North Central London
Joint Formulary Committee

NCL JFC Position Statement

November 2022

Choice of Direct Oral Anticoagulant (DOAC) for prevention of stroke & systemic embolism in patients with non-valvular atrial fibrillation (NVAF)

Update November 2022

The NCL Joint Formulary Committee are aware of recent evidence relating to the comparative efficacy and safety of DOACs for the prevention of stroke & systemic embolism in patients with non-valvular atrial fibrillation published in the Annals of Internal Medicine *(Lau WCY et al. Comparative Effectiveness and Safety Between Apixaban, Dabigatran, Edoxaban, and Rivaroxaban Among Patients with Atrial Fibrillation: A Multinational Population-Based Cohort Study. Ann Intern Med. 2022 Nov;175(11):1515-1524)*

The Committee will be writing to NICE to raise awareness of the new evidence and to request an updated evaluation and cost-effectiveness analysis; and to NHSE to clarify if the new evidence will affect the current NHSE commissioning recommendations which place edoxaban first line, where clinically appropriate.

The current NCL position statement (outlined below) remains unchanged.

Before reading this position statement, please consider the following:

This position statement on the choice of DOAC for prevention of stroke and systemic embolism in patients with NVAF supersedes previous versions.

All DOACs should be used with caution in patients at higher risk of bleeding, e.g. the elderly or in patients with low body weight or renal impairment.

Anticoagulation may **NOT** be clinically appropriate for some patients with NVAF.

This position statement **does NOT apply** to DOAC use for treatment of ***Venous Thromboembolism.***

This position statement is not intended to replace local Trust or NCL guidance, which should be referred to for further information.

1. Patients to be newly initiated on a DOAC for stroke prevention in NVAF

Where a DOAC is to be initiated for prevention of stroke & systemic embolism in patients with NVAF, **edoxaban should be considered as the first line option across NCL** (*where clinically appropriate*); since (1) all DOACs are endorsed as treatment options by NICE; and (2) edoxaban currently has the lowest acquisition cost, is a once daily dose, and does not need to be taken with food.

Consider initiating once-daily rivaroxaban in preference to edoxaban for NVAF:

- for patients who have a CrCL >95ml/min (Cockcroft Gault)
- where drug interactions preclude the use of edoxaban

Consider initiating twice-daily apixaban in preference to edoxaban or rivaroxaban for NVAF:

- in the frail / frail elderly / patients with low body weight and or renal impairment
- for individuals at high-risk of gastrointestinal or other mucosal bleeding
- where potential drug interactions preclude the use of edoxaban or rivaroxaban

** In line with NICE TAs, all anticoagulant options will be available if clinically appropriate **

2. Patients already established on rivaroxaban for NVAF

NCL high-risk criteria to exclude adult patients from a RIVAROXABAN to edoxaban switch for stroke prevention in NVAF

- Patients in primary care with NVAF currently receiving rivaroxaban for prevention of stroke or systemic embolism can be considered for switching to edoxaban **unless they meet one or more high-risk criteria (see below).**
- Patients taking other oral anticoagulants (e.g., apixaban, dabigatran, warfarin) are outside the scope of this position statement and are **not suitable** for consideration of a switch within the context of the criteria outlined below.

The following patients taking rivaroxaban **should NOT be switched to edoxaban**:

- Patients with contraindications and cautions listed in the edoxaban SmPC: https://www.medicines.org.uk/emc/product/6905/smpc
- Where a haematologist or the anticoagulation clinic have specifically advised/indicated a clinical reason for using an oral anticoagulant other than edoxaban
- Where a drug-drug interaction precludes the use of edoxaban
- CrCL >95mL/min (estimated via Cockcroft Gault) as this may reduce the efficacy of edoxaban
- Patients with BMI >40 or weight >120kg
- Active malignancy or chemotherapy (and where rivaroxaban is appropriate to continue)
- Cognitive dysfunction, e.g., if there are concerns regarding patient understanding

On review of high-risk criteria, some patients may be identified who are **NOT suitable for either edoxaban or rivaroxaban.** Such patients might include those with:

- Severe renal impairment CrCL <30mL/min (estimated via Cockcroft Gault*) not eGFR

  [Nb: NCL currently advises against the routine use of DOAC in severe renal impairment unless discussed with a haematologist. All DOACs are contraindicated with CrCL <15mL/min (<30mL/min for dabigatran)]
- High risk of gastrointestinal or other mucosal bleeding
- Frail or frail elderly (as indicated by EMIS flag or clinical judgement)
- Patients with low body weight (<50kg)

These patients should be re-evaluated for their suitability for anticoagulation by their GP. Some such patients may be suitable for apixaban or warfarin as an alternative to edoxaban or rivaroxaban. Patients should be referred to haematology/AC services in the usual manner if needed.

- **If it is unclear if a patient is suitable to switch from rivaroxaban to edoxaban, or if the patient declines to switch, then continue with rivaroxaban where it is safe and appropriate to do so.**
- **If there are concerns regarding the appropriateness of any anticoagulation regimen, please discuss with the patient's GP in the first instance. Local haematology team can be contacted for advice/support.**

References

1. NICE NG196. Atrial fibrillation: diagnosis and management (April 2021, last updated June 2021) https://www.nice.org.uk/guidance/ng196/chapter/Recommendations
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7. MHRA. Direct-acting oral anticoagulants (DOACs): reminder of bleeding risk, including availability of reversal agents (June 2020) https://www.gov.uk/drug-safety-update/direct-acting-oral-anticoagulants-doacs-reminder-of-bleeding-risk-including-availability-of-reversal-agents
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9. British National Formulary. Edoxaban (accessed Sept 2022) https://bnf.nice.org.uk/drug/edoxaban.html
10. FDA. Drug Trials Snapshot: Savaysa (edoxaban) for Prevention of Stroke in Atrial Fibrillation (September 2017) https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshot-savaysa-edoxaban-prevention-stroke-atrial-fibrillation
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12. Summary of Product characteristics for rivaroxaban 20mg tablets (January 2022) https://www.medicines.org.uk/emc/product/2793/smpc#gref

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