose in a single day to make up for the missed dose.

If you are not sure what to do or if have missed more than one dose of rivaroxaban, ask your doctor, pharmacist, or nurse.

If you take too much rivaroxaban

You may be at risk of bleeding if you take more rivaroxaban than you have been prescribed.
Contact NHS 111 or tell your doctor, pharmacist, or nurse immediately.

Further Information

Always read the patient leaflet that comes with your medicine and remember to carry your alert card with you at all times.
If you have any questions about this change in medicine or would like to discuss it further, please speak to your GP or practice pharmacist, or your local community pharmacist.

19. Appendix 4 – Clinical Systems Resources

SystmOne	EMIS Web
A search for patients with a current repeat for Edoxaban is available in the F12 group of searches: • Zz F12 Drug DB • •E • Edoxaban (repeat) # { Practices can choose how to configure the output from the search. There is a pre-defined report output available to use if practices so wish: MSO AF DOAC MONITORING 2024	A search for patients with a current repeat for Edoxaban is available in the EMIS library of searches: • SNOMED searches • EMIS Clinical Utilities • Drug Monitoring • Edoxaban There is also a search for patients with a current repeat for a DOAC available from the ICB Medicines Optimisation Team as part of the MSO DOAC Dosing 24-25 workstream. Please contact your ICB MOT pharmacist or technician if you would like to use this search and the associated auto report.

Disclaimer:

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