EDOXABAN switch programme for Atrial Fibrillation

In order to switch safely from one DOAC to another, the prescriber would need to ensure they had upskilled their knowledge sufficiently in this area. There are a number of agents on the market, all with different indications, doses, cautions and monitoring requirements etc. DOACs can be viewed as straightforward by some, whilst in reality the prescribing can be complicated and confusing.

Patients would also need additional counselling and therefore careful planning is needed as to who would do this, how it will be managed and to ensure there is sufficient time available. Currently the anticoagulation service absorb all this workload but there is potential for shared care agreements to be introduced.

In AF - apixaban 5mg has been shown to be more efficacious when compared to warfarin. Edoxaban showed similar efficacy to warfarin. There have been no head-to head trials comparing different DOACs.

Criteria

Individual patient considerations
Which patients should not be prescribed Edoxaban?

- Creatinine Clearance (CrCl) <15ml/min – patients should be reviewed to determine if a DOAC is appropriate and warfarin should be used if required.
- CrCl 30-50mls/min - whilst edoxaban can be initiated in this patient population as per the license and NICE TA355, a cautious approach has been taken to avoid changing patients from full treatment dose (e.g. apixaban 5mg twice daily) to a reduced dose of edoxaban (30mg daily). Therefore new initiation for this patient group is appropriate however a switch to edoxaban is excluded from this programme.
- A non-significant trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin and the SPC advises that it should be used with caution. For patients with a Cockcroft-Gault equation CrCl >95 mL/min, edoxaban should not be used due to lesser efficacy compared with warfarin in preventing stroke in this group due to high renal clearance. For such patients, another DOAC is an alternative.
- Metallic heart valves – warfarin is recommended for these patients.
- Diagnosis of DVT/PE- apixaban remains the first choice for these patients as per local policy. Edoxaban requires five days of initial treatment with parenteral anticoagulation. In long term secondary prevention of VTE – there is no reduced dose for edoxaban (as opposed to apixaban 2.5mg or rivaroxaban 10mg). A reduced dose of DOAC is associated with a reduced bleeding risk. This group will not be included in the switch.
- Patients with a BMI > 40 kg/m2 or weight >120kg should be considered for warfarin as 1st line due to limited evidence for efficacy in this patient population. If it has already

been determined that a DOAC is more appropriate then the patient can still be switched to edoxaban. Peak and trough assay must be considered in this group.

- If a patient is stable and tolerating dabigatran 150mg twice daily, they should be excluded from a potential switch to edoxaban. Dabigitran is the only DOAC to show a significant reduction in ischaemic stroke and therefore should be continued unless the patient is not tolerating the treatment (gastro effects, despite use of PPI). • See the SPC for edoxaban for full list of contraindications www.medicines.org.uk

Undertaking individual patient reviews

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.
- Renal function should be calculated using the Cockcroft and Gault equation using actual body weight as per the trials and licensed information.
- Creatinine clearance must be used for calculating renal function using the Cockcroft and Gault equation (see below). eGFR is **not** a suitable alternative:
- CrCl (ml/min)= (140 – age) x wt (kg) x 1.04 (female) or 1.23 (male) serum creatinine (micromol/l). A calculator is in built into DAWN AC database. If unavailable us MDCAL
- The actual body weight must be used to calculate CrCl.

What happens if a patient has more than one indication 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 NICE 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.
- Apixaban remains the first choice agent depending on local formulary for the treatment of DVT and PE. The use of edoxaban to treat DVT/PE requires initial treatment with heparin for 5 days and is not necessarily a suitable first choice for this indication.

If clinically appropriate how do I switch a patient to edoxaban?

- If patients meet the criteria for switching, discuss the change and issue a prescription for edoxaban with verbal and written explanation of how to switch.
- Advise to use up the supply of existing DOAC before switching to edoxaban.
- Advise to switch to edoxaban when the next dose of the existing DOAC would be due
- 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 in prescribing

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 concomitant use of edoxaban with P-gp inducers (e.g. rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort) may lead to reduced edoxaban plasma concentrations and should be used with caution.
- 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 that is already dose-reduced due to either weight or renal function, there is no further dose reduction required in relation to the above interacting drugs i.e. if patient 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.
- As with other anticoagulants the possibility may exist that patients are at increased risk of bleeding in case of concomitant use with SSRIs or SNRIs due to their reported effect on platelets.
- Chronic use of NSAIDs with edoxaban is not recommended due an increased clinically relevant risk of bleeding.

Can edoxaban go into a patient compliance device?

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

Is there an antidote to DOACs?

- There are reversal agents available for both thrombin inhibitors and Xa inhibitors which can be used if rapid reversal is required – see local policy for management of major bleeding.
- Andexanet alpha is a reversal agent for factor Xa inhibitors and is licensed for apixaban and rivaroxaban. It may be used off-license for patients on edoxaban as it is also a factor Xa inhibitor although this must be documented in the notes and the patient informed.
- Idarucizumab is a reversal agent for dabigatran, a thrombin inhibitor.

Ongoing review of patients prescribed DOACs

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.
- Edoxaban and other DOACs are not recommended if the CrCl 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.

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

- At initiation of treatment or when switching DOACs the renal function should have been confirmed within the last 3 months.
- At initiation of treatment or when switching DOACs the weight should be recorded . If there has been recent acute illness or there is evidence of a suspicion of weight loss/gain, a more recent weight should be obtained.
- Thereafter the weight should be checked annually, once the patient has been reviewed and confirmed to be on the appropriate dose of DOAC.
- 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.
- Monitoring Interval will initially be after 3 months of switching to a DOAC then annually.
- Establish if other disciplines request renal function,Hb and/or LFTs to reduce need to over test the patients and help with cost savings.