BNSSG Shared Care Guidance

Section 1: Heading

Drug	Rivaroxaban (Xarelto®)
Amber *one month*	
Indication	Co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine, for the prevention of atherothrombotic events in adult patients after an acute coronary syndrome (ACS) with elevated cardiac biomarkers
Speciality / Department	Cardiology
Trust(s)	North Bristol NHS Trust
	University Hospitals Bristol NHS Trust
	WAHT

Section 2: Treatment Schedule

Usual dose and frequency of administration	2.5 mg twice daily.
Route and formulation	Oral, tablet
Duration of treatment	12 months unless indicated. Very little experience of use post 24 months

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate
Renal function. Use with caution in patients with a CrCL<30ml/min. Not recommended if CRCl <15ml/min. Liver function tests. Rivaroxaban is contraindicated in patients with hepatic disease associated with coagulopathy.
Subsequent tests - where appropriate

1. Renal function

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	The main adverse effects for rivaroxaban include bleeding events, epistaxis, anaemia, haematoma, haematuria, decreased haemoglobin, hypotension, syncope, dyspepsia and gastrointestinal upsets. Also raised LFTs, pruritus, fatigue, dizziness and headaches. For full details please see the summary of product characteristics available from: www.medicines.org.uk and the BNF. Rivaroxaban is currently a black triangle medicine and so is monitored intensively by the CHM and MHRA. All suspected reactions (including those not considered to be serious) should be reported through the yellow card scheme http://yellowcard.mhra.gov.uk/.
Referral back to specialist	Serious bleed, or other side effects resulting in premature termination of treatment

Section 5: Drug Interactions

Please list clinically significant drug interactions (view rivaroxaban spc here)

Significant Drug Interactions	1. Care should also be taken if patients are treated concomitantly with medicines affecting haemostasis such as non-steroidal anti-inflammatory medicinal products (NSAIDs), acetylsalicylic acid, platelet aggregation inhibitors or other antithrombotic agents. 2. Co-administration of rivaroxaban with the strong CYP3A4 inducer rifampicin has been shown to decrease rivaroxaban levels, with parallel decreases in its pharmacodynamic effects. The concomitant use of rivaroxaban with other strong CYP3A4 inducers (e.g. phenytoin, carbamazepine, phenobarbital or St. John's Wort) may also lead to reduced rivaroxaban plasma concentrations. 3. Strong CYP3A4 inducers should therefore be co-administered with caution. Given the limited clinical data available with dronedarone, co-administration with rivaroxaban should also be avoided. 4. The use of rivaroxaban is not recommended in patients receiving concomitant systemic treatment with azole-antimycotics (such as ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (e.g. ritonavir). These active substances are strong inhibitors of both CYP3A4 and P-gp and therefore may increase rivaroxaban plasma concentrations which may lead to an increased bleeding risk. Please note this list is not exhaustive and prescribers should refer to the following sources for a complete list of interactions; an up to date version of the British National Formulary (BNF), the Summary of Product Characteristics (SPC) available via the electronic medicines compendium (http://emc.medicines.org.uk/) or drug interaction texts such as Stockley. 5. Recent communications from the European Medicines Agency has highlighted that dabigatran must not be used in patients using any other anticoagulant, unless the patient is being switched to or from dabigatran. The same principles would apply to rivaroxaban.

Reminder to ask patient about specific problems	New oral anticoagulant counselling required – please use suitable checklist e.g. http://www.bnssgformulary.nhs.uk/includes/documents/FINAL%20SOP%20counselling%20anticoagulants%20version%2030012013%20(3).pdf

Section 6: Contra-indications, Cautions and Special Recommendations

Rivaroxaban contraindications include:

- Patients with severe renal impairment (CrCl < 15 ml/min)
- Active clinically significant bleeding
- Hepatic disease associated with coagulopathy & clinically relevant bleeding risk
- Including cirrhotic patients with Child Pugh B &C
- Hypersensitivity to rivaroxaban or to any of the excipients
- Concomitant treatment with systemic ketoconazole, itraconazole, voriconazole and ritonavir
- Pregnancy & breast feeding

Recommendations if bleeding occurs:

- Should a bleeding complication arise in a patient taking rivaroxaban, the next administration of rivaroxaban should be delayed or treatment discontinued as appropriate. Management should be individualised according to the severity and location of haemorrhage.
- In cases of suspected overdose it would be recommended to seek advice from secondary care as it would be advisable for the patient's anticoagulation status to be assessed. An urgent PT may help decide whether significant amounts of anticoagulant effect remains (but cannot be used to monitor levels). Within two hours of ingestion oral activated charcoal may reduce absorption of the drug.
- Traditional blood products (fresh frozen plasma particularly if volume is needed) and an antifibrinolytic agent such as tranexamic acid may be used initially. Theoretically prothrombin complex concentrate may reverse the anticoagulant action of rivaroxaban; however, there is very limited clinical experience with the use of these products.

Minor bleeding such as epistaxis or menorrhagia can be managed with simple withdrawal of the anticoagulant for one or more days, allowing definitive interventions (where available) to be applied.

Moderate bleeding (such as upper or lower GI bleeding) should be managed with withdrawal of the anticoagulant, careful clinical monitoring, interventions to identify and definitively treat the bleeding source, and consideration of an extended period of withdrawal of the oral anticoagulant (perhaps with the addition of a parenteral anticoagulant for patients at particularly high risk of thrombosis) to allow healing. Transfusion therapy with RBCs might be required to treat symptomatic anaemia.

Section 7: Advice to the patient

Advice for prescribing clinician to inform patient

1. The need for careful follow up to reinforce the importance of taking this medication as well as to discuss any concerns is essential.
2. Please counsel the patient using an approved checklist for New oral anticoagulants e.g. UHB: http://www.bnssgformulary.nhs.uk/includes/documents/FINAL%20SOP%20counselling%20anticoagulants%20version%2030012013%20(3).pdf
   NBT: http://www.bnssgformulary.nhs.uk/includes/documents/NBT%20NOAC%20counselling%20checklist%20final.pdf

Section 8: Responsibilities for Secondary Care

Core responsibilities

1. Initiating treatment and prescribing for the first month
2. Undertaking the clinical assessment and monitoring for the first month.

3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of Rivaroxaban.
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. To counsel patient on use of rivaroxaban.
2. To determine and communicate the length of treatment with apixaban required.
3. What to do in the case of any moderate bleeds or serious side effects serious enough for patient to abandon treatment (GP to arrange urgent care for any serious bleeds).

Section 9: Responsibilities for Primary Care

Core responsibilities

1. Responsible for taking over prescribing after the first month
2. Responsible for the clinical assessment and monitoring after the first month
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. Respond to any patient concerns or problems regarding their treatment, being alert to any signs of bleeding.
2. Reinforce new oral anticoagulant safety messages to patients if/when reviewing treatment with them.
3. Monitor renal function on an at least annual basis, or more frequently is decline in function is suspected.

Section 10: Contact Details

Name	Organisation	Telephone Number	E mail address
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At Weston, contact Consultant who initiated the NOAC.	Weston Area Healthcare NHS Trust	01934 636363 ext. 3300 (Pathology Secretaries)	Anna.morris3@nhs.net

Also Anna Morris, Lead Haematologist			

Section 11: Document Details

Date prepared	June 2015
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Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

1. Shared amongst secondary and primary care colleagues prior to agreement

Section 13: References

1. Summary of product Characteristics, Xarelto 2.5mg. https://www.medicines.org.uk/emc/medicine/29371 Accessed June 2015
2. NICE Technology appraisal 335. Rivaroxaban for preventing adverse outcomes after acute management of acute coronary syndrome http://www.nice.org.uk/guidance/ta335 Accessed June 2015