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.
- When transferred, the patient will be given a supply of dronedarone sufficient for 4 weeks maintenance therapy

2. AREAS OF RESPONSIBILITY

GP responsibilities	Consultant/ specialist responsibilities
1. If NOT participating in shared care reply to the request from the consultant/specialist as soon as practicable. **2.** Prescribe dronedarone at the dose determined by the secondary care specialist **3.** Refer to secondary care physician if the patient's condition deteriorates. **4.** Perform monitoring tests as outlined in section VI. **5.** Manage adverse effects as detailed in section v and discuss with specialist team when required. **6.** 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. **7.** Stop treatment on the advice of the specialist or immediately if any urgent need to stop treatment arise. **8.** To receive ECG monitoring results from the specialist. **9.** Refer the management back to the specialist if the patient becomes or plans to become pregnant. **10.** Report any adverse effects to the referring specialist and the MHRA yellow card scheme	**1.** Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol. **2.** To confirm the patient has no contra-indications to treatment and consider the relevance of any cautions. **3.** Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling to enable the patient to reach an informed decision. **4.** Perform monitoring tests as outlined in section VI. **5.** To initiate dronedarone for the licensed indication in accordance with the manufacturer's Summary of Product Characteristics (SPC) and retain overall responsibility for the patient and the prescribing for the **first twelve months** 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. **11.** Advising women of child bearing age to use reliable contraceptive methods whilst taking dronedarone. Reassume prescribing responsibilities if a woman becomes or wishes to become pregnant.

Patient responsibilities

1. Report to the specialist or GP if he/she does not have a clear understanding of the treatment and share any concerns in relation to treatment with dronedarone.
2. Take dronedarone as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
3. Attend regularly for monitoring and review appointments with primary care and specialists. Be aware that medicine may be stopped if they do not attend.

4. Present rapidly to the GP or secondary care specialist should their condition significantly worsen. 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)
   - Signs or symptoms of lung toxicity- Breathlessness and non-productive cough, or deterioration in general health (e.g. fatigue, weight loss, fever)
   - Signs or symptoms of heart failure- Swollen feet or legs, trouble breathing when lying down or sleeping, shortness of breath when moving around, or weight increase
   - Signs or symptoms of bradycardia (slow heartbeat) - dizziness, fatigue, fainting, shortness of breath, chest pain or palpitations, confusion or trouble concentrating
   - 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.
6. Report the use of any over the counter medicines to their prescriber and be aware they should discuss the use of dronedarone with their pharmacist before purchasing any OTC medicines.
7. Avoid grapefruit juice while taking dronedarone
8. Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

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

iii. Patient information
British Heart Foundation – Anti-arrhythmics**:** https://www.bhf.org.uk/informationsupport/heart-matters-magazine/medical/drug-cabinet/anti-arrhythmics

4. CLINICAL INFORMATION

i. Prescribed indications	Dronedarone 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.
	
	NICE TA 197 recommends dronedarone as an option in patients:
	• whose AF is not controlled by 1st line therapy (usually including beta-blockers) and
	• who have at least 1 of the following cardiovascular risk factors:
	  ○ hypertension requiring drugs of at least 2 different classes
	  ○ diabetes mellitus
	  ○ previous transient ischaemic attack, stroke or systemic embolism
	  ○ left atrial diameter of 50 mm or greater or
	  ○ age 70 years or older and
	• who do not have left ventricular systolic dysfunction and do not have a history of, or current, heart failure

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. Tablets should be swallowed whole with a drink of water during a meal. The tablet cannot be divided into equal doses and should not be split.
iv. Duration of treatment	Indefinite

v. Adverse effects

Refer to the SPC for a full list of adverse effects & further information http://www.medicines.org.uk

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit https://yellowcard.mhra.gov.uk/

In clinical trials, the most frequently observed adverse reactions with dronedarone were diarrhoea, nausea, vomiting, fatigue and asthenia.

Adverse effect	Suggested action for primary care
Cardiovascular: Bradycardia: • Heart rate 50 - 60bpm without symptoms • HR ≤50bpm or ≤60bpm with symptoms	Continue dronedarone. Repeat monitoring. No action required if hear rate remains >50 without symptoms. Discuss with specialist team; dose reduction may be required.
Worsening of arrhythmia, new arrhythmia, or heart block	**Stop dronedarone.** Urgent referral to specialist team.
Recurrence of atrial fibrillation (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. Discontinue dronedarone if patient develops permanent AF with a duration of six months or more.
Signs or symptoms of congestive heart failure, e.g. weight gain, dependent oedema, or increased dyspnoea.	**Stop dronedarone** if congestive heart failure is suspected and refer urgently to specialist team.
Heart failure symptoms Symptoms such as weight gain, dependent oedema, increased dyspnoea	Discontinue treatment if congestive heart failure is suspected and refer urgently to specialist team.
Symptoms of **hepatic injury** (e.g. hepatomegaly, weakness, ascites, jaundice)	check LFTs urgently; Proceed as per monitoring section below
Pulmonary toxicity new/worsening cough, shortness of breath or deterioration in general health (e.g. fatigue, weight loss, fever)	Continue dronedarone. Urgent referral to initiating specialist and respiratory specialist.
Gastrointestinal disturbance: diarrhoea, nausea, vomiting, abdominal pain, dyspepsia	Continue dronedarone. May require dose reduction; discuss with specialist if persistent.
General disorders: fatigue, asthenia	Continue dronedarone. May require dose reduction; discuss with specialist.
Dermatological disorders: rashes, pruritus, photosensitivity	Continue dronedarone. Reinforce appropriate self-care, including sun avoidance and purchasing of a broad spectrum sunscreen (at least SPF30) if photosensitivity occurs. May require dose reduction; discuss with specialist.

vi. Monitoring Requirements

Consultant/ specialist (12 month responsibility)

Baseline monitoring:

- Ensure any Potassium and Magnesium deficiency is corrected before initiation with Dronedarone
- LFT
- U&E (specifically plasma creatinine)
- ECG

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 serum creatinine continues to increase, further investigations and consider withdrawal of treatment.
- Monitor concurrent medicines as appropriate e.g. anticoagulants, digoxin

Further monitoring of consultant (includes prescribing responsibilities for 12 months)

- LFT to then be monitored at 1 month after treatment initiation, then monthly for 6 months, month 9 and 12.
- ECG monitoring 6 monthly
- Chest X-ray and pulmonary function tests, if respiratory symptoms or toxicity suspected

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

- 6monthly LFT and U&E (includes creatinine and Mg) 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
- Ongoing monitoring for symptoms of heart failure e.g. weight gain, dependent oedema or dyspnoea

Action for GPs

Parameter	Action
Liver function tests	ALT>5x ULN or symptoms of hepatic injury- stop amiodarone. Urgent referral to initiating specialist and hepatologist If ALT is elevated to ≥3 upper limit of normal (ULN) but no symptoms- 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. CrCl<30ml/min- seek advice urgently from specialist
Hypokalaemia/ hypomagnesaemia	Continue dronedarone. Correct deficiency as per local guidelines (see SCP guideline)
ECG	If QTc interval ≥ 500 milliseconds (Contact consultant responsible)

As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance

vii. Contra-indications and cautions

Contraindications:

- Known hypersensitivity to dronedarone or 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 less than 50 beats per minute
- Permanent atrial fibrillation (AF) with an AF duration ≥6 months (or duration unknown), and attempts to restore sinus rhythm no longer considered by the physician
- Unstable haemodynamic conditions
- History of or current heart failure, or left ventricular systolic dysfunction
- Patients with liver or lung toxicity related to previous use of amiodarone
- Co-administration with potent cytochrome P450 3A4 (CYP3A4) inhibitors, such as ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, nefazodone and ritonavir
- Co-administration with medicinal products inducing torsades de pointes, including phenothiazines, cisapride, bepridil, tricyclic antidepressants,

	terfenadine and certain oral macrolides (such as erythromycin), class I and III anti-arrhythmics • Co-administration with dabigatran • QTc Bazett interval greater than 500 milliseconds • Severe hepatic or renal impairment (CrCl <30 mL/min) **Cautions:** • Dronedarone can cause serious adverse reactions; clinical monitoring for development of congestive heart failure, left ventricular systolic dysfunction, QTc prolongation, liver injury, and respiratory disease are required.
viii. Clinically relevant drug interactions Refer to the SPC for more detailed information on drug interactions http://www.medicines.org.uk.	**Dronedarone is associated with a large number of interactions, some of which are significant enough to contradict concurrent use, require dose adjustment and/or additional monitoring.** Dronedarone is contraindicated when co-administered with potent cytochrome P450 3A4 (CYP3A4) inhibitors, medicinal products inducing torsades de pointes, and dabigatran (see above). Dronedarone is an enzyme inhibitor and can increase exposure to a number of medicines including: • P-glycoprotein (PgP) substrates (e.g. digoxin, dabigatran, apixaban, rivaroxaban, edoxaban). • CYP3A4 substrates (e.g. ciclosporin, statins, fentanyl, sildenafil, tacrolimus, sirolimus, everolimus, apixaban, rivaroxaban, edoxaban). • CYP2D6 substrates (e.g. metoprolol). Dronedarone interacts with other medicines that: • Induce Torsade de Points or prolong qtc (e.g. Phenothiazines, cisapride, bepridil, tricyclic antidepressants, certain oral macrolides (such as clarithromycin and erythromycin), terfenadine and Class I and III anti-arrhythmics). Concomitant use is contraindicated. • Lower heart rate (e.g. Beta-blockers, calcium channel blockers). • Induce hypokalaemia (e.g. Diuretics, stimulant laxatives). • Induce hypomagnesaemia (e.g. Diuretics). Other interactions include: • CYP3A4 inhibitors – may increase exposure to dronedarone (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, ritonavir, clarithromycin, grapefruit juice). Concomitant use is contraindicated. • Potent CYP3A4 inducers – may reduce exposure to dronedarone and are not recommended (e.g. rifampicin, phenobarbital, carbamazepine, phenytoin, St John's Wort). • Anticoagulants – vitamin K antagonist and direct oral anticoagulant (DOAC) exposure may be increased by dronedarone (e.g. warfarin, rivaroxaban, edoxaban). 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. **NOACs** • Edoxaban: reduce edoxaban dose to 30mg if concomitant use with dronedarone • Rivaroxaban: Concomitant use of rivaroxaban and dronedarone is not recommended.

	• Apixaban: no dose adjustment for apixaban is required when co-administered 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
ix. Pregnancy, paternal exposure and breastfeeding	**Pregnancy:** There are limited data on the use of dronedarone in pregnant women. Studies in animals have shown reproductive toxicity. Use is not recommended during pregnancy and in women of childbearing potential not using contraception. **Breastfeeding:** Low levels of dronedarone are anticipated in breast milk. Use is cautioned while breast feeding; infants should be monitored for adverse events such as diarrhoea, vomiting, weakness, bradycardia. Information for healthcare professionals: https://www.sps.nhs.uk/medicines/dronedarone/
x. Additional information	Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed **To be read in conjunction with the following documents** • RMOC Shared Care Guidance • NHSE/NHSCC guidance – items which should not be routinely prescribed in primary care: guidance for CCGs • NHSE policy- Responsibility for prescribing between Primary & Secondary/Tertiary Care
xi. Supply of ancillary equipment ; Supply, storage & reconstitution instructions	Not applicable
xii. Prepared by **Reviewed 2023**	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 Derbyshire Guideline group in consultation with Dr. Julia Baron, consultant cardiologist UHDBFT Dr. Paul Sheridan, consultant cardiologist CRHFT In line with NHSE/ RMOC Shared Care Protocols- Dronedarone for patients in adult services, July 2022. https://www.england.nhs.uk/publication/shared-care-protocols/

This does not replace the SPC, which should be read in conjunction with it.
Date Prepared: October 2019 **Reviewed August** 2023 **Next review** July 2026

Document control	Date

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_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_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 explained and agreed	*Yes / No*
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}

Please send a copy of this response to the specialist/consultant requesting shared care