City and Hackney Clinical Commissioning Group
Homerton University Hospital Foundation Trust

DRUG NAME: RIVAROXABAN (XARELTO ®)
Transfer of Care document
Prevention of stroke and embolism for nonvalvular atrial fibrillation

INTRODUCTION – Indication and Licensing

Rivaroxaban is a non-vitamin K antagonist oral anticoagulant (NOAC) that works through highly selective inhibition of factor Xa. It is 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, such as:

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

Initiation would be by secondary care only and in accordance with its licensed indication and NICE guidelines.

A NOAC can be initiated in either primary or secondary care in accordance with its licensed indication and NICE guidelines. Initiation must be done by a suitably qualified healthcare professional. This transfer of care document is a guidance document for when prescribing has been initiated in secondary care.

Due to its selective inhibition of one clotting factor, the anticoagulation effects are more predictable and as such there is no requirement for regular monitoring, unlike vitamin K antagonists (VKA) such as warfarin. Other potential advantages compared to VKAs include a standard dosing regimen and a lower likelihood of drug interactions. Disadvantages of rivaroxaban are its higher cost (partially offset by the reduced need for INR monitoring) and limited clinical experience of long-term use. Additional disadvantages are; there is no antidote as yet in case of life threatening bleeding, no available test for measuring residual activity before operation and no test for monitoring of patient adherence. However, in studies comparing against warfarin, less fatal bleeding was shown in comparison to warfarin in both atrial fibrillation and acute venous thromboembolism (VTE) and unlike warfarin has far shorter half-life and is therefore cleared quicker than warfarin, which may explain the less fatal bleeding seen in clinical trials.

PATIENT PATHWAY

Clinical Speciality / Indication	**Prescribing Initiated by**	**Prescribing Continued by** ***(detail when suitable for transfer to occur)***	**Monitored by** ***(detail when suitable for transfer to occur IF APPROPRIATE)***	**Duration of treatment**
Haematology/ Cardiology/ Stroke	Secondary care prescriber	Hospital after 4 weeks of initiation, where a further 4 weeks supply will be issued to patients	GP after 8 weeks	Lifelong

(N.B. a temporary discontinuation for surgical procedures is advised, see below for further details).

Patients are to be initiated in the first instance by a clinician who has expertise in initiating anticoagulant therapy for stroke prevention in AF. The clinician is responsible for the safe prescribing of rivaroxaban and ensuring the patient meets the defined criteria for use as outlined above. If rivaroxaban is suitable, 4 weeks supply will be issued alongside the anticoagulation alert card and patient booklet.

Amended for use at HUHFT by: N. Chauhan, R.Holland S.Hashi: 06/ 2016
Approved by Joint Prescribing Group on 07/2016. Review date: 07/2018

The patient will return to anticoagulation clinic after the initial 4 weeks to ensure adequate follow up during the initiation phase providing adherence counselling addressing any patients concerns regarding therapy. If rivaroxaban is tolerated, then a further 4 weeks of treatment will be supplied by the hospital, after which the GP will continue the supply and monitoring. If the patient has concerns prior to commencing continuation with the GP they should contact the hospital anticoagulant team.

The patient will be advised to contact their GP within 8 weeks of initiation. A NOAC initiation letter will also be forwarded to GP confirming transfer of care. Treatment should continue indefinitely on confirmation of nonvalvular atrial fibrillation that requires anticoagulation. Treatment should be reviewed at least annually by the GP 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. Ongoing adherence should be reviewed on a regular basis, the duration and method of adherence assessment should be determined by the GP and taking into account individual patient circumstances and factors. The GP is to re-educate the patient each time for the need to stop their rivaroxaban and seeing any doctor as soon as possible in case of bleeding.

ORAL DOSE AND ADMINISTRATION

Rivaroxaban film coated tablets are available in 2 strengths for this indication: 15mg and 20mg.

Usual dose:

	Renal function*		
	CrCl ≥50ml/min	**CrCl: 15 to 49ml/min**	**CrCl <15ml/min**
Dose	**20mg once daily**	**15mg once daily**	**Not recommended**

*Cockroft and Gault to be used – see below for formula

Increased risk of bleed:

- If bleeding risk is assessed as high (in accordance with HAS-BLED score), patients are to be considered for 15mg tablet once daily. 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.
- 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 (as CHA2DS2VASc score increases, the benefits of treatment with anticoagulation increase).
- If clinically relevant bleeding occurs, treatment should be interrupted and reviewed prior to re-initiation.

Cockroft and Gault formula to calculate CrCl (ml/min)

$$\frac{K \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (µmol/L)}}$$

K = 1.23 in males
K = 1.04 in females

DRUG NAME: RIVAROXABAN (XARELTO ®)
Transfer of Care document
Prevention of stroke and embolism for nonvalvular atrial fibrillation

MONITORING

Parameter	**Renal function (Creatinine clearance - CrCl)** Using Cockroft and Gault equation (see above)
Action Required	CrCl 15-49ml/min: Dose reduction to 15 mg once a day. CrCL <15mls/min; contraindicated – avoid use.
Frequency of monitoring	Assess renal function prior to treatment to ensure appropriate starting dose. Then: • Annually (alongside Hb and liver function tests) • 6 monthly o >75years o Frail (defined as ≥3 of the following criteria: unintentional weight loss, self-reported exhaustion, weakness assessed by handgrip test, slow walking speed/gait apraxia, low physical activity) o If CrCl 30–60ml/min • 3 monthly o If CrCl 15-29ml/min More frequent renal function monitoring maybe needed 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. Routine clotting tests (PT and APTT) are not very reliable indicators of the level of rivaroxaban and should not be used for monitoring purposes. If measurement of a rivaroxaban level is required it should be with an anti-Xa assay following discussion with the haematology.
Action	If numerous episodes of minor bleeding are observed or patient at high risk of bleed discuss with haematology

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

Please note: Rivaroxaban has an inverted Black Triangle ▼displayed in the patient information leaflet and in the summary of product characteristics (SPC). This means that it is a medicine subject to additional monitoring by regulatory authorities in the European Union (EU).

DRUG NAME: RIVAROXABAN (XARELTO ®)
Transfer of Care document
Prevention of stroke and embolism for nonvalvular atrial fibrillation

KEY ADVERSE EFFECTS & ACTIONS

Adverse effects	Symptoms/signs	Actions)
Minor Bleeding	Self-terminating minor bleeding from scratches, cuts, nosebleeds, 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 concerns are raised - liaise with haematology for advice.
Clinically significant 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 consider omitting a dose. If concerns are raised - liaise with haematology for advice. For bleeding that does not stop with intervention, send patient to local A&E.
Gastrointestinal	Dyspepsia	Consider gastro protection in accordance with local guidance. If no further improvement, consider alternatives or referral to specialist.

This only lists the key important ADRs-For comprehensive information on cautions, contra-indications and interactions please refer to the current British National Formulary and Summary of Product Characteristics.

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. If an invasive procedure or surgical intervention is required, rivaroxaban should be stopped at least 24hours before the intervention. See SPC for further details. If surgery cannot be delayed the case should be discussed with haematology for advice on reversal if required.

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.

For comprehensive information please refer to the current British National Formulary and Summary of Product Characteristics.

Evidence

Rivaroxaban has been shown to be as effective as standard anticoagulant therapy comprising of low molecular weight heparin in combination with a vitamin K antagonist (VKA) e.g. warfarin; it has similar levels of bleeding and a similar adverse effect profile.

Amended for use at HUHFT by: N. Chauhan, R.Holland S.Hashi: 06/ 2016
Approved by Joint Prescribing Group on 07/2016. Review date: 07/2018

DRUG NAME: RIVAROXABAN (XARELTO ®)
Transfer of Care document
Prevention of stroke and embolism for nonvalvular atrial fibrillation

Use of rivaroxaban to reduce the incidence of ischemic stroke has been studied in a large multinational, randomised control trial enrolling at least 14,000 patients with $CHADS_2$ score >2. The primary endpoint was a composite of prevention of stroke and systemic embolism. The ROCKET trial demonstrated noninferiority with respect the primary endpoint (1.7% vs. 2.2%, P<0.001 for non inferiority, for rivaroxaban and warfarin respectively) with similar rates of minor and major bleeding.

TRANSFER OF CARE

This document 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 transfer of care should be explained to the patient. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. 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/Anticoagulant team

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) and follow up that is required (using advocacy if appropriate).
3. Ensure baseline investigations are satisfactory before commencing treatment. Give the patient an anticoagulant alert card patient booklet.
4. Counsel the patient on the risks and benefits of treatment with rivaroxaban as well as importance of adherence to treatment.
5. Initiate treatment, prescribe and monitor for the first 7 weeks.
6. Send a NOAC initiation letter to the GP.
7. Clear documentation should be made as to reason for dose reduction.
8. Report any abnormal blood results to the GP where appropriate.
9. Evaluation of any reported adverse effects by GP or patient.
10. Advise GP on review, duration or discontinuation of treatment where necessary.
11. Ensure a 3 to 6 months follow up is arranged with haematologist.
12. Ensure that backup advice is available at all times.
13. Inform the patient to make a GP appointment within 8 weeks of initiation for further supplies.

General Practitioner

1. Reinforce the patient understands the nature, effect and potential side effects of rivaroxaban before prescribing 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 and monitor the drug treatment as described and stop the drug at the specified time. Consider managing the drug as an acute prescription as oppose to a repeat.

Clinical Commissioning Group

1. To provide feedback to trusts via Joint Prescribing Group.
2. To support GPs to prescribe rivaroxaban safely and effectively.
3. To support trusts in resolving issues that may arise as a result of transferred care.

Amended for use at HUHFT by: N. Chauhan, R.Holland S.Hashi: 06/ 2016
Approved by Joint Prescribing Group on 07/2016. Review date: 07/2018

DRUG NAME: RIVAROXABAN (XARELTO ®)
Transfer of Care document
Prevention of stroke and embolism for nonvalvular atrial fibrillation

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. Administer rivaroxaban as prescribed and attend hospital/GP for assessment and monitoring as required.

Costs

Drug Product	Cost in primary care
Rivaroxaban tablets [15mg and 20mg]	£766.50 / year*

Based on BNF February 2016

RESOURCES AVAILABLE

EHRA practical guide (see references)

Relevant contact details	
Doctor via switchboard Registrar on-call out of hours	Dr Neil Chauhan (clinical lead for anticoagulation) via switchboard Contact on-call haematology registrar out of hours via switchboard
Clinical Nurse Specialist/pharmacist	020 8510 4413 or 020 8510 4114 or via email huh-tr.Antico@nhs.net
Trust Homerton University Hospital NHS Foundation Medicines Information	020 8510 7000 or via email mipharmacy@homerton.nhs.uk
City and Hackney Medicines Management Team	020 3816 3224

Amended for use at HUHFT by: N. Chauhan, R.Holland S.Hashi: 06/ 2016
Approved by Joint Prescribing Group on 07/2016. Review date: 07/2018

References
With thanks to Barts Health NHS Trust,

- Barts Health NHS Trust SCG adapted for local use.
- EHRA practical guide, Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation, August 2015. Available at: http://europace.oxfordjournals.org/content/europace/early/2015/08/29/europace.euv309.full.pdf. Accessed 08/12/15.
- Patel MR, Mahaffey KW et al. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation (ROCKET-AF). *The New England Journal of Medicine*. 2011;365(10):883-891.
- Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation, May 2012, NICE technology appraisal guidance [TA256]. Available at: https://www.nice.org.uk/guidance/ta256, accessed 20/12/15.
- Summary of Product Characteristics, Xarelto 20mg film-coated tablets, Bayer plc, Date of revision of the text Jul 2015, accessed 20/12/15.

SCG template adopted from NELMMN and Barts Health NHS Trust (updated by JPG February 2015)