Basildon and Thurrock University Hospitals NHS
NHS Foundation Trust

Rivaroxaban Shared Care Guideline (SCG)

Rivaroxaban shared care guidelines for the prevention of stroke and embolism in adult patients with nonvalvular atrial fibrillation.

Introduction

Indication and licensing

Rivaroxaban is an oral anticoagulant that works through highly selective inhibition of factor Xa. It belongs to a small number of agents that are licensed for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation with one or more of the following risk factors:

- Congestive heart failure
- Hypertension
- Age > 75 years
- Diabetes mellitus
- Prior stroke, transient ischemic attack

Patient pathway

Clinical speciality	Prescribing initiated by	Prescribing continued by	Monitored by	Duration of treatment
Cardiology Haematology Stroke	Hospital consultant	GP following initiation by hospital	GP following initiation by hospital	Life long*

*temporary discontinuation for surgical procedures advised.

Patients are to be initiated in the first instance via a consultant (cardiology, haematology, stroke). One month supply to be made by hospital when initiated.

Treatment should continue indefinitely on confirmation of nonvalvular atrial fibrillation that requires anticoagulation. Treatment should be reviewed (at least annually) and an assessment made for new contraindications to ongoing anticoagulation with Rivaroxaban (e.g. temporary discontinuation for surgery, marked decline in renal function and increased bleeding risk (see below for further advice on bleeding risk)). Where new contraindications are found, treatment is to be reviewed and anticoagulation therapy withdrawn if risks are deemed to outweigh benefits. If therapy is to be withdrawn, refer to specialist to assess and initiate suitable antithrombotic therapy.

Ongoing compliance should be reviewed on a regular basis, the duration and method of compliance assessment should be determined by the GP and patient characteristics.

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Date approved: 22nd Feb 2013

Normal dose and administration

Rivaroxaban is available as 2 strengths for prevention of stroke and systemic embolism in atrial fibrillation. Both are film coated tablets containing Rivaroxaban 15mg or 20mg.

Usual dose:

20mg tablet once daily* to be swallowed whole with food.

*Unless dose reduction indicated as below

Dose alterations:

Increased risk of bleed:

-If bleeding risk is assessed as high (in accordance with HAS-BLED score, see Appendix I), patients are to be considered for 15mg tablet once daily or no anticoagulation (if no anticoagulation refer to specialist for antithrombotic of choice). Clear documentation should be made as to reason for dose reduction.
-For subjects with gastritis, oesophagitis, or gastroesophageal reflux, a dose of 15mg tablet once daily may be considered due to the increased risk of major gastro-intestinal bleeding.
-Individuals at low body weight (<50kg) may be more prone to bleeding and as such monitored closely and dose reduction (15mg once daily) considered.
-Patients with an increased bleeding risk should be closely monitored clinically (looking for signs of bleeding or anaemia, more details below). Dose adjustment should be decided at the discretion of the physician, following assessment of the potential benefit and risk to an individual patient.
-If clinically relevant bleeding occurs, treatment should be interrupted and reviewed prior to re initiation.

Renal impairment:

-Renal function should be assessed by calculating creatinine clearance prior to initiation of treatment with Rivaroxaban to exclude patients with severe renal impairment (i.e. CrCL < 15 ml/min).
-CrCl > 50mls/min; no adjustment although consider dose reduction if risk factors for bleed
-CrCl 15 to 49mls/min; dose reduction, 15mg once daily
-CrCL <15mls/min; contraindicated

Monitoring standards for rivaroxaban

Parameter	**Renal function (Creatinine clearance - CrCl)**
Action required	CrCl >50mls/min; no adjustment required, but for patients at high risk of bleeding, consider dose reduction to 15mg once daily. CrCl 15 to 49mls/min; 15mg once daily. CrCl <15mls/min; contraindicated, avoid use
Frequency of monitoring	Assess renal function prior to treatment to ensure appropriate starting dose then while on treatment renal function should be assessed at least once a year (or more frequently as needed in certain clinical situations when it is suspected that the renal function could decline or deteriorate such as hypovolemia and dehydration.
Further action	Dose reduction may be required based on initial renal function. If renal function declines rapidly may need to temporarily withhold therapy and review prior to restarting.

Parameter	**Minor bleeding (or those at high risk of bleed on treatment)**
Haematological tests	Dose-dependent inhibition of Factor Xa activity was observed in humans. Prothrombin time (PT) is influenced by Rivaroxaban in a dose dependent way with a close correlation to plasma concentrations (r value equals 0.98) if Neoplastin is used for the assay, other reagents would provide different results. If clinically indicated rivaroxaban levels can be measured by calibrated quantitative anti-Factor Xa tests but liaise with haematology prior to requesting.
Frequency of monitoring	Only if numerous episodes of minor bleeding is observed or patient at high risk of bleed and on 20mg once daily, a raised PT should prompt a dose reduction if clinically indicated
Action	Dose reduction if clinically indicated and / or liaison with haematology

Parameter	**Compliance**
Target level	100%
Frequency of monitoring	Prior to initiation, likely compliance should be considered and discussed with the patient. Following initiation, compliance should be checked and reinforced at a minimum of annually although this is left at the discretion of the physician.
Action	If compliance likely to be low, consider alternative anticoagulation that can be monitored.

Adverse effects

Adverse effects	Symptoms/signs (specify what would prompt action)	Actions
Minor Bleeding	Self terminating minor bleeding from scratches, cuts, nose bleeds, gum bleeding etc. may be experienced. If these are frequent or patient / physician concerned - contact local haematology department for advice	The degree of bleeding will dictate action. If minor bleeding is infrequent and self terminates, patient can be reassured. If already on lower dose or concerns are raised - liaise with haematology for advice.
Moderate bleeding	Bleeding that does not stop with reasonable intervention should be referred to local A&E, if in doubt contact local haematology department for advice.	The degree of bleeding will dictate the action. If bleeding stops spontaneously and patient taking 20mg once daily, consider omitting a day's dose and reducing to 15mg once daily. If already on lower dose or concerns are raised - liaise with haematology for advice. For bleeding that does not stop with intervention, send patient to local A&E.
Major bleeding	Major bleeding in the ROCKET trial was defined as a reduction in haemoglobin of at least 20g/L or leading to a transfusion of at least 2 units of blood or bleeding at a critical site or with a fatal outcome. If bleeding presents as clinically significant send patient to local A&E or call 999	Immediate referral to secondary care.
GI	Dyspepsia	Consider gastro protection in accordance with local guidance. If no further improvement, consider alternatives or referral to specialist.

Key adverse events and actions

This lists the key adverse drug reactions, for comprehensive information on cautions, contra- indications and interactions. Please refer to the current British National Formulary and Summary of Product Characteristics for further information.

Important cautions

Surgery and invasive procedures

Patients on rivaroxaban who undergo surgery or invasive procedures are at increased risk for bleeding. Therefore surgical interventions may require temporary discontinuation of rivaroxaban with or without bridging management as per local guidance and protocols for anticoagulation depending on the surgery and thromboembolic risks involved.

For further information refer to the Trust's peri-operative management of drug therapy guidelines.

Drug interaction

Rivaroxaban is metabolised via CYP 3A4 and CYP 2J2, for this reason strong CYP 3A4 inducers and inhibitors should be avoided as these can cause significant under and over anticoagulation effect. Inducers such as rifampicin, St. John`s Wort, carbamazepine, or phenytoin, and inhibitors such as ketoconazole and ritonivir are to be avoided. No clinically significant pharmacokinetic or pharmacodynamic interactions were observed when rivaroxaban was co-administered with midazolam (substrate of CYP3A4), digoxin (substrate of P-gp), atorvastatin (substrate of CYP3A4 and P-gp) or omeprazole (proton pump inhibitor). Rivaroxaban neither inhibits nor induces any major CYP isoforms like CYP3A4. A full list of interactions can be obtained from Summary of Product Characteristics.

Pregnancy and breast feeding

The safety of rivaroxaban has not been established in pregnant or lactating women; as such use in these patients is to be avoided.

Shared care of rivaroxaban

Shared care guideline: is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets out responsibilities for each party. The intention to shared care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and cooperation in the management of patients. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use.

Consultant

1. Ensure that the patient/carer is an informed recipient of Rivaroxaban.

2. Ensure that patients understand Rivaroxaban treatment and monitoring (e.g. renal function) or follow up that is required (using advocacy if appropriate).

3. Ensure baseline investigations are normal before commencing treatment. Give the patient a patient held anticoagulant card.

4. Initiate treatment and prescribe until the GP formally agrees to shared care. Supply the first month of treatment at initiation.

5. Send a letter to the GP requesting shared care

6. Send a letter/results notification to the GP after the clinic meeting confirming the current dose and most recent blood results.

7. Evaluation of any reported adverse effects by GP or patient.

8. Advise GP on review, duration or discontinuation of treatment where necessary.

9. Ensure that backup advice is available at all times.

General Practitioner

1. Reinforce the patient understands the nature, effect and potential side effects of Rivaroxaban before prescribing it as part of the shared care programme and contact the specialist for clarification where appropriate.

2. Monitor patient's overall health and well-being.

3. Report any adverse events to the consultant, where appropriate.

4. Report any adverse events to the CSM, where appropriate.

5. Help in monitoring the progression of disease

6. Prescribe the drug treatment as described.

CCG

1. To provide feedback to trusts via Trust Medicines Committee.

2. To support GPs in decision making and facilitate appropriate use and monitoring of Rivaroxaban.

3. To support trusts in resolving issues that may arise as a result of shared care.

Patient/ Carer

1. Report any adverse effects to their GP and/or specialist
2. Ensure they have a clear understanding of their treatment (Rivaroxaban).
3. Carry an anticoagulation card with them at all times
4. Report any changes in disease symptoms to GP and/or specialist
5. Alert GP and/or specialist of any changes of circumstance which could affect management of disease
6. Take/ administer rivaroxaban as prescribed

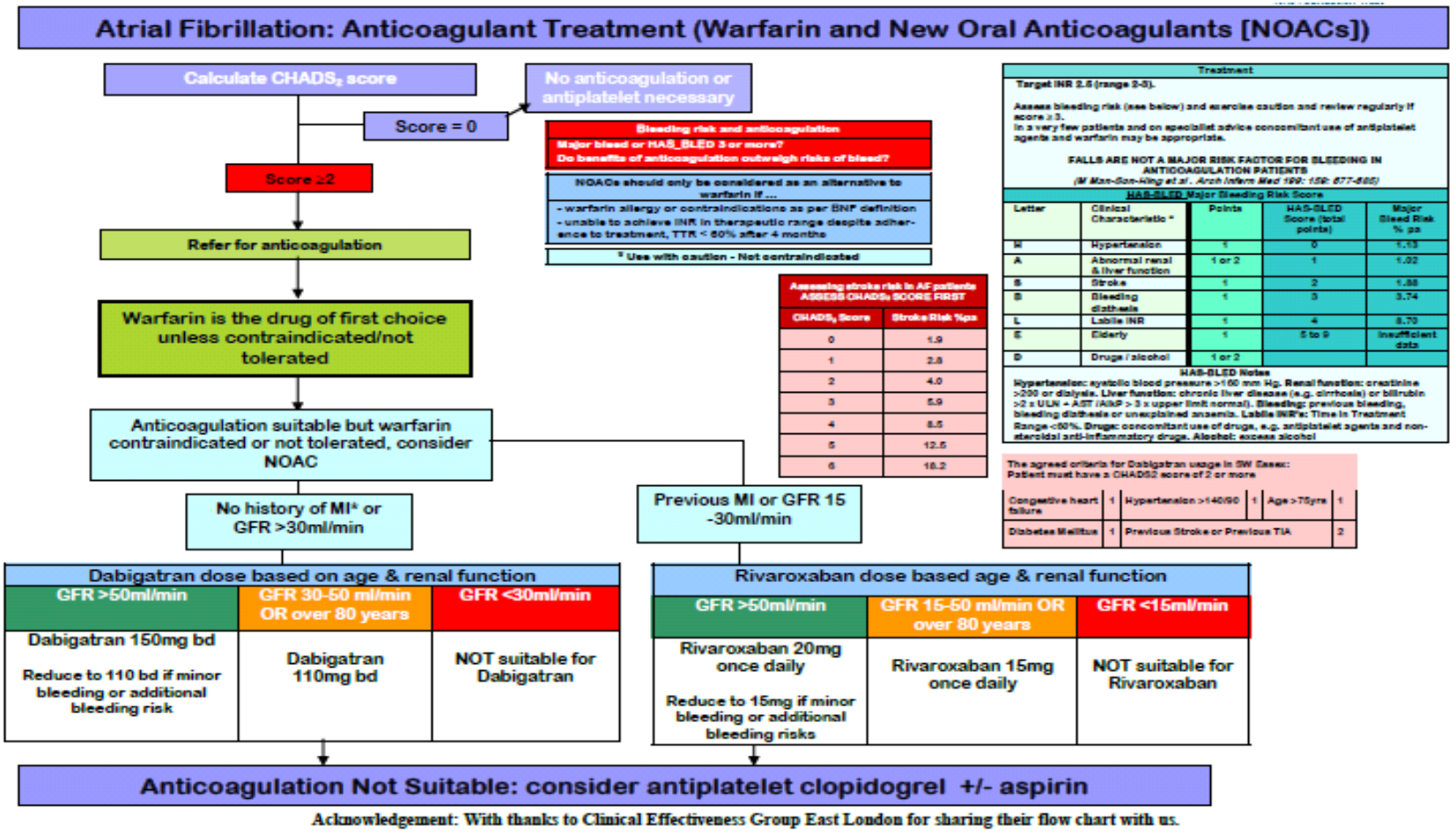
Contact details

Initial contact should be made with the initiating consultant. Contact consultant haematologist if haematologist is the initiating consultant or on the advise of the initiating consultant.

Initiating consultant at BTUH Name (please print):	Please insert: Contact details:
CCG prescribing team	Contact details:

Acknowledgement:
These shared care guidelines are based on the shared care guidelines by NHS North East London Cardiovascular and Stroke Network

Appendix I



Acknowledgement: With thanks to Clinical Effectiveness Group East London for sharing their flow chart with us.

Approved by: Medicines Management Committee
Date approved: 22nd Feb 2013

Appendix II

Approval Form for Dabigatran and Rivaroxaban Usage in Atrial Fibrillation Patients

Patient name: DOB:

Patient Hospital no: NHS no:

This form is for completion by **haematology, stroke and cardiac consultants ONLY**. Forms filled in by any other grade or speciality will be declined. Only patients meeting the agreed criteria will be supplied with NOACs (a prescription is also required).

The agreed criteria for Dabigatran usage in SW Essex are:

Patient must have a CHADS2 score of 2 or more

Congestive heart failure	1	Hypertension >140/90	1	Age >75yrs	1
Diabetes Mellitus	1	Previous Stroke or Previous TIA			2

**Please circle the relevant risk factors*

Plus the patient should have **one** of the following
**Please circle which apply*

Clinical contraindications to warfarin causing drug discontinuation

Yes	No	The C/Is are:

Allergy to warfarin

Yes	No	The allergy is:

Experience of substantial side effects with warfarin causing drug discontinuation

Yes	No	The S/Es are:

A further embolic event whilst on warfarin if eligible for 150 mg dabigatran

Yes	No

Time in therapeutic range for warfarin of less than 60% for 4 months i.e. poor control (Note: concordance issues must be fully explored and resolved before looking at poor control)

Yes	No

Patient requiring domiciliary phlebotomy

Yes	No

Please send completed form with the prescription to Fatemeh Leedham, pharmacy department

Consultant name: Signature: Date …../…../……

PCT advisor name: Signature Date …../…../……

Approved:

Yes	No

Fatemeh leedham Signature Date …../…../……

Please only dispense when all above signatures are complete and approval received from PCT

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Appendix III

Shared care agreement letter

Name of Trust: Basildon and Thurrock University Hospital NHS FT
Rivaroxaban (Xarelto ®)
Prevention of stroke and embolism in adult patients with nonvalvular atrial fibrillation

Name of GP …… Address ……
……...
……
..……
Dear GP

Re: Patient's Name……..……Date of Birth…….
NHS Number……..
Hospital Number……..……

Indication for oral Rivaroxaban 20 or 15mg mg (delete as appropriate) once daily for prevention of stoke and embolism in adult patients with nonvalvular atrial fibrillation.

Enclosed is a copy of the shared care guidelines for Rivaroxaban to be retained in the patient's notes.
Should you agree to shared care, we will send a letter containing the details of the patient's treatment plan, the dose to be prescribed and all relevant blood results.

Please sign below and return this letter to the Hospital Specialist if you agree to the shared care arrangements for this patient.

Many thanks

Hospital Specialist	GP
Signature……...	Signature……...
Name ……..……..	Name ……...
Date……..	Date……..……..

If you are not taking on shared care for this patient please state the reason why and return this letter to the Hospital Specialist.
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