Edoxaban Switch Programme - Frequently Asked Questions

What should I tell patients?

- NHS Tayside is reviewing all patients currently receiving a Direct Oral Anticoagulant (DOAC) for stroke prevention in NV-AF(non-valvular atrial fibrillation)
- Edoxaban has been identified as the first choice DOAC. It is similarly effective to the other DOAC options but costs considerably less
- Clinical experts in Tayside are supporting the use of edoxaban
- All newly diagnosed NV-AF patients will be started on edoxaban as 1st choice for those unsuitable for warfarin
- Existing patients already on a DOAC for NV-AF are to be reviewed and considered for switch to edoxaban
- This will help to ensure that the money available to spend on medicines is being used appropriately

Is edoxaban as good as the other DOACs?

- Yes, the evidence is that it is as effective as warfarin and the other DOACs. It is licensed for this indication and has been recommended by the Scottish Medicines Consortium
- Other Scottish Health Boards are also considering the use of edoxaban
- A recent Health Improvement Scotland (HIS) summary (http://www.healthcareimprovementscotland.org/our_work/cardiovascular_disease/programme_resources/doac_review_report.aspx) is consistent with this Tayside switch recommendation
- Lead clinicians from cardiology, stroke, vascular medicine, relevant MCN's and haematology are all supportive of this Tayside guidance on the basis of current evidence

Will we need to do a further switch if the price of other DOACs falls?

- The rebate on edoxaban is in place for five years
- The manufacturers of other DOAC's have not reduced the price or offered sufficient rebates to review the decision to switch to edoxaban
- A further switch will only be considered if clinical evidence emerges that another DOAC is more effective and/or safer than edoxaban; in the unlikely event of a very significant price change of an equivalent product or; when a generic DOAC is available
- No generic versions of the DOACs we currently use are expected until 2021 at the earliest

Which patients should not be on edoxaban?

- Creatinine clearance<30ml/min unless on specialist advice
- Creatinine clearance<15ml/min – these patients should be on warfarin
- Metallic heart valves – warfarin is recommended for these patients
- For a diagnosis of DVT/PE without AF-rivaroxaban remains the first choice
- AF patients who require intervention for acute coronary syndrome may be discharged on a combination of rivaroxaban and one or more antiplatelets based on current evidence

How do I switch patients to edoxaban?

- If patients meet the criteria for switching and have agreed to the switch they should be issued with a prescription for edoxaban
- They should be advised to use up the supply of existing DOAC before switching to edoxaban. They should switch to edoxaban the day after they use up their existing supply.
- If they are switching from apixaban they should take both the morning and evening dose on the day before switching to edoxaban
- Edoxaban should be taken once daily. The precise time of day is not important, neither is the timing in relation to food. The patient should decide the most convenient time of day for them. It is important to take edoxaban every day
- Community pharmacists are being informed of this change and will be supplied with all the relevant support materials

Why are we excluding patients who have a creatinine clearance<30ml/min from an automatic switch to edoxaban, and suggesting that if a switch is considered it should be on specialist advice?

- There is limited evidence as to which DOAC performs best in patients who have a creatinine clearance<30ml/min
- The first line anticoagulant for patients with NV-AF who have a creatinine clearance<30ml/min is warfarin however DOACs can be used, if clinically indicated, if the creatinine clearance is 15-30ml/min
- Because of the limitations of evidence in this group, if a patient has a creatinine clearance of 15-30ml/min and is on a DOAC it is best to refer for specialist advice if a switch is envisaged
- Patients with a creatinine clearance<15ml/min should not be on a DOAC. These patients should receive warfarin

What happens if renal function changes?

- If renal function decreases significantly then the DOAC dose may need to be reviewed.
- For edoxaban the important value for review of treatment is 50ml/min which should trigger a dose reduction to 30mg once daily

- If the creatinine clearance is <30ml/min it may be appropriate to use edoxaban but this should only be done on specialist advice as these patients were excluded from clinical trials.
- Edoxaban, and other DOACs are not recommended if the creatinine clearance is <15ml/min. These patients should receive warfarin if there is a clinical indication for long-term anticoagulation
- Alternatively, if a reduced dose of a DOAC has been started during an acute impairment of renal function, then the dose will need to be reviewed if renal function subsequently improves

Do I need to use the Cockcroft-Gault equation to estimate renal function or can I use eGFR?

- All DOACs require a dose adjustment based on renal impairment
- NHS Tayside has endorsed the eGFR as an appropriate indicator of renal function. The Cockcroft-Gault equation is an alternative method of estimating renal function which may generate a different value for creatinine clearance. Both methods make assumptions to allow calculations to be made. The different values generated are only important if this influences the appropriate dose of DOAC for each patient
- If the eGFR is within 10% of the value which would trigger a dose change then it may be appropriate to calculate estimated creatinine clearance using the Cockcroft-Gault equation to help with decision-making
- The Cockcroft-Gault equation may be the best option for patients >75 years old (see BNF recommendation)

How often do I need to check weight and renal function?

- At initiation of treatment or when switching DOACs. Both weight and renal function should have been confirmed within the last 6 months
- Check annually, once the patient has been reviewed and confirmed to be on the appropriate dose of edoxaban
- For new patients and those switching to edoxaban, the dose should be reduced to 30mg once daily if the creatinine clearance is <50ml/min or if the patient weighs less than 60kg
- Caution when prescribing any other new medicines which may interact with edoxaban and require the dose of edoxaban to be reduced to 30mg once daily - ciclosporin, dronedarone, erythromycin or ketoconazole

What about patients with liver disease?

- All DOAC's 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
- Liver function tests are recommended prior to treatment for those patients with elevated liver enzymes (ALT/AST > 2 x ULN) or total bilirubin ≥ 1.5 x ULN
- Edoxaban should be used with caution in patients with mild to moderate hepatic impairment

- Periodic monitoring of liver function is recommended if treatment continues beyond one year

What happens if a patient has more than one reason to be on a DOAC?

- There are several reasons why a patient might be taking a DOAC either for a fixed period of time or for the long-term
- All DOACs are licenced and approved by the Scottish Medicines Consortium for stroke prevention in NV-AF and treatment of a DVT/PE. Some DOACs are also used for thromboprophylaxis following joint replacement. This switch programme is focussing on patients receiving a DOAC for stroke prevention in NV-AF. If a patient is on a long-term DOAC for another indication this should be discussed with the relevant specialist before switching.
- Rivaroxaban remains the first choice agent in Tayside for the treatment of DVT and PE in the absence of AF. The use of edoxaban to treat DVT/PE requires initial treatment with heparin for 5 days and for this reason is not considered a suitable first choice for this indication at the outset of treatment.
- If a patient has NV-AF and is already established on rivaroxaban for DVT/PE it would be appropriate to consider them for a switch to edoxaban

What drugs interact with edoxaban and what should I do about them?

- There are no drugs which should be avoided in combination with edoxaban except other anticoagulants
- The dose of edoxaban should be reduced to 30mg daily if the patient is taking any of the following medicines - ciclosporin, dronedarone, ketoconazole or erythromycin (when erythromycin is started the dose reduction to edoxaban 30 mg should be done immediately and the same is true in reverse. In other words, no 'lag' time required). This is irrespective of renal function and weight. See edoxaban SPC for further details.
- If you have a patient already on a lower dose due to either weight or renal function, there is no further dose reduction required in relation to the above interacting drugs therefore if a patient is already on 30mg then do not reduce to 15mg.
- As with other anticoagulants, the risk of bleeding is increased if edoxaban is used in combination with one or more antiplatelet drugs. This combination is clinically appropriate in certain circumstances but this should only be done on the advice of a specialist and a clear treatment plan describing the intended duration of treatment

What is non-valvular atrial fibrillation (NV-AF)?

- The most recent European Society Cardiology guidance on AF (2016) suggests replacing the historic term ‘non-valvular’ AF with reference to the specific underlying conditions.
- 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 OAC could include either warfarin or a DOAC.

Can edoxaban go into a patient compliance device?

- There are no known issues with using edoxaban in a compliance device

How can patients feed back if they wish to raise concerns or make a complaint?

- Any patient feedback or complaints should be routed through local practice procedures in the first instance.
- Where the feedback received relates primarily to the NHS Tayside recommendation for a switch program, patients should be directed to the NHS Tayside Complaints and Feedback Team (feedback.tayside@nhs.net or telephone 0800 027 5507) who will record all feedback and facilitate a response from the Chairs of the NHS Tayside Prescribing Management Group.

For further advice on the switching process contact the Clinical Director for your HSCP. For clinical advice contact Ron Kerr, Lead Clinician for Anticoagulation (ronkerr@nhs.net) or the appropriate clinical specialist