Edoxaban Switch Programme – Key information

This document covers DOAC use in Non-Valvular Atrial Fibrillation (NVAF) ONLY

What should I tell patients?

- PCNs across Lancashire & South Cumbria are reviewing all patients currently receiving a Direct Oral Anticoagulant (DOAC) for stroke prevention in NVAF (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 Lancashire & South Cumbria are supporting the use of edoxaban
- All newly diagnosed NVAF patients will be started on edoxaban as the 1st choice anti-coagulant wherever suitable
- Existing patients already on a DOAC for NVAF 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

What is non-valvular atrial fibrillation (NVAF)?

- 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

Is edoxaban as good as the other DOACs?

- The evidence suggests it is as effective as the other DOACs. It is licensed for this indication and has been recommended by NICE (NG196 April 21)
- Across England other areas will be using edoxaban as the 1st choice anti-coagulant wherever suitable
- Optimising the anticoagulant pathway aligns with work already underway to reduce stroke rates in line with the NHS Long Term Plan
- NHS England & Improvement (NHSEI) has made commissioning recommendations to use edoxaban where this is clinically appropriate which is consistent with this switch recommendation
- Clinicians from across the health economy are all supportive of this guidance based on current evidence

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

- NHSEI completed a national procurement to give all DOAC suppliers an opportunity to update their value proposition to the NHS
- Three of the four DOAC suppliers (Bayer, Bristol Myers Squibb and Daiichi Sankyo) responded to the procurement and have been awarded national framework agreements **effective from 1 January 2022**
- The Daiichi Sankyo (edoxaban) offer included significantly better prices, investment and support than that offered individually or collectively by other suppliers
- A further switch will only be considered if clinical evidence emerges that another DOAC is more effective and/or safer than edoxaban, or in the unlikely event of a very significant price change of an equivalent product
- The DOACs that are currently prescribed for more than 95% of patients will remain patent protected until at least 2026. Dabigatran usage is c.3% of all DOAC prescribing in England and is not expected to increase once generic products become available in 2023

Is there an antidote to DOACs?

- There are reversal agents available for both thrombin inhibitors and Xa inhibitors which could be considered if rapid reversal is required
- Andexanet alpha is a reversal agent for factor Xa inhibitors and is licensed for apixaban and rivaroxaban
- Andexanet alpha may be used *off-license* for patients on edoxaban as it is also a factor Xa inhibitor. The national procurement of edoxaban took into consideration the lack of a licensed antidote, but the availability and *off-license* use of andexanet alpha was sufficient for a licensed edoxaban-specific antidote not to be a barrier to recommending it as a first line DOAC

Is secondary care on board with switching to edoxaban?

- NHSEI are engaging with secondary care via a number of channels
- Locally the Cardiac Network has disseminated the information to all the acute trusts in L&SC to ensure all cardiology teams are aware of the national procurement of edoxaban so that it is considered first line wherever possible
- Chief pharmacists at the hospitals are regularly informed of the work undertaken in primary care to ensure a joint approach is continued
- Across L&SC we have a joint position statement for edoxaban) as the DOAC of choice

Which patients should not be on edoxaban? https://www.medicines.org.uk/emc/product/6906/smpc#PRODUCTINFO

- CrCl <15ml/min. [NOTE: there is evidence of decreasing efficacy with increasing CrCl, seek advice if CrCl >95 ml/min]
- Metallic heart valves
- Moderate to severe mitral stenosis
- Severe hepatic impairment, hepatic disease associated with coagulopathy and clinically relevant bleeding risk – *see below*
- Concomitant treatment with any other anticoagulants – *see below*
- Uncontrolled severe hypertension
- Pregnant or nursing
- Triple positive antiphospholipid syndrome (APS)
- Clinically significant active bleeding or if any significant risk for major bleeding

How do I switch patients to edoxaban?

- If patients meet the criteria for switching, and following a discussion with the clinician they have agreed to the switch they should be issued with a prescription for edoxaban
- Patients 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 switching from apixaban patients 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
- Local community pharmacists should be informed of this change

What happens if renal function changes?

- If renal function decreases significantly then the DOAC dose should be reviewed
- For edoxaban the important value for review of treatment is 50ml/min which should trigger a dose reduction to 30mg once daily
- Creatinine clearance must be used for calculating renal function using the Cockcroft and Gault equation. eGFR is not a suitable alternative
- The actual body weight must be used to calculate CrCl. Always use the most up to date values and check the default units are correct when entering weight and serum creatinine

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 3 months
- Check annually, or sooner if indicated (see Appendix 1 of supporting information), once the patient has been reviewed and confirmed to be on the appropriate dose of 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 e.g. ciclosporin, dronedarone, erythromycin or ketoconazole

What about DOAC use in extremes of weight?

- Patients with a BMI up to 40 kg/m2, or weight up to 120 kg, can be prescribed a DOAC
- The BTH cardiology team advise against any patient <40kg or >over 120kg being switched to edoxaban: under 40kg warfarin would be first choice, if over 120kg warfarin would be considered the first choice followed by apixaban or rivaroxaban. Exclude these groups or seek further guidance

What about patients with 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
- 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 long-term
- All DOACs are licenced and approved by NICE for stroke prevention in NVAF 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 NVAF**. If a patient is on a long-term DOAC for another indication this should be discussed with the relevant specialist before switching

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
- Assess regularly for new P-glycoprotein inhibitors/inducers. 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 the patient is 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

For further advice on the switching process contact the Clinical Director for your PCN.

Medicines Optimisation Teams may be contacted on:

Pennine Lancashire	elccg.adminmmt@nhs.net tel. 01282 644799
Fylde coast CCGs	blackpool.medicinesoptimisation@nhs.net
Morecambe Bay	sue.bennett22@nhs.net
Central Lancs	philip.haydock@nhs.net
West Lancs	barry.lloyd1@nhs.net nicola.baxter1@nhs.net