Derbyshire Medicines Management UPDATE

www.derbyshiremedicinesmanagement.nhs.uk

Date: June 2017

Novel Oral Anticoagulants (NOACs) for Stroke Prevention in non-valvular Atrial Fibrillation

Warfarin or NOACs?*

***For information regarding when stroke prevention is indicated please see full atrial fibrillation guideline.**

Considerations include:

- Currently no licensed antidotes for NOACs except for dabigatran.
- NOACS are relatively new drugs so all potential problems are not known. All adverse effects should be reported via the yellow card system except for dabigatran and apixiban where only serious incidents need to be reported.
- NOACs may improve efficacy if warfarin, (despite good compliance) has been within range less than 65% of the time in 6 months**.**
- NOACs have short half-lives so missing doses has a significant impact on efficacy.
- Cannot measure compliance with NOACs. Recent studies suggest compliance may be poor with NOACs so it is important to assess compliance at least 3 monthly.
- Patient choice.
- A high proportion of the excretion of NOACS is renal – see overleaf for more on dosing. There are no studies of NOACs with creatinine clearance less than 30ml/min.
- NOAC drug interactions –warfarin maybe preferred as dose can be adjusted and INR monitored.
- There is no evidence for NOACs with antiplatelet agents therefore warfarin should be used where possible.
- Warfarin is locally recommended ahead of NOAC in patients with BMI>40kg/m^2 or weight >120kg because there are limited clinical data available for patients at the extreme of weight.

Which NOAC?

There have been no head to head trials so any recommendations are based on indirect comparisons.

Clinicians should consider clinical, logistical and patient preference when choosing a NOAC.
(See full guideline for further information).

- Rivaroxaban and edoxaban can be given once daily.
- Dabigatran is not suitable for monitored dosing systems.
- The packaging for dabigatran has to be opened in a specific way which may be a problem for patients with dexterity issues.
- Dabigatran should be swallowed whole.
- Rivaroxaban and apixaban can be crushed and mixed with water or apple puree immediately prior to administration.
- Rivaroxaban can be crushed as above for gastric tube patients as long as the tube terminates in the stomach.
- Apixaban can be given by a nasogastric tube.

Important Counselling Points for NOACs

Please note some of these will apply to other anticoagulants.

- Rivaroxaban should be taken with food to increase bioavailability.
- Monitoring requirements – see overleaf.
- Reporting any symptoms of bleeding.
- Before any hospital or dental procedure, make sure the hospital or dentist is aware of the NOAC. NOACs may need stopping beforehand depending on the bleeding risk of the procedure.
- Seek emergency care if they suffer a blow to the head, major trauma or prolific or sustained bleeding.
- Seek urgent medical advice if they have taken too many tablets.
- Let their health care professionals know if they are taking any OTC or herbal medicines and get advice from a pharmacist when buying medicines.
- What to do if they have missed a dose. Rivaroxaban and edoxoban can be taken up to 12 hours after scheduled intake and dabigatran and apixiban 6 hours. After this time they will need to skip a dose and take at the next scheduled time.
- Avoid binge drinking

Patients should be given an anticoagulant alert card available from NHS stationery suppliers. A patient information leaflet is also available from the MMT website: Patient information leaflet and NHS choices have information too: http://www.nhs.uk/Conditions/Anticoagulant-medicines/Pages/Introduction.aspx

NOTE Unlike warfarin where compliance can be monitored with INR testing, NOACs cannot. A 6 month follow up study shows that non-compliance rates were around 30% of patents started on NOACs increasing the risk of Stroke/TIA/death. Patients should be counselled on adherence.

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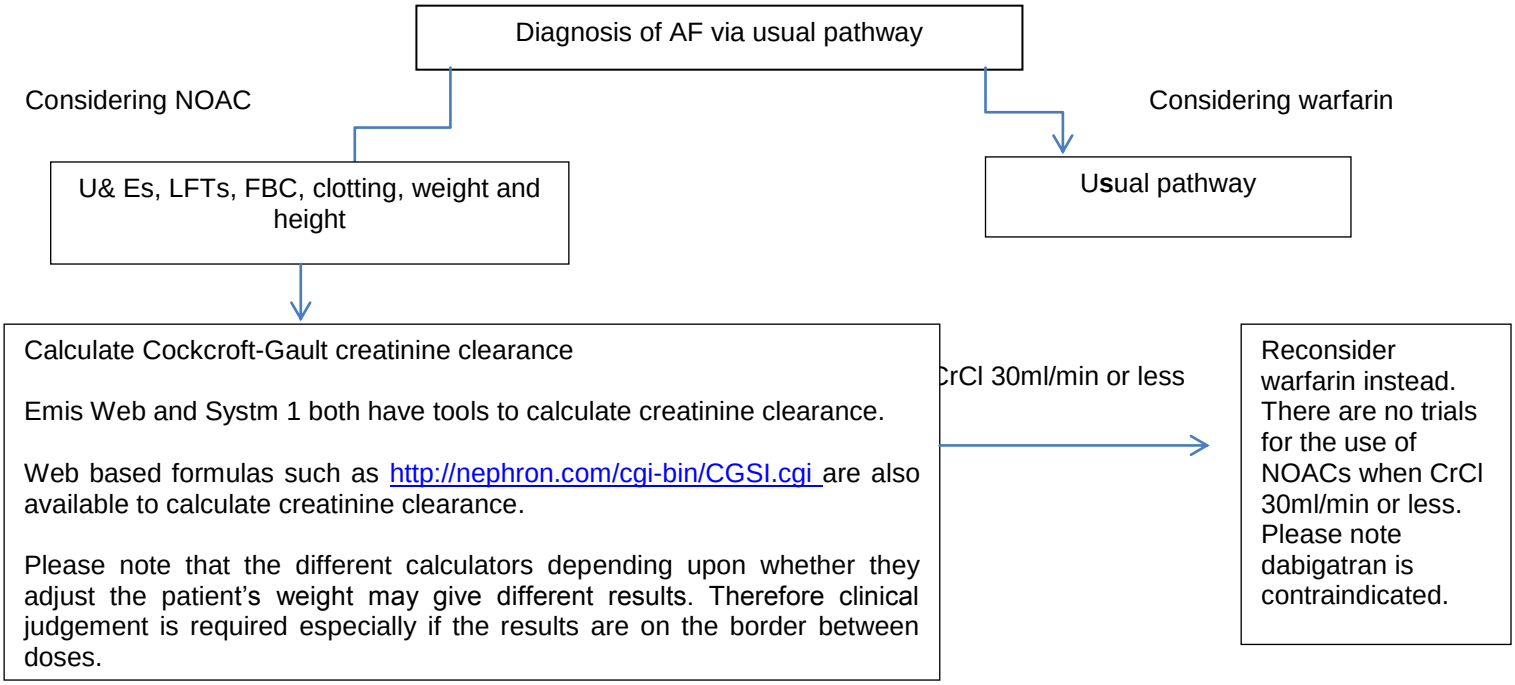
Flowchart to aid NOAC dosing and monitoring for Non-valvular AF only

Doses for other indications may differ. The choice of anticoagulation should be a shared decision process with the patient.



Apixaban	Dabigatran	Edoxaban	Rivaroxaban
5mg twice daily CrCl 15-29mL/min: **2.5mg twice daily (use with caution)** Patients with **2 or more** of the following give **2.5mg twice daily**: ▪ age >80 yrs ▪ body weight ≤60kg ▪ serum Cr >133micromol/L	Age < 80 yrs: **150mg twice daily** Age ≥ 80 yrs or taking verapamil : **110mg twice daily** **Also consider 110 mg twice daily if:** ▪ thromboembolic risk is low & bleeding risk is high ▪ age 75-80 yrs ▪ patients with gastro-oesophageal reflux, oesophagitis or gastritis ▪ CrCL 30-50mL/min N.B. dabigatran must be stored in original packaging and is therefore unsuitable for use in monitored dosage systems.	**60mg once daily** CrCl 15-50ml/min: **30mg once daily** **Also 30mg once daily if:** ▪ body weight ≤60kg ▪ concomitant use of ciclosporin, dronedarone, erythromycin and ketoconazole	**20mg once daily** CrCl 30-49 mL/min: **15mg once daily** CrCl 15-29mL/min: **15mg once daily (use with caution)**

Every 3 months

Check adherence and reinforce advice regarding the importance of a regular dosing schedule. Check for:

- Adverse effects (e.g. bleeding)
- Thromboembolic events (e.g. symptoms of stroke or breathlessness)

If CrCl 15-30ml/min repeat U & Es, weight and recalculate Cockcroft-Gault to check dose still appropriate

Every 6 months

As above, in addition if CrCl 30-60ml/min repeat U & Es, weight and recalculate Cockcroft-Gault to check dose still appropriate. (6 monthly monitoring for dabigatran is also recommended in the fragile or over 75s).

At 12 months

As above, in addition check FBC, U & E's and LFTs. Re-do weight and calculate CrCl to check dose still appropriate.

U&Es and LFTs may have to be checked more frequently if there is an intercurrent illness that may impact on renal or hepatic function