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

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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.

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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

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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%**

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.

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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

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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 follow-up
Manage missed appointments
Reporting
Audit

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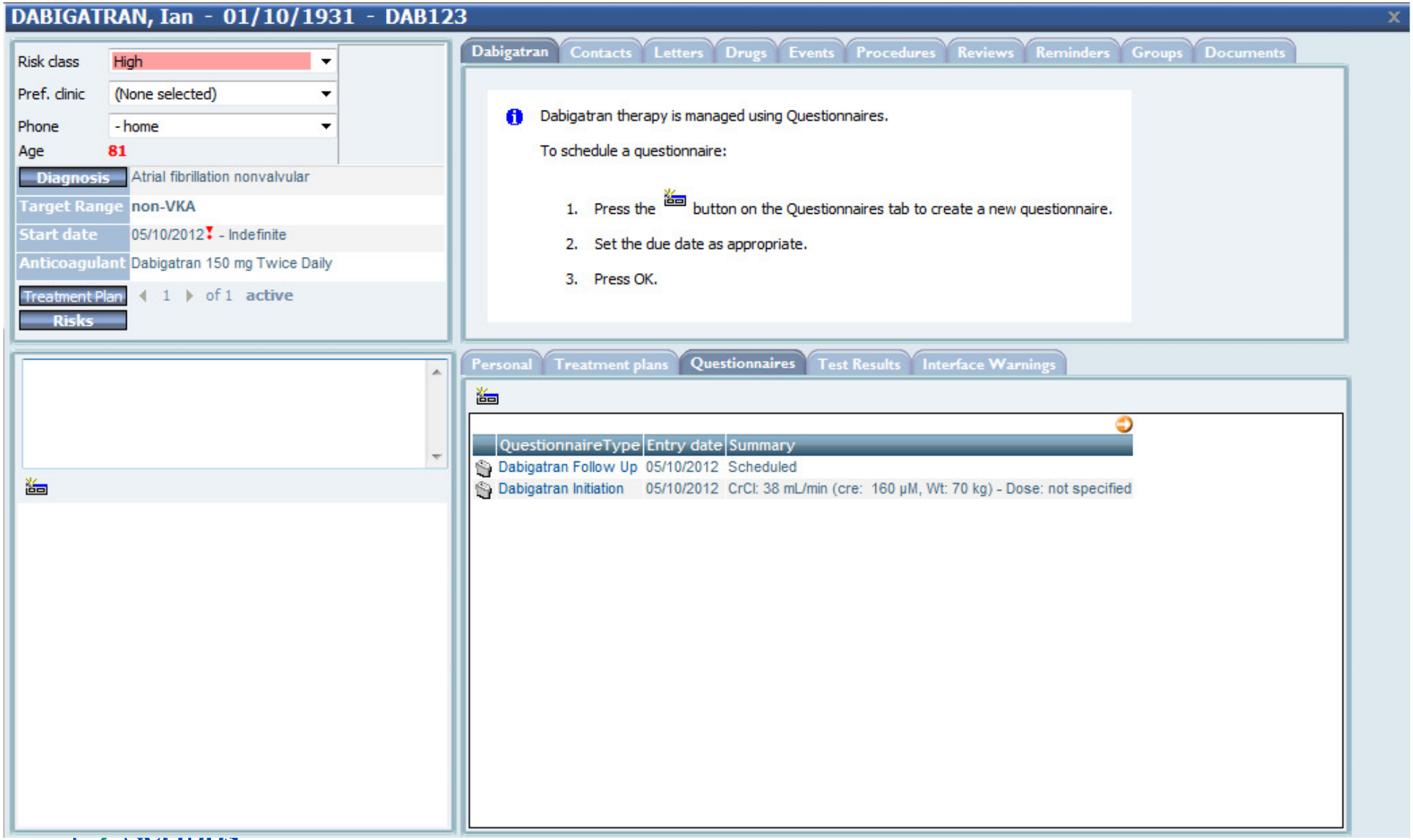
DABIGATRAN, Ian - 01/10/1931 - DAB123
Risk class
High
Pref. clinic
(None selected)
Phone
- home
Age
81
Diagnosis
Atrial fibrillation nonvalvular
Target Range
non-VKA
Start date
05/10/2012 - Indefinite
Anticoagulant
Dabigatran 150 mg Twice Daily
Treatment Plan
1 of 1 active
Risks
Dabigatran
Contacts
Letters
Drugs
Events
Procedures
Reviews
Reminders
Groups
Documents
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

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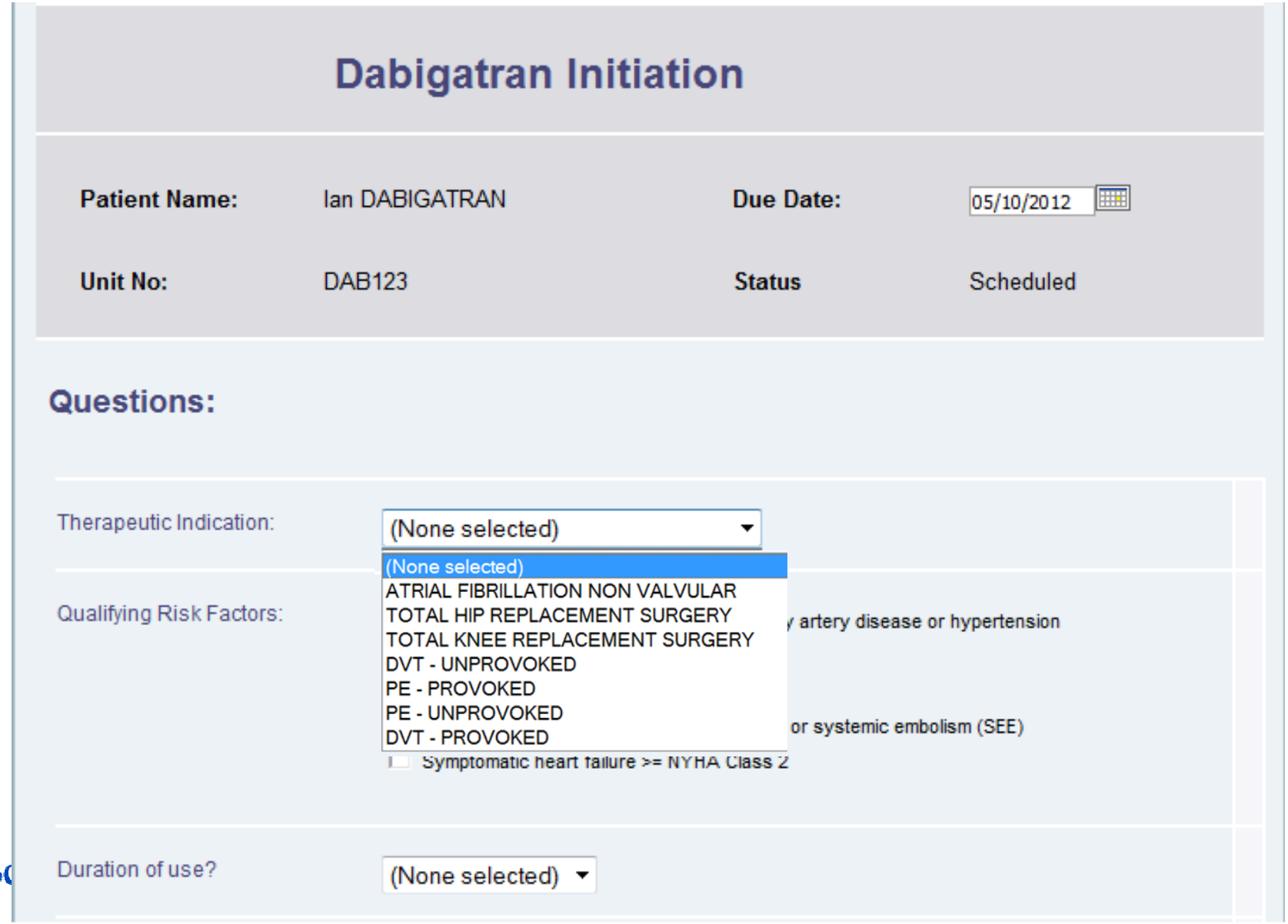

Dabigatran Initiation
Patient Name:
Ian DABIGATRAN
Due Date:
05/10/2012
Unit No:
DAB123
Status
Scheduled
Questions:
Therapeutic Indication:
(None selected)
(None selected)
ATRIAL FIBRILLATION NON VALVULAR
TOTAL HIP REPLACEMENT SURGERY
TOTAL KNEE REPLACEMENT SURGERY
DVT - UNPROVOKED
PE - PROVOKED
PE - UNPROVOKED
DVT - PROVOKED
Qualifying Risk Factors:
artery disease or hypertension
or systemic embolism (SEE)
Symptomatic heart failure >= NYHA Class 2
Duration of use?
(None selected)

Measured Creatinine Clearance: [ ] mL/min

Cockcroft-Gault estimate of 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 µmol/L High

Body Weight: 70 kg

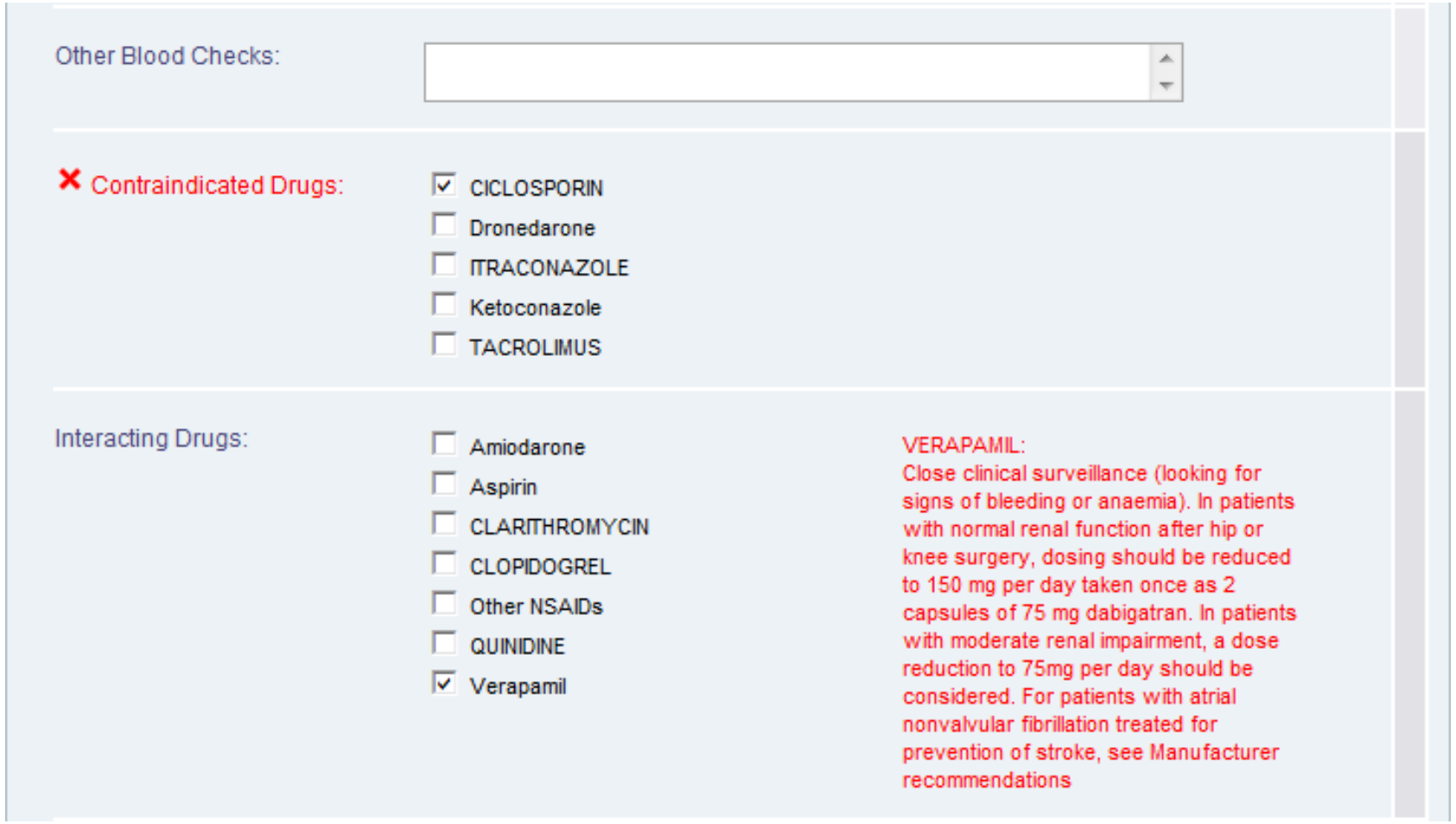
Gender: Male

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

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✖ Other contraindications:

- [ ] Active clinically significant bleeding
- [ ] Hepatic impairment or liver disease expected to have any impact on survival
- [ ] Hypersensitivity to dabigatran etexilate
- [x] 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:

- [x] 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

CHA_2DS_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
A_2	Age ≥ 75 years	2
D	Diabetes Mellitus	1
S_2	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 > 200uM or > 2.6mg/dL)	1
	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
	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)	2 ▾	

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:

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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*

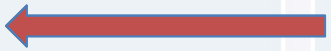
If switching from VKA, please enter the current INR:

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.

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
- [x] 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

New Delete Save To list Print 1 / 1

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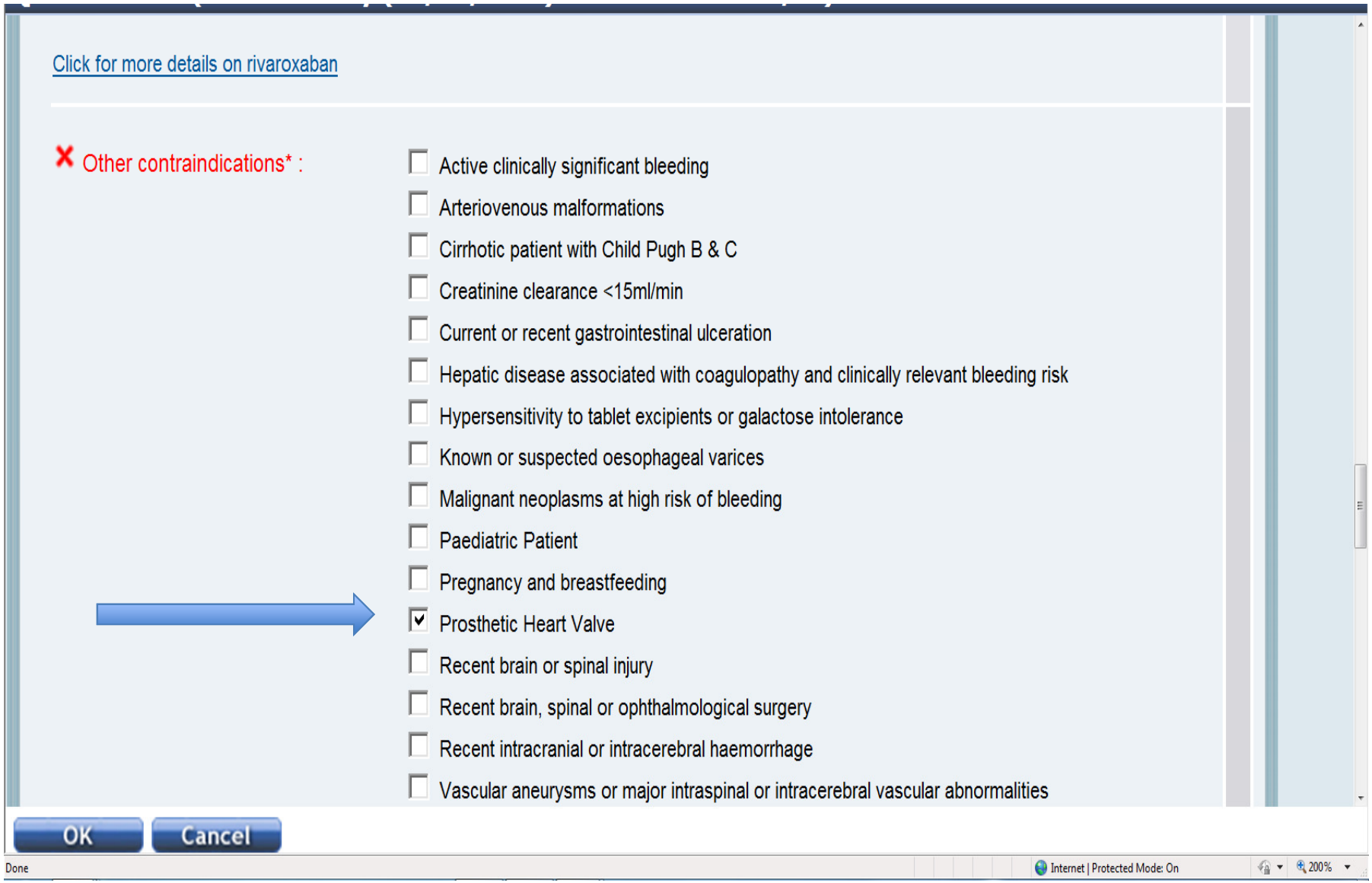
Case 2

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%

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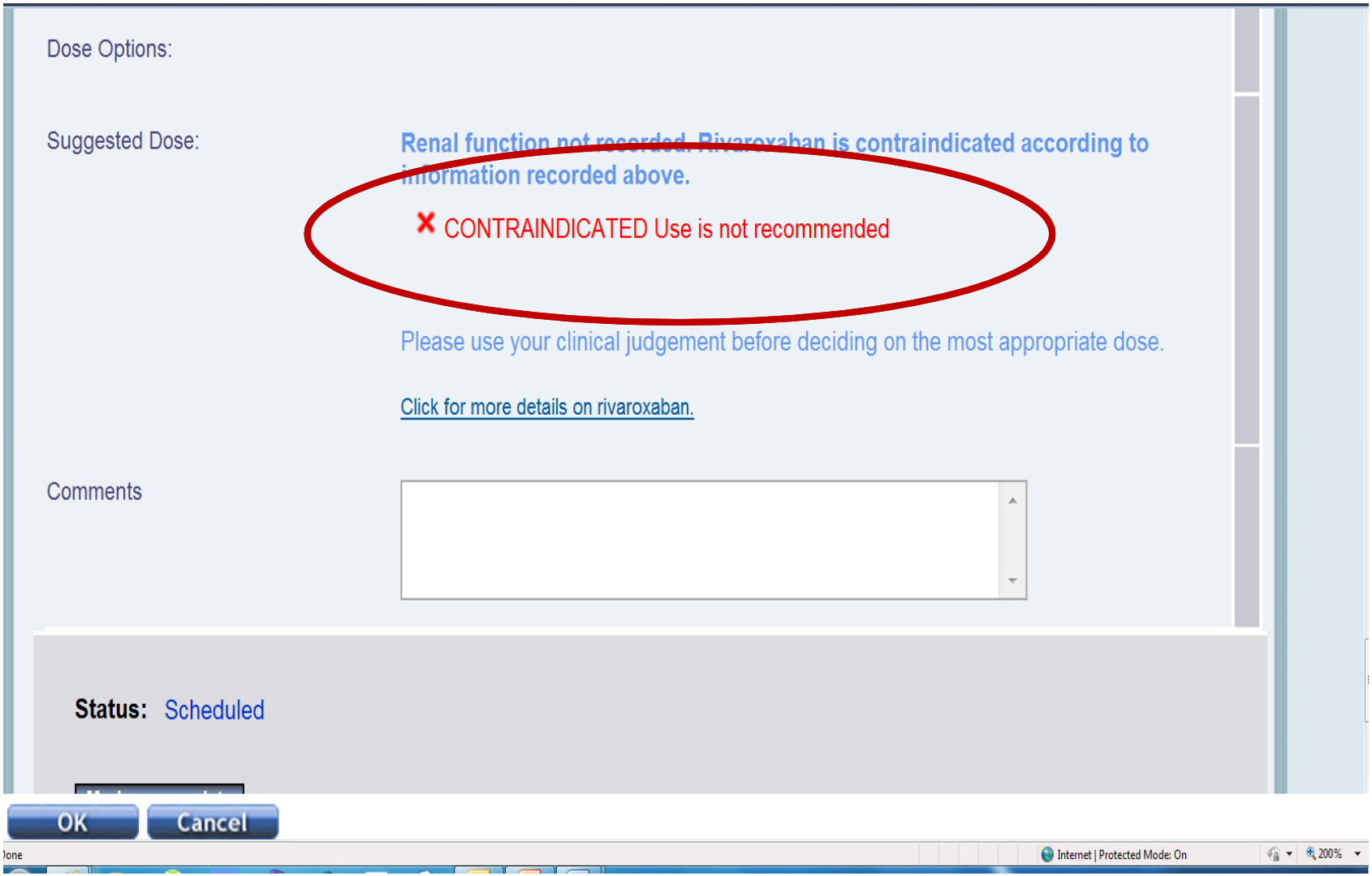
Dose Options:
Suggested Dose:
Renal function not recorded. Rivaroxaban is contraindicated according to information recorded above.
CONTRAINDICATED Use is not recommended
Please use your clinical judgement before deciding on the most appropriate dose.
Click for more details on rivaroxaban.
Comments
Status: Scheduled
OK
Cancel
Done
Internet | Protected Mode: On
200%

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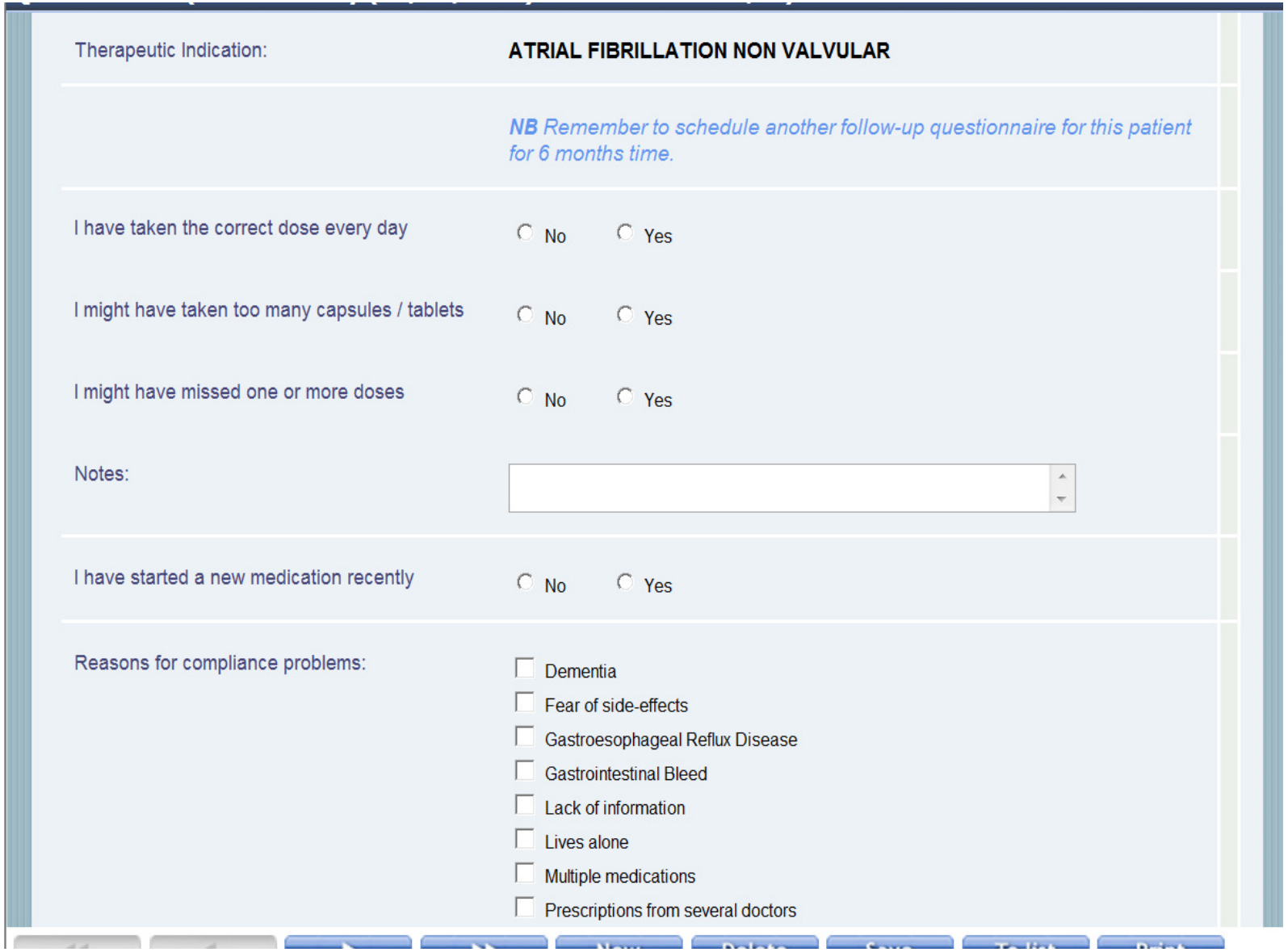
Case 3

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

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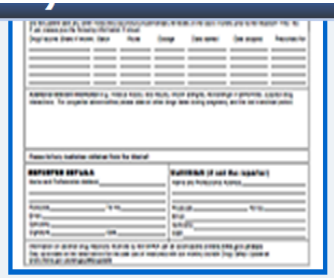

Measured Creatinine Clearance: 48 mL/min

eGFR: mL/min

Cockcroft-Gault estimate of CrCl:

$$\frac{1.23 \times (140 - \text{age years}) \times \text{weight kg (x 0.85 if female)}}{\text{serum creatinine µmol/L}}$$

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

Serum Creatinine: µmol/L

Body Weight:

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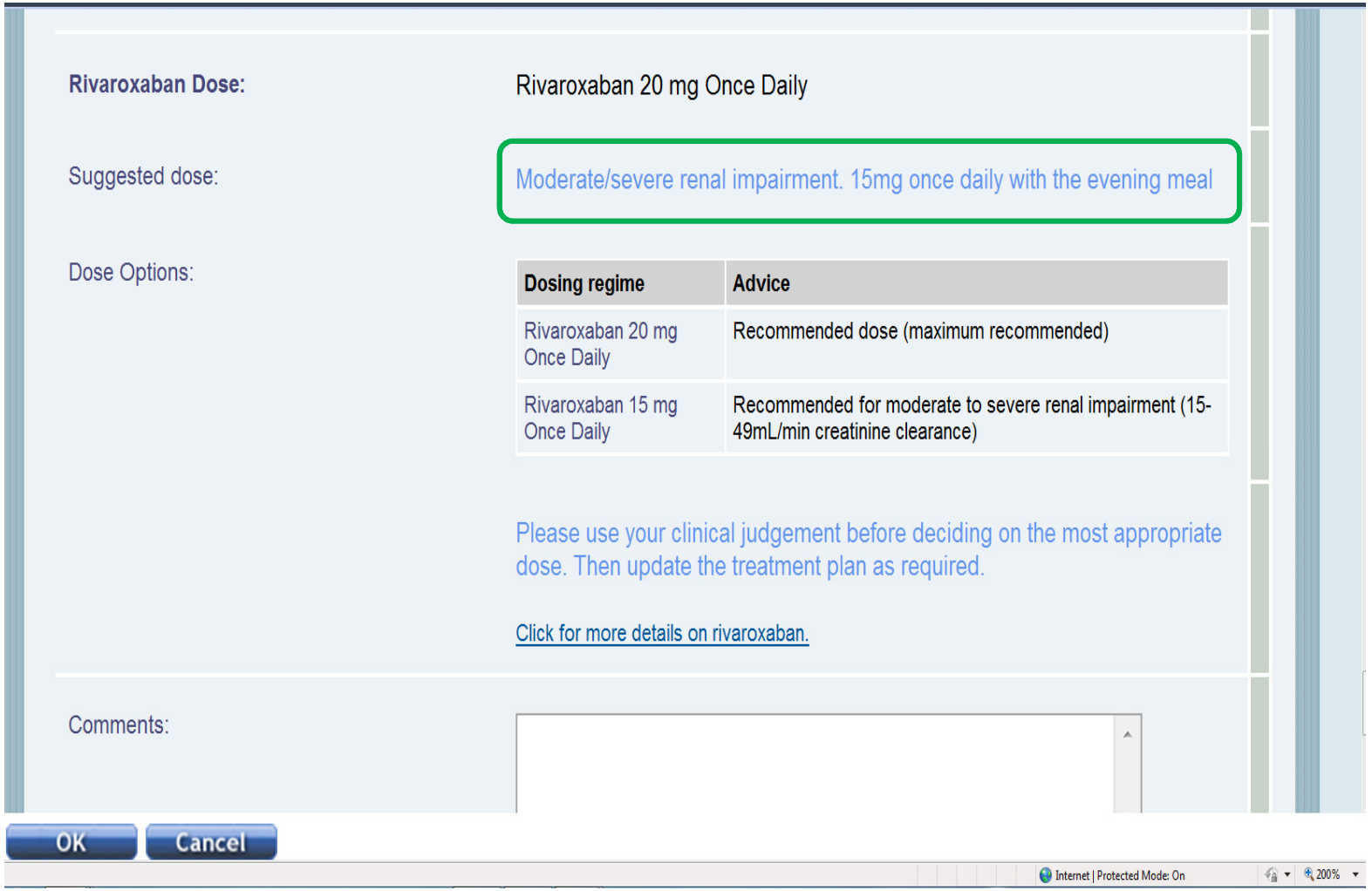
Rivaroxaban Dose:
Rivaroxaban 20 mg Once Daily
Suggested dose:
Moderate/severe renal impairment. 15mg once daily with the evening meal
Dose Options:
Dosing regime
Advice
Rivaroxaban 20 mg Once Daily
Recommended dose (maximum recommended)
Rivaroxaban 15 mg Once Daily
Recommended for moderate to severe 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
Internet | Protected Mode: On
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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