NHS
South West London

Anticoagulation Selection for Stroke Prevention in Non-valvular Atrial Fibrillation (NVAF) in adults

This document is aimed at healthcare professionals with experience in the prescribing and monitoring of oral anticoagulation.

This guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Introduction

- Vitamin K antagonists (e.g. warfarin) and Direct Oral Anticoagulants (DOACs) are available for stroke prevention in NVAF. DOACs include apixaban, edoxaban, dabigatran and rivaroxaban and have shown advantages over warfarin therefore recommended as the agents of choice in NVAF when clinically appropriate.
- There are no published randomised controlled trials comparing one DOAC against another, so no direct comparison of effectiveness and safety is available. A network meta-analysis has compared the DOACs, however the heterogenicity of the data in the underlying studies limit comparison.
- NICE guidance for stroke prevention and atrial fibrillation does not advise on a specific DOAC. The choice should be based on clinical appropriateness of the DOAC e.g. contraindications, renal impairment, availability of reversal agents and monitoring requirements.

This document is part of the available resources within SWL to help support with the prescribing of DOACs. The scope of this document does not cover switching between DOAC preparations.

DOAC initiation for stoke prevention NVAF

- To maximise affordability and support treatment for the greatest number of patients NHS England's Commissioning recommendations for the national procurement of direct acting oral anticoagulants (DOACs) outlines the highest-ranked joint best-value treatment choices:
    - generic Apixaban tablets: twice a day **or**
    - generic Rivaroxaban tablets: once a day.
- Edoxaban is ranked next if either of the highest-ranked DOACs are contraindicated or not clinically appropriate for the specific patient.
- With increased diagnosis of AF, the recommendations aim to:
    - improve availability of DOACs.
    - support uptake of DOAC medicines.

Please use the guidance below in conjunction with:

- NICE NG196 Atrial Fibrillation.

- NHS England. Operational note: Commissioning recommendations for national procurement for DOACs.
- NHS England. National medicines optimisation opportunities 2024/25.
- SWL DOAC Initiation Guidance for NVAF & Guidance for HCPs monitoring DOACs Prescribed in all Indications and DOAC FAQs for Primary Care
- SWL Joint Medicines Formulary.
- and the individual DOAC Technology Appraisals and Summary of product characteristics (SPCs).

Links to NHS Specialist Pharmacy Service (SPS) resources:

- Managing interactions with direct oral anticoagulants (DOACs)
- Understanding direct oral anticoagulant (DOAC) interactions
- DOACs (Direct Oral Anticoagulants) monitoring

The clinician, in conjunction with the patient, will continue to determine the most appropriate treatment for their clinical needs (shared decision making).

Initiating anticoagulation for NVAF following NHSE DOAC commissioning recommendations

This guidance is also available as a visual summary comparison chart to support anticoagulation shared decision-making with patients.

Exclusion criteria

For patients with NVAF requiring oral anticoagulation, consider a DOAC as first line, unless the patient has any of the following exclusion criteria:

- Mechanical prosthetic heart valves.
- Moderate to severe mitral valve stenosis (warfarin preferred).
- Antiphospholipid syndrome (APLS) (warfarin preferred)- except where advised by an anticoagulant specialist.
- Severe renal impairment with creatinine clearance (CrCl) less than 15ml/min (warfarin preferred).
- Patient requiring a higher international normalised ratio (INR) (greater than 2 to 3).
- Concomitant use of drugs which are contraindicated with DOACs- see interactions sections below, individual SPCs.

Special circumstances

For patients with NVAF requiring oral anticoagulation, consider a DOAC as first line; unless the patient has any of the following (Note. list not exhaustive):

- Bioprosthetic heart valves/ repair -within three months post-operative.
    - Note: For transcatheter aortic valve implantation (TAVI) patients- a DOAC is acceptable post procedure.
- Extremes of body weight less than 50kg and greater than 150kg.
- Renal impairment: CrCl less than 30ml/min.
- High CrCl greater than 95ml/min (caution for edoxaban, consider alternative DOAC in line with SPC- eg. rivaroxaban preferred).

- Raised liver function tests (LFTs):
    - Aspartate transaminase (AST) or Alanine transaminase (ALT) over 2 times the upper limit of normal.
    - Total bilirubin over 1.5 times the upper limit of normal.
- Active malignancy/ chemotherapy.
- Patients also prescribed antiplatelets.
- Significant bleeding issues abnormal clotting screen, low Hb with no identifiable cause, platelets less than 100 units, menorrhagia.
- Previous serious bleed (consider a lesion or condition that is a significant risk for major bleeding e.g. current or recent gastrointestinal ulceration, known or suspected oesophageal varices).
- Post coronary event/intervention/other venous thromboembolism (VTE) event.
- Absorption problems.
- Complex drug interactions (e.g. antiepileptics, antiretrovirals, azole antifungals).
- Pregnancy/breastfeeding (Lower molecular weight heparin preferred).

Considering the appropriate agent

For patients with NVAF requiring oral anticoagulation who fall within the exclusion criteria or special circumstances criteria check if warfarin is mandated:

- Initiate warfarin where appropriate with INR monitoring. (Note: A higher INR target may be required if mechanical prosthetic heart valve/antiphospholipid syndrome) **or**
- Seek specialist advice on the appropriate choice of anticoagulation.

Monitoring of DOACs

- DOACs are not without a need for surveillance as their dosing is determined by renal function.
- Local guidance on recommended monitoring frequencies outlined in Direct Oral Anticoagulant: Calculating renal function.

Before prescribing, please consult the SPC for each individual DOAC for a complete list of cautions, contraindications, interactions, dosage adjustments e.g. in liver, renal impairment.

Apixaban Tablet (Best Value DOAC)

Dosing

- Standard: 5mg twice daily.
- Reduced dosing: 2.5mg twice daily if:
    - CrCl is 15 to 29 ml/min **or**
    - if 2 or more of the following:
        - age greater than or equal to 80 years
        - body weight less than or equal to 60 kg
        - serum creatinine greater than or equal to 133 micromol/l.

Contraindication in renal disease

- Avoid if CrCl is less than 15ml/min.

Drug interactions
Note: list is not exhaustive- use BNF, SPC, HIV Drug interaction, current EHRA practical guide on NOACs in AF:

- HIV protease inhibitors, ketoconazole, itraconazole, voriconazole, posaconazole- Avoid use.
- Rifampicin, antiepileptics, St. John's Wort- use with Caution.

Compliance aid

- Suitable for use in a compliance aid.

Licensed reversal agent

- Available.

Patients with swallowing difficulties or enteral tubes

- Tablets can be crushed -see SPC/ NEWT guidelines for additional advice.

Dabigatran Capsule

Dosing

- Standard: 150mg twice daily if any of the following:
  - age less than 75 years.
  - CrCl greater than 50ml/min.
  - low risk of bleeding.
- Reduced dosing: 110mg twice daily if any of the following:
  - aged greater than or equal to 80 years.
  - prescribed verapamil.
- **Consider** 110mg twice daily if any of the following:
  - based on individual assessment of thrombotic risk and the risk of bleeding in patients aged between 75 and 80 years.
  - with CrCl 30 to 50ml/min.
  - with increased risk of bleeding (including gastritis, oesophagitis, gastro-oesophageal reflux).

Contraindication in renal disease

- Avoid if CrCl is less than 30ml/min.

Drug interactions

Note: list is not exhaustive- use BNF, SPC, HIV Drug interaction, current EHRA practical guide on NOACs in AF:

- HIV protease inhibitors, ketoconazole, ciclosporin, itraconazole, tacrolimus, dronedarone, rifampicin, St John’s Wort, antiepileptics- Avoid use.
- Amiodarone, quinidine, ticagrelor, posaconazole, verapamil (use reduced dose)- use with Caution.
- Antidepressants: SSRIs and SNRIs- increased bleeding risk- use with Caution.

Compliance aid

- Not suitable for use in a compliance aid.

Licensed reversal agent

- Available.

Patients with swallowing difficulties or enteral tubes

- Capsules cannot be crushed- see SPC/ NEWT guidelines for additional advice.

Edoxaban Tablet

Dosing

- Standard: 60mg once daily.
- Reduced dosing: 30mg once daily if 1 or more of the following:
    - weight less than or equal to 60kg.
    - CrCl 15 to 50ml/min.
    - on ciclosporin, dronedarone, erythromycin, ketoconazole.

Contraindication in renal disease

- Avoid if CrCl is less than 15ml/min.
- Caution in patients with CrCl greater than 95ml/min.

Drug interactions

Note: list is not exhaustive- use BNF, SPC, HIV Drug interaction, current EHRA practical guide on NOACs in AF:

- HIV protease inhibitors- No data on co-administration.
- Rifampicin, antiepileptics, St. John's Wort- use with Caution.
- Ciclosporin, dronedarone, erythromycin, ketoconazole- see reduced dosing section.

Compliance aid

- Suitable for use in a compliance aid.

Licensed reversal agent

- No licensed antidote. See SPC for options.

Patients with swallowing difficulties or enteral tubes

- Tablets can be crushed- See SPC/ NEWT guidelines for additional advice.

Rivaroxaban Tablet (Best Value DOAC)

Dosing

- Standard: 20mg once daily with food.
- Reduced dosing: 15mg once daily with food if CrCl 15 to 49ml/min.

Contraindication in renal disease

- Avoid if CrCl is less than 15ml/min.

Drug interactions
Note: list is not exhaustive- use BNF, SPC, HIV Drug interaction, current EHRA practical guide on NOACs in AF:

- HIV protease inhibitors, ketoconazole, itraconazole, voriconazole, posaconazole, dronedarone- Avoid use.
- Rifampicin, antiepileptics, St. John's Wort- use with Caution.

Compliance aid

- Suitable for use in a compliance aid.

Licensed reversal agent

- Available.

Patients with swallowing difficulties or enteral tubes

- Tablets can be crushed- See SPC/ NEWT guidelines for additional advice.

References/resources

- NICE (2021). Atrial fibrillation: diagnosis and management. National Institute for Health and Care Excellence.
- NICE (2021). Apixaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation. National Institute for Health and Care Excellence.
- NICE (2021). Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. National Institute for Health and Care Excellence.
- NICE (2021). Edoxaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation. National Institute for Health and Care Excellence.
- NICE (2021). Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation. National Institute for Health and Care Excellence.
- NHS England (September 2024). Operational note: Commissioning recommendations for national procurement for direct-acting oral anticoagulant(s) (DOACs).
- Summary of product characteristics.
- PCCS/ PCPA/ UKCPA (July 2022). Anticoagulation for non-valvular atrial fibrillation (NVAF) following NHSE DOAC commissioning recommendations.

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