



Use of Novel Oral Anticoagulants (NOACs) and the new DAWN modules at Scripps

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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: concern during long term anticoagulation

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%**

Kimmel SE, et al., The influence of patient adherence on anticoagulation control with warfarin: results from the International Normalized Ratio Adherence and Genetics (IN-RANGE) study. Arch Intern Med 2007; 167: 229-35.

Van der Meer FJ, et al., The role of compliance as a cause of instability in oral anticoagulant therapy. Br J Haematology 1997; 98: 893-900.

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?

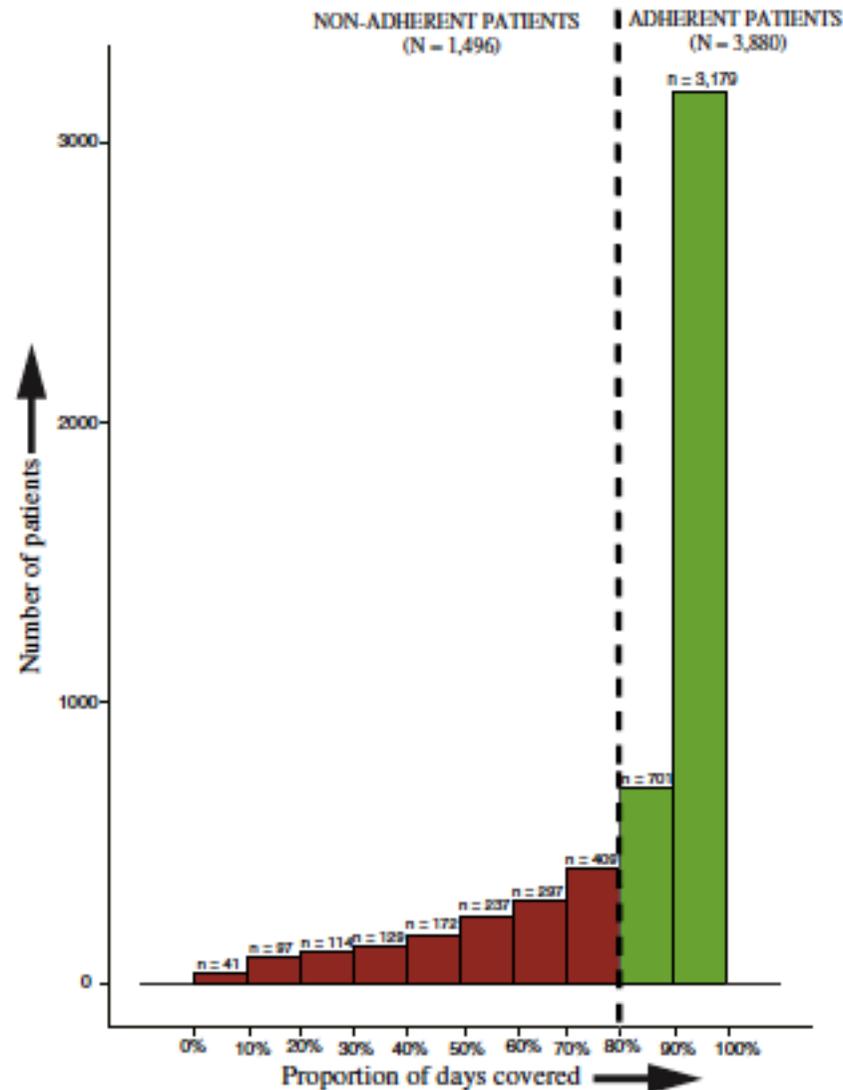
Einstein PE: adherence was >80% in 94.2% of patients treated with rivaroxaban (Xarelto)

The EINSTEIN-PE Investigators, N Engl J Med, 2012; 366:1287-97

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

Agnelli, G. and AMPLIFY Investigators., N Engl J Med 2012; 368: 699-708

Adherence to Dabigatran Therapy in Longitudinal Veterans Administration Cohort



Distribution of Proportion of days covered across study cohort. x-axis displays proportion of days covered in increments of 10%, y-axis displays number of patients. Patients with PDC <80% were classified as non-adherent. Patients with PDC \geq 80% were classified as adherent.

Current Scripps NOAC Anticoagulation Service Experience

Diagnosis	Indications
Pradaxa [®] (dabigatran)	Non-valvular atrial fibrillation Treatment and Prevention of DVT/PE
Xarelto [®] (rivaroxaban)	Non-valvular atrial fibrillation Treatment and Prevention of DVT/PE
Eliquis [®] (apixaban)	Non-valvular atrial fibrillation Treatment and Prevention of DVT/PE

DAWN New Oral Anticoagulant Modules

NOAC Management using DAWN AC

- Full anticoagulant history
- Ensure patients are on appropriate drug and dose
- Schedule followups
- Manage missed appointments
- Reporting
- Audit

DABIGATRAN, Ian - 01/10/1931 - DAB123

Risk class **High**
Pref. clinic (None selected)
Phone - home
Age **81**

Diagnosis Atrial fibrillation nonvalvular

Target Range non-VKA

Start date 05/10/2012 - Indefinite

Anticoagulant Dabigatran 150 mg Twice Daily

Treatment Plan 1 of 1 active

Risks

Dabigatran Contacts Letters Drugs Events Procedures Reviews Reminders Groups Documents

i 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.

Personal Treatment plans **Questionnaires** Test Results Interface Warnings

QuestionnaireType	Entry date	Summary
 Dabigatran Follow Up	05/10/2012	Scheduled
 Dabigatran Initiation	05/10/2012	CrCl: 38 mL/min (cre: 160 µM, Wt: 70 kg) - Dose: not specified

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

Patient Name:	Ian DABIGATRAN	Due Date:	05/10/2012 
Unit No:	DAB123	Status	Scheduled

Questions:

Therapeutic Indication:	<input type="text" value="(None selected)"/>
Qualifying Risk Factors:	<input type="text" value="(None selected)"/> ATRIAL FIBRILLATION NON VALVULAR TOTAL HIP REPLACEMENT SURGERY TOTAL KNEE REPLACEMENT SURGERY DVT - UNPROVOKED PE - PROVOKED PE - UNPROVOKED DVT - PROVOKED <input type="checkbox"/> Symptomatic heart failure >= NYHA Class 2
Duration of use?	<input type="text" value="(None selected)"/>

Measured Creatinine Clearance: mL/min

Cockcroft-Gault estimate of CrCl:

$1.23 \times (140 - \text{age years}) \times \text{weight kg} \times 0.85 \text{ if female}$

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

serum creatinine $\mu\text{mol/L}$

Serum Creatinine: $\mu\text{mol/L}$ **High**

Body Weight: kg

Gender: **Male**

Age (at due date): **43**

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
- Hypersensitivity to sunset yellow (E110)
- Organic lesion at risk of bleeding
- 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

CHA₂DS₋₂VASc score?

3 ▼

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
A₂	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?

1: Risk was 3.4% in one study ▼

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

Dabigatran Dose:

Dabigatran 150 mg Twice Daily ▾

Valid dosing regimes for this indication are:

Dosing regime	Advice
Dabigatran 150 mg Twice Daily	Normal dose
Dabigatran 110 mg Twice Daily	Patients aged 80 or over, or at risk of bleeding

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

Patient Name: Ian DABIGATRAN

Due Date:

05/10/2012



Unit No: DAB123

Status

Scheduled

Questions:

Therapeutic Indication: Atrial fibrillation nonvalvular

Duration of use? Indefinite

Age (at due date): 43

Dabigatran Dose: Dabigatran 150 mg Twice Daily

Over the past two weeks:

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

I take more than 3 other medications regularly No Yes

Stomach upset / burning / pain (0-9)

- 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 Lovenox 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

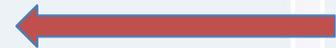
Notes:

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.

[Click for more details on Apixaban](#)

Contraindicated Drugs* :

- ANTIMYCOTIC (ITRACONAZOLE, KETACONAZOLE...)
- ANTITHROMBOTIC (WARFARIN, DABIGATRAN...)
- HIV PROTEASE INHIBITOR (RITONAVIR...)

Interacting drugs*:

INTERACTION
[click for more details](#)

- Agent associated with serious bleeding
- ASPIRIN
- CLOPIDOGREL
- CYP3A4 and P-gp inducers (RIFAMPICIN,PHENYTOIN...)
- OTHER NSAIDs

CYP3A4 AND P-GP INDUCERS (RIFAMPICIN,PHENYTOIN...):
Use with caution.
Not to be used for treatment of DVT and PE

Other anticoagulant or platelet inhibitor* :

- Abciximab
- Eptifibatide
- Heparin

Care is to be taken if patients are

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.

[Click for more details on rivaroxaban](#)

✖ 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



OK

Cancel

Done

Internet | Protected Mode: On

200%

Dose Options:

Suggested Dose:

Renal function not recorded. Rivaroxaban is contraindicated according to information recorded above.

✘ CONTRAINDICATED Use is not recommended

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

[Click for more details on rivaroxaban.](#)

Comments

Status: Scheduled

OK

Cancel

Done

Internet | Protected Mode: On

200%

Case 3

73 yo female on Xarelto 20mg qpm 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

Rivaroxaban Dose:

Rivaroxaban 20 mg Once Daily

Suggested dose:

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

Dose Options:

Dosing regime	Advice
Rivaroxaban 20 mg Once Daily	Recommended dose (maximum recommended)
Rivaroxaban 15 mg Once Daily	Recommended for moderate to severe renal impairment (15-49mL/min creatinine clearance)

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.](#)

Comments:

OK

Cancel

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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.”

Edith A. Nutescu, Pharm.D, et.al., Transitioning from traditional to novel anticoagulants: the impact of oral direct thrombin inhibitors on anticoagulation management. Pharmacotherapy 2004; 24: 199S-202S.

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