Management of Novel Oral Anticoagulants (NOACs) with the DAWN AC modules

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Anticoagulation Services
Scripps Clinic and Scripps Green Hospital
La Jolla, California
Pharmacist Management of Novel Oral Anticoagulants (NOACs)

- The role of pharmacists at Scripps as anticoagulation specialists includes NOAC management.

- Our dedicated Anticoagulation Services uses DAWN-AC modules for NOAC management.

- Patients are referred to us by outpatient physicians, inpatient physicians and urgent care.
Pharmacist Management of Novel Oral Anticoagulants (NOACs)

- Encourage Adherence
- Drug dose adjustment and follow up renal function
- Adverse drug reactions
- Pre and post op therapy instructions
- Follow-up of bleeding complications
- Track drug discontinuation and transition back to warfarin
Non-adherence to NOACS

Poor adherence is an important factor to consider when explaining instability of anticoagulation control and places the patient at risk for thrombotic events.

For Vitamin K Antagonist (VKAs)- rates of non-adherence have been reported between 22-58%


Medication adherence to NOACs has been poorly documented and may be an issue now that these drugs are used with increased frequency outside of clinical trials.

Efficacy of NOACs are expected to be lower in non-adherent patients.
What Information is Available from the NOAC Clinical Trials about Adherence?

**Einstein PE**: adherence was >80% in 94.2% of patients treated with rivaroxaban (Xarelto)


**Amplify (DVT & PE)**: adherence was >80% in 96% of patients treated with apixaban (Eliquis)

# Current Scripps NOAC Anticoagulation Service Experience

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pradaxa® (dabigatran)</td>
<td>Non-valvular atrial fibrillation Treatment and Prevention of DVT/PE</td>
</tr>
<tr>
<td>Xarelto® (rivaroxaban)</td>
<td>Non-valvular atrial fibrillation Treatment and Prevention of DVT/PE</td>
</tr>
<tr>
<td>Eliquis® (apixaban)</td>
<td>Non-valvular atrial fibrillation Treatment and Prevention of DVT/PE</td>
</tr>
</tbody>
</table>
DAWN New Oral Anticoagulant Modules

NOAC Management using DAWN AC

- Full anticoagulant history
- Ensure patients are on appropriate drug and dose
- Schedule follow-up
- Manage missed appointments
- Reporting
- Audit
Dabigatran therapy is managed using Questionnaires.

To schedule a questionnaire:

1. Press the button on the Questionnaires tab to create a new questionnaire.
2. Set the due date as appropriate.
3. Press OK.
DAWN New Oral Anticoagulant Modules

NOAC patients are managed using specific forms set up as questionnaires.

Initiation
• Identify valid Indications
• Identify contraindications
• Identify haemorrhagic risks
• Advise on dose

Follow Up
• Check drug and dose still appropriate
• Check compliance
# Dabigatran Initiation

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Ian DABIGATRAN</th>
<th>Due Date:</th>
<th>05/10/2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unit No:</td>
<td>DAB123</td>
<td>Status:</td>
<td>Scheduled</td>
</tr>
</tbody>
</table>

## Questions:

**Therapeutic Indication:** (None selected)

**Qualifying Risk Factors:**
- ATRIAL FIBRILLATION NON VALVULAR
- TOTAL HIP REPLACEMENT SURGERY
- TOTAL KNEE REPLACEMENT SURGERY
- DVT - UNPROVOKED
- PE - PROVOKED
- PE - UNPROVOKED
- DVT - PROVOKED
- Symptomatic heart failure >= NYHA Class 2
- Other cardiopulmonary disease, hypertension or systemic embolism (SEE)

**Duration of use?** (None selected)
<table>
<thead>
<tr>
<th>Measured Creatinine Clearance:</th>
<th>mL/min</th>
</tr>
</thead>
</table>

### Cockcroft-Gault estimate of CrCl:

\[
\text{CrCl} = \frac{1.23 \times (140 - \text{age years}) \times \text{weight kg} \times 0.85 \text{ if female}}{\text{serum creatinine } \mu\text{mol/L}}
\]

Cockcroft D, Gault MD. Nephron, 16:31-41, 1976

| Serum Creatinine: | 160 \(\mu\text{mol/L} \quad \text{High} \)
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight:</td>
<td>70 kg</td>
</tr>
<tr>
<td>Gender:</td>
<td>Male</td>
</tr>
<tr>
<td>Age (at due date):</td>
<td>43</td>
</tr>
</tbody>
</table>

| Calculate Cockcroft-Gault CrCl | 52 mL/min | Mild renal impairment |

Please be aware of the limitations of estimates of renal function in relation to muscle mass, race and diet.

### Hepatic Impairment:

- [ ] Liver Enzymes > 2ULN
Other Blood Checks:

Contraindicated Drugs:
- CICLOSPORIN
- Dronedarone
- ITRACONAZOLE
- Ketoconazole
- TACROLIMUS

Interacting Drugs:
- Amiodarone
- Aspirin
- CLARITHROMYCIN
- CLOPIDOGREL
- Other NSAIDs
- QUINIDINE
- Verapamil

VERAPAMIL:
Close clinical surveillance (looking for signs of bleeding or anaemia). In patients with normal renal function after hip or knee surgery, dosing should be reduced to 150 mg per day taken once as 2 capsules of 75 mg dabigatran. In patients with moderate renal impairment, a dose reduction to 75mg per day should be considered. For patients with atrial nonvalvular fibrillation treated for prevention of stroke, see Manufacturer recommendations.
### Other contraindications:

- Active clinically significant bleeding
- Hepatic impairment or liver disease expected to have any impact on survival
- Hypersensitivity to dabigatran etexilate
- Organic lesion at risk of bleeding
- Hypersensitivity to sunset yellow (E110)
- Severe renal impairment (CrCl<30mL/min)
- Spontaneous or pharmacological impairment of haemostasis

### Haemorrhagic Risks:

- Active ulcerative GI disease
- Bacterial endocarditis
- Brain, spinal or ophthalmic surgery
- Congenital or acquired coagulation disorder
- Recent biopsy or major trauma
- Recent gastrointestinal bleeding
- Recent ICH
- Thrombocytopenia or functional platelet defects
**CHA₂DS₂-VASc score?**

- C: Congestive heart failure (or left ventricular systolic dysfunction) - 1
- H: Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication) - 1
- A₁: Age ≥ 75 years - 2
- D: Diabetes Mellitus - 1
- S₂: Prior Stroke or TIA or thromboembolism - 2
- V: Vascular disease (e.g., peripheral artery disease, myocardial infarction, aortic plaque) - 1
- A: Age 65-74 years - 1
- Sc: Sex category (i.e., female gender) - 1

**HASBLED score?**

- H: Hypertension? systolic blood pressure > 160 mmHg or uncontrolled - 1
- A: Renal Disease? (creatinine > 200μM or > 2.6mg/dL) - 1
- L: Liver Disease? (cirrhosis, bilirubin > 2xULN, AST/ALT/AP > 3xULN) - 1
- S: Stroke History? - 1
- B: Prior Major Bleeding or Predisposition to Bleeding? - 1
- E: Labile INR? - 1
- D: Age ≥ 65 years - 1
- A: Medication Usage Predisposing to Bleeding? (Antiplatelet agent / NSAIDs) - 1
- E: Alcohol Usage History? - 1

1: Risk was 3.4% in one study
Dabigatran Dose:

- Dabigatran 150 mg Twice Daily

Valid dosing regimes for this indication are:

<table>
<thead>
<tr>
<th>Dosing regime</th>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran 150 mg Twice Daily</td>
<td>Normal dose</td>
</tr>
<tr>
<td>Dabigatran 110 mg Twice Daily</td>
<td>Patients aged 80 or over, or at risk of bleeding</td>
</tr>
</tbody>
</table>

Comments:

Status: Complete

Last marked as complete: 05/10/2012 11:29 by Brenda Nicol

Unlock to edit

Information in this questionnaire is used to influence dosing and therapy decisions. Please ensure all answers are accurate and complete.
## Dabigatran Follow Up

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Ian DABIGATRAN</th>
<th>Due Date:</th>
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</table>

### Questions:

<table>
<thead>
<tr>
<th>Therapeutic Indication:</th>
<th>Atrial fibrillation nonvalvular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of use?</td>
<td>Indefinite</td>
</tr>
<tr>
<td>Age (at due date):</td>
<td>43</td>
</tr>
<tr>
<td>Dabigatran Dose:</td>
<td>Dabigatran 150 mg Twice Daily</td>
</tr>
</tbody>
</table>
### Over the past two weeks:

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have taken the correct dose every day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I might have taken too many capsules / tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I might have missed one or more doses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I take more than 3 other medications regularly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach upset / burning / pain (0-9)</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

### Reasons for compliance problems:
- Cost
- Dementia
- Fear of side-effects
- Gastroesophageal Reflux Disease
- Gastrointestinal Bleed
- Lack of information
- Lives alone
- Multiple medications
- Prescriptions from several doctors
Has the patient reported any adverse event (potentially due to current anticoagulant)?

- [ ] Anaemia
- [ ] Bruising
- [ ] Change in color of stools
- [ ] Epistaxis
- [ ] Haematoma
- [ ] Vomiting blood

Comments:
Case 1

66yo male referred from Urgent Care for acute unprovoked PE/DVT. Patient was given one dose of enoxaparin and prescribed apixaban 10mg BID x 7 days then apixaban 5mg BID.

PMH: CAD, HTN, HPL, H/O seizures
Labs: CMP unremarkable, CBC normal
    INR=1.0    Scr=0.9
Meds: atorvastatin, omeprazole, phenytoin and vit D
Questions:

Therapeutic Indication: PE - UNPROVOKED

Duration Of Use: 6 months

NB Remember to schedule a follow-up questionnaire for this patient once the Apixaban treatment plan is activated

If switching from VKA, please enter the current INR:

Delay starting Apixaban until INR<2.0

Notes:

Enter the start date of Apixaban or other anticoagulant: 06/02/2015

Day 7 will be on Monday 6/8/2015 - adjust dose as appropriate.

Measured Creatinine Clearance: 80 mL/min
The following lists are for guidance only and are not exhaustive. Please use your clinical judgement before decision making.

**Contraindicated Drugs**:  
- ANTIMYCOTIC (ITRACONAZOLE, KETACONAZOLE...)
- ANTITHROMBOTIC (WARFARIN, DABIGATRAN...)
- HIV PROTEASE INHIBITOR (RITONAVIR...)

**Interacting drugs**:  
- Agent associated with serious bleeding
- ASPIRIN
- CLOPIDOGREL
- CYP3A4 AND P-GP INDUCERS (RIFAMPICIN, PHENYTOIN...): Use with caution. Not to be used for treatment of DVT and PE
- OTHER NSAIDs

**Other anticoagulant or platelet inhibitor**:  
- Abciximab
- Eptifibatide
- Heparin

*Click for more details on Apixaban*
Case 2

65 yo male with atrial fibrillation previously on warfarin but recently switched to Xarelto by his cardiologist. Wife called concerned because she saw commercial that Xarelto is indicated for nonvalvular atrial fibrillation and patient has bioprosthetic mitral heart valve.
Other contraindications*:

- Active clinically significant bleeding
- Arteriovenous malformations
- Cirrhotic patient with Child Pugh B & C
- Creatinine clearance <15ml/min
- Current or recent gastrointestinal ulceration
- Hepatic disease associated with coagulopathy and clinically relevant bleeding risk
- Hypersensitivity to tablet excipients or galactose intolerance
- Known or suspected oesophageal varices
- Malignant neoplasms at high risk of bleeding
- Paediatric Patient
- Pregnancy and breastfeeding
- Prosthetic Heart Valve
- Recent brain or spinal injury
- Recent brain, spinal or ophthalmological surgery
- Recent intracranial or intracerebral haemorrhage
- Vascular aneurysms or major intraspinal or intracerebral vascular abnormalities
Renal function not recorded. Rivaroxaban is contraindicated according to information recorded above.

✗ CONTRAINDIATED Use is not recommended

Please use your clinical judgement before deciding on the most appropriate dose.

Click for more details on rivaroxaban.
Case 3

73 yo female on Xarelto 20mg once daily for atrial fibrillation due for follow up. Patient has been having borderline CRCL around 51 ml/min. Upon checking current SCR, CRCL = 48 ml/min.
Therapeutic Indication:

**ATRIAL FIBRILLATION NON VALVULAR**

*NB Remember to schedule another follow-up questionnaire for this patient for 6 months time.*

I have taken the correct dose every day  
- ☐ No  ☐ Yes

I might have taken too many capsules / tablets  
- ☐ No  ☐ Yes

I might have missed one or more doses  
- ☐ No  ☐ Yes

Notes:

I have started a new medication recently  
- ☐ No  ☐ Yes

Reasons for compliance problems:

- ☐ Dementia
- ☐ Fear of side effects
- ☐ Gastroesophageal Reflux Disease
- ☐ Gastrointestinal Bleed
- ☐ Lack of information
- ☐ Lives alone
- ☐ Multiple medications
- ☐ Prescriptions from several doctors
<table>
<thead>
<tr>
<th><strong>Measured Creatinine Clearance:</strong></th>
<th>48 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>eGFR:</strong></td>
<td>ml/min</td>
</tr>
<tr>
<td><strong>Cockcroft-Gault estimate of CrCl:</strong></td>
<td>1.23 x (140 - age years) x weight kg (x 0.85 if female) serum creatinine μmol/L</td>
</tr>
<tr>
<td><strong>Cockcroft D, Gault MD.</strong></td>
<td>Nephron, 16:31-41, 1976</td>
</tr>
<tr>
<td><strong>Serum Creatinine:</strong></td>
<td>μmol/L</td>
</tr>
<tr>
<td><strong>Body Weight:</strong></td>
<td>102.7 kg</td>
</tr>
</tbody>
</table>
Rivaroxaban Dose:

Rivaroxaban 20 mg Once Daily

Suggested dose:

Moderate/severe renal impairment. 15mg once daily with the evening meal

Dose Options:

<table>
<thead>
<tr>
<th>Dosing regime</th>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban 20 mg</td>
<td>Recommended dose (maximum recommended)</td>
</tr>
<tr>
<td>Once Daily</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban 15 mg</td>
<td>Recommended for moderate to severe renal impairment (15-49 mL/min creatinine clearance)</td>
</tr>
<tr>
<td>Once Daily</td>
<td></td>
</tr>
</tbody>
</table>

Please use your clinical judgement before deciding on the most appropriate dose. Then update the treatment plan as required.

Click for more details on rivaroxaban.
Re-Design of the “Coumadin Clinic”

“Clinics that survive the introduction of novel agents will likely be those that shift from a primary focus on monitoring warfarin to management of thrombotic disease and coordination of all antithrombotic therapy in the form of multidisciplinary comprehensive antithrombosis centers.”

A Comprehensive Pharmacist Managed Anticoagulation Service at Scripps

- NOACs have been incorporated into the scope of practice: Pradaxa (dabigatran), Xarelto (rivaroxaban), Eliquis (apixaban)
- Development of expertise in the full range of antithrombotic agents
- Peri-procedural management
- Transition between agents
- Drug-drug interactions
- Compliance management
- Knowledge of intervention to avoid or minimize complications and maximize efficacy of therapy