DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE
SHARED CARE AGREEMENT

DRONEDARONE

For the maintenance of sinus rhythm after successful cardioversion in adult clinically stable patients with paroxysmal or persistent atrial fibrillation (AF) when alternative treatments are unsuitable

1. REFERRAL CRITERIA

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP that the patient's condition is stable or predictable.
- Patients will only be referred to the GP once the GP has agreed in each individual case.
- When transferred, the patient will be given a supply of dronedarone sufficient for 4 weeks maintenance therapy

2. AREAS OF RESPONSIBILITY

GP responsibilities	Consultant responsibilities
1. Prescribe dronedarone at the dose determined by the secondary care specialist **2.** Refer to secondary care physician if the patient's condition deteriorates. **3.** Perform monitoring tests as outlined in section VI. **4.** Primary care physician to report adverse events to the specialist and MHRA. **5.** Due to the potential for significant drug-drug interactions, the primary care physician must ensure that interacting drugs are not taken following initiation with dronedarone. **6.** Stop treatment on the advice of the specialist or immediately if any urgent need to stop treatment arise. **7.** To receive ECG monitoring results from the specialist. **8.** Report any adverse effects to the referring specialist and the MHRA yellow card scheme	**1.** To confirm the patient has no contra-indications to treatment and consider the relevance of any cautions. **2.** To discuss the benefits and possible side-effects of treatment with the patient, advising women of child bearing age to use reliable contraceptive methods whilst taking dronedarone. **3.** To initiate dronedarone for the licensed indication in accordance with the manufacturer's Summary of Product Characteristics (SPC) and provide at least 4 weeks' supply upon transferring prescribing responsibility to GP. **4.** To retain overall responsibility for the patient and the prescribing for the first twelve months as outlined in section VI. **5.** Perform monitoring tests as outlined in section VI. **6.** To discuss the possibility of sharing prescribing and monitoring of dronedarone with the patient's GP; to provide a copy of this shared care agreement for their consideration and not to transfer prescribing responsibility until the GP has formally agreed to share care in this way. **7.** To advise on the clinical relevance of concomitant medication after initiation of dronedarone, as well as potential drug interactions (e.g. with dabigatran, digoxin, beta-blockers etc). **8.** To ensure that arrangements are in place for GPs to obtain advice and support where needed. **9.** To communicate promptly with the GP the results of any monitoring undertaken in secondary care and any changes to treatment made by the specialist. **10.** Communicate to the GP results of the 6 monthly ECG monitoring.

Patient responsibilities

1. Report to the specialist or GP if he/she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with dronedarone.
3. Present rapidly to the GP or secondary care specialist should their condition significantly worsen.
4. The patient must notify the GP or secondary care specialist if they develop any of the following:

- symptoms of potential liver injury (such as sustained new-onset abdominal pain, anorexia, nausea, vomiting, fever, malaise, fatigue, jaundice, dark urine or itching)
- Breathlessness and non-productive cough
- Swollen feet or legs, trouble breathing when lying down or sleeping, shortness of breath when moving around, or weight increase
- any symptoms suggesting that the medication has become ineffective such as a sudden deterioration in condition / notice a new persistently irregular pulse or detect newly occurring

palpitations
5. Report any other adverse effects to the specialist or GP whilst taking dronedarone.

3. COMMUNICATION AND SUPPORT

i. Hospital contact:	**ii. Out of hours contact and procedures:**
University Hospitals of Derby and Burton Foundation Trust Consultant/nurse via switchboard:01332 340131 **Chesterfield Royal Hospital Foundation Trust** Consultant via switchboard: 01246 277271	Pharmacy, UHDB, ask for on-call pharmacist via switchboard: 01332 340131 Cardiology, UHDB, ask for on-call Cardiology Consultant via switchboard: 01332 340131 Contact the CRH on-call Medic for the relevant speciality via switchboard: 01246 277271

4. CLINICAL INFORMATION

i. Prescribed indications	Dronedarone (Multaq®) is indicated for the maintenance of sinus rhythm after successful cardioversion in adult clinically stable patients with paroxysmal or persistent atrial fibrillation (AF) when alternative treatments are unsuitable.
ii. Therapeutic summary	Dronedarone is a multichannel blocker inhibiting the potassium currents and thus prolonging cardiac action potential and refractory periods (Class III). It also inhibits the sodium currents (Class Ib) and the calcium currents (Class IV). It non-competitively antagonises adrenergic activities (Class II).
iii. Dose & Route of administration	400 mg twice daily orally, with breakfast and evening meal. Do not take with grapefruit juice.
iv. Duration of treatment	Indefinite
v. Adverse effects	**Very common (≥1/10):** • Congestive heart failure, increased plasma creatinine, prolonged QTc interval **Common (≥1/100 to <1/10):** • Bradycardia, diarrhoea, vomiting, nausea, abdo pain, dyspepsia, LFT abnormalities, rashes, pruritus, fatigue, asthenia **Uncommon (≥1/1,000 to <1/100):** • Dysgeusia, erythemas, eczema, photosensitivity reaction, allergic dermatitis, dermatitis, Interstitial lung disease including pneumonitis and pulmonary fibrosis **Rare (≥1/10,000 to <1/1,000):** • Ageusia, hepatocellular liver injury (including life-threatening acute liver failure), Vasculitis, including leukocytoclastic vasculitis, Anaphylactic reactions including angioedema In clinical trials, the most frequently observed adverse reactions with dronedarone 400 mg po bd were diarrhoea, nausea, vomiting, fatigue and asthenia. Refer to the SPC for a full list of adverse effects & further information http://www.medicines.org.uk
vi. Monitoring Requirements	**Consultant (12 month responsibility)** **Baseline monitoring:** • Ensure any Potassium and Magnesium deficiency is corrected before initiation with Dronedarone • LFT • U&E (specifically plasma creatinine) **Day 7 after treatment initiation** • LFT • U&E's (specifically plasma creatinine). If increase measure again after 7 days and take as new baseline. If continues to increase, further investigations and consider withdrawal of treatment. **Further monitoring of consultant (includes prescribing responsibilities)** • LFT to then be monitored at 1 month after treatment initiation, then monthly for 6 months, month 9 and 12.

- ECG monitoring 6 monthly

GP monitoring (taking prescribing and monitoring responsibility for patient after 12 months)

- Annual LFT and U&E (specifically creatinine) monitoring
  (LFT's should also be taken if the patient presents with signs or symptoms of potential liver injury (such as sustained new-onset abdominal pain, anorexia, nausea, vomiting fever, malaise, fatigue, jaundice, dark urine or itching)

Parameter	Action
Liver function tests	If ALT is elevated to ≥3 upper limit of normal (ULN), re-check level in 48-72 hrs. If ALT is then confirmed as ≥3 ULN, contact Specialist for urgent advice on other treatment options then stop dronedarone.
U&E's specifically Plasma creatinine (Cr)	If Cr is less than agreed threshold for this patient, take no further action. If Cr is more than agreed threshold for this patient, refer to Specialist for review.
ECG	If QTc interval ≥ 500 milliseconds (Contact consultant responsible)
To be aware of the potential for persistent (rather than paroxysmal) AF to develop.	Referred back to secondary care for a further adjustment of their medication or formulation of new management plan.
Pulmonary toxicity Symptoms such as dyspnoea or non-productive cough should be assessed as may be pulmonary toxicity.	If suspected the patient should be referred back to the specialist for relevant lung examinations and treatment discontinued.
Heart failure symptoms Symptoms such as weight gain, dependent oedema, increased dyspnoea	Discontinue treatment

vii. Clinically relevant drug interactions

Patients should be warned to avoid grapefruit juice beverages while taking dronedarone.

Dronedarone tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption, should not take this medicine.

Dronedarone will increase plasma levels of digoxin, and thus may precipitate symptoms and signs of digoxin toxicity. Clinical, ECG and biological monitoring is recommended, and digoxin dose should be halved. A synergistic effect on heart rate and atrio-ventricular conduction is possible.

Beta-blockers and calcium antagonists with depressant effect on sinus and AV node should be co-administered with caution. In patients on dronedarone, they should be initiated at low dose, and titrated only after ECG assessment. In patients on calcium antagonists/ beta blockers at time of dronedarone initiation, an ECG should be performed and doses adjusted if necessary.

Medicines which induce torsades de pointes (such as phenothiazines and tricyclic antidepressants), certain oral macrolides (such as erythromycin), and Class I & III antiarrhythmics are contraindicated due to risk of proarrhythmia.

	Statins should be used with caution. Lower starting and maintenance doses of statins should be considered, and patients monitored for clinical signs of muscular toxicity. MAO inhibitors may decrease clearance of the active metabolite of dronedarone, and should be used with caution. Concomitant potent CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, St John's Wort) are not recommended. **NOACs** Dronedarone is likely to increase the exposure of rivaroxaban (a CYP3A4 and P-gp substrate) and consequently concomitant use may increase the risk of bleedings. Concomitant use of rivaroxaban and dronedarone is not recommended. Apixaban: No information about concomitant use. Edoxaban: See SPC for dose adjustment when used concomitantly with dronedarone. Dabigatran: Contra-indicated. **Warfarin** Clinically significant INR elevations (≥5) usually within 1 week after starting dronedarone were reported in patients taking oral anticoagulants. Consequently, INR should be closely monitored after initiating dronedarone in patients taking vitamin K antagonists as per their label Refer to the SPC for more detailed information on drug interactions http://www.medicines.org.uk.
viii. Contra-indications	• Hypersensitivity to the active substance or to any of the excipients • Second- or third- degree atrio-ventricular block, complete bundle branch block, distal block, sinus node dysfunction, atrial conduction defects, or sick sinus syndrome (except when used in conjunction with a functioning pacemaker) • Bradycardia <50 beats per minute (bpm) • Permanent AF with an AF duration ≥6 months (or duration unknown) and attempts to restore sinus rhythm no longer considered by the physician • Patients in unstable hemodynamic conditions, • History of, or current heart failure or left ventricular systolic dysfunction • Patients with liver and lung toxicity related to the previous use of amiodarone • Co-administration with potent cytochrome P 450 (CYP) 3A4 inhibitors, such as ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, nefazodone and ritonavir • Medicinal products inducing torsades de pointes such as phenothiazines, cisapride, bepridil, tricyclic antidepressants, terfenadine and certain oral macrolides (such as erythromycin), Class I and III antiarrhythmics • QTc Bazett interval ≥500 milliseconds • Severe hepatic impairment • Severe renal impairment (CrCl <30 ml/min) • Co-administration with dabigatran
ix. Supply of ancillary equipment	Not applicable
x. Supply, storage and reconstitution instructions	Not applicable
xi. Prepared by	Dominic Moore, Advanced Pharmacist Specialist Medicine, University Hospitals of Derby and Burton NHS Foundation Trust Dr Rob McIntosh, Consultant Cardiologist University Hospitals of Derby and Burton NHS Foundation Trust

This does not replace the SPC, which should be read in conjunction with it.
Date Prepared: October 2019 **Review Date**: September 2022 (Extended to March 2023)

Document control	**Date**
Rivaroxaban interaction information updated as per SPC	June 2020

Sample transfer letter

{Insert Hospital Logo here}

Hospital No: «HOSPITAL_NUMBER»
NHS No: «NHS_NUMBER»

{Insert date}

PRIVATE & CONFIDENTIAL
«GP_TITLE» «GP_INITIALS» «GP_SURNAME»
«GP_ADDRESS_1»
«GP_ADDRESS_2»
«GP_ADDRESS_3»
«GP_ADDRESS_4»
«GP_POSTCODE»

DERBYSHIRE JAPC SHARED CARE AGREEMENT LETTER

Dear «GP_TITLE» «GP_SURNAME»

«FORENAME_1» «SURNAME» «DATE_OF_BIRTH»
«CURRENT_ADDRESS_1» «CURRENT_ADDRESS_2» «CURRENT_ADDRESS_3»
«CURRENT_ADDRESS_4» «CURRENT_POSTCODE»

Your patient was seen on ***{Insert date}*** with a diagnosis of ***{Insert diagnosis}***. I have initiated the following medication ***{Insert drug name}*** and am writing to ask you to participate in the shared care for this patient.

This medication has been accepted as suitable for shared care by the Derbyshire Joint Area Prescribing Committee (JAPC). I agree to the secondary care responsibilities set out in the shared care agreement for this medication (available from www.derbyshiremedicinesmanagement.nhs.uk/clinical_guidelines/shared_care_guidelines). I am therefore requesting your agreement to share the care of this patient. Where preliminary tests are set out in the agreement I have carried these out and results are below.

Dose Regimen	Date ***{Insert medicine name}*** started	Date for GP to start prescribing ***{Insert medicine name}*** from
The baseline test results are (if applicable):		

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been	*Yes / No*

explained and agreed	
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

If you do **NOT** wish to participate in shared care for this patient, usually under clinical grounds, please complete the attached form.

Yours sincerely

{Consultant name}

GP RESPONSE TO SHARED CARE (only complete & send if **NOT** participating in shared care*)

* For completeness please record medication on GP clinical system as per guidance- 'Recording medicines prescribed and issued by other Healthcare Providers'

Shared care is produced by GPs and specialists knowledgeable in the field of that drug usage. The shared care has been approved by the JAPC. This allows a more convenient service to the patient and cost effective use of NHS resources.

Patient:	NHS No:
Consultant:	Medicine requested for shared care:

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care guideline. My clinical reasons for declining shared care for this patient are listed in the box below:

		Tick which apply
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patients primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	
2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	
3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	
5.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure	

	that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed**.** For this reason I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible.

Yours sincerely

{GP name}
{Surgery}