Extended Shared Care Agreement (Dronedarone)

For patients to be eligible for a shared care prescribing arrangement, the following points must be met beforehand:

- Prescribing responsibility is only transferred when there is mutual agreement between the specialist and patient's GP that the patient's condition is stable.
- Patient will be given adequate supply from the provider to allow enough time for the shared care process to be completed.

1. Areas of responsibility		
Specialist/Consultant	**GP**	**Patient**
1. Confirm patient has no contraindications to treatment (and review any cautions). 2. Discuss the benefits and side effects of treatment with the patient ensuring patient understands which warning symptoms to report, ensuring patient understands the dosing regimen. 3. Initiate and stabilise treatment with dronedarone. 4. Ask the GP whether he or she is willing to participate in shared care, and discuss the shared care arrangement with the patient, and provide the patient with a monitoring and dosage record. 5. Perform and provide results of baseline tests and recommend frequency of monitoring as outlined in the monitoring section (3f). Perform baseline tests, U+Es and eGFR-repeat plasma creatinine and LFT 7 days and one month after initiation. 6. Periodically review the patient's condition (initially annually) and communicate promptly with the GP when treatment is changed. 7. Perform 6 monthly ECG to exclude asymptomatic reversion to AF and communicate the results to the GP. 8. Periodically monitor for signs and symptoms of HF and Lung Fibrosis 9. Advise the GP on when to adjust the dose, stop treatment, or consult with specialist. 10. Report adverse events through the MHRA yellow card scheme and GP. 11. Ensure that clear arrangements exist for GPs to obtain advice and support.	1. Reply to the request for shared care as soon as practicable. 2. Prescribe dronedarone at the dose recommended and adjust the dose as advised by the specialist 3. Ensure compatibility with other concomitant medication (making sure interacting drugs are not taken following initiation with dronedarone). 4. Ensure that the patient understands the dosing regimen, and which warning symptoms to report. 5. Periodically monitor for signs and symptoms of HF and Lung Fibrosis. 6. Perform monitoring tests as outline in the monitoring section below (3f). 7. Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises (e.g. Stevens Johnson reaction, marked systemic side effects etc.). 8. Report adverse events to the specialist and the MHRA yellow card scheme. 9.Receive ECG monitoring results from the specialist. 10. Ensure periodic monitoring of hepatic and renal function. -See above for frequency of hepatic monitoring. 11. Refer to specialist/consultant if patients condition worsens.	1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment. 2. Share any concerns in relation to treatment with dronedarone 3. Inform specialist or GP of any other medication being taken, including over-the-counter products. 4. Report any adverse effects, warning symptoms or if their condition worsens to the specialist or GP whilst taking dronedarone - Increasing swelling of the feet or legs - Wheezing, chest tightness or coughing up frothy sputum at rest, night time or after minor exertion - Shortness of breath when moving around - Using more pillows to prop themselves up at night so they can breathe more easily - Gaining more than 5 pounds or 2-3 kilograms in weight in a short period of time 5. Patients should not stop dronedarone unless told to do so.

2. Communication and Support

Contact details	Telephone No	Bleep	Email address
Cardiology Consultant	Manor ext 6504/7543	Mobile via switch	E referral
Hospital Pharmacy Dept.:…			
Other:……..			

3. Clinical Information

(a) Indication	Maintenance of sinus rhythm after successful cardioversion in clinically stable patients with paroxysmal or persistent atrial fibrillation, when alternative treatments are unsuitable (initiated under specialist supervision).
(b) Therapeutic Summary	Multi-channel blocking anti-arrhythmic drug. It inhibits the potassium currents, therefore prolonging cardiac action potential and refractory periods (Class III). In addition, it also inhibits sodium and calcium currents (Class Ib, Class IV respectively). It antagonises adrenergic activities (non-competitively, Class II).
(c) Dose & route of administration	Recommended dose: 400mg twice daily in adults (one tablet with the morning meal and one tablet with the evening meal). Do not take with grapefruit juice. If a dose is missed, the next dose should be taken at the regular scheduled time (do not double the dose).
(d) Duration of treatment	As per specialist advice.
(e) Adverse effects	In clinical trials as per SPC, the most frequently observed adverse reactions were diarrhoea, nausea, vomiting, fatigue and asthenia. Refer to the SPC for a full list of adverse effects and more information. **Very common (≥1/10):** Congestive heart failure, increased plasma creatinine, prolonged QTc interval **Common (≥1/100 to <1/10):** Bradycardia, diarrhoea, vomiting, nausea, abdominal pain, dyspepsia, LFT abnormalities, rashes (including generalised, macular, maculo-papular), pruritus, fatigue, asthenia (abnormal physical weakness/lack of energy) **Uncommon (≥1/1,000 to <1/100):** Dysgeusia, interstitial lung disease including pneumonitis and pulmonary fibrosis, erythemas (including erythema and rash erythematous), eczema, photosensitivity reaction, allergic dermatitis, dermatitis **Rare (≥1/10,000 to <1/1,000):** Anaphylactic reactions including angioedema, ageusia, vasculitis (including leukocytoclastic vasculitis), hepatocellular liver injury (including life-threatening acute liver failure)
(f) Monitoring requirements	**Specialist/Consultant (first 12 months)** Specialist should undertake monitoring of the patient's hepatic, renal and cardiac function prior to initiation of dronedarone and during treatment to confirm absence of severe renal failure, hepatic failure, AF (symptomatic/permanent), congestive heart failure and left ventricular dysfunction. **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 this has increased, measure again after 7 days and take as new baseline. If this continues to increase, further investigations should be carried out and consideration for treatment to be stopped.

Further specific monitoring

LFTs: 1 month after treatment initiation, then monthly for 6 months, then at the 9-month interval and 12 month. After this it should be reviewed periodically.

If alanine transaminase (ALT) levels are elevated to ≥3 upper limit of normal (ULN), levels should be re-measured within 48 to 72 hours. If ALT levels are confirmed to be ≥3 ULN after re-measurement, dronedarone treatment should be withdrawn. Appropriate investigation and close observation of patients should continue until the enzyme levels return to normal.

ECG: 6 monthly, if symptomatic AF reoccurs discontinuation of dronedarone should be considered, if patients treated with dronedarone develop permanent AF, treatment with dronedarone should be discontinued.

U&E's (specifically plasma creatinine): this should continue to be reviewed periodically thereafter and to consider further investigations as needed.

GP monitoring (for patients after 12 months)

Parameter	Frequency	Action
LFTs	Annually and also if patient presents with signs or symptoms of liver injury	If ALT levels are elevated to ≥3 ULN, levels should be re-measured within 48 to 72 hrs. If levels are confirmed to be ≥3 ULN after re-measurement, contact specialist for urgent advice on options and dronedarone treatment discontinued.
U & E's specifically plasma creatinine	Annually	If plasma creatinine is more than the agreed levels then refer to specialist for review/advice.
ECG	6 monthly	If QT prolonged (As per SPC ≥500 milliseconds) contact specialist consultant cardiologist
AF management	At every review opportunity	Consider cessation and substitution with specialist advice if persistent (in place of paroxysmal) AF develops.
Heart Failure	At every review opportunity	If patient develop heart failure symptoms (e.g. weight gain, dependent oedema, increased dyspnoea) – discontinue treatment.
Pulmonary toxicity	At every review opportunity	If patient develop signs or symptoms of pulmonary toxicity (e.g. dyspnoea, non-productive cough) – these should be assessed, if suspected the

			patient should be referred to specialist for relevant lung examinations and treatment discontinued.	
(g) Clinically relevant drug interactions (as per SPC)	Beta-blockers and calcium antagonists: The co-administration of beta-blockers or calcium antagonists with depressant effect on sinus and atrio-ventricular node should be undertaken with caution. In clinical studies, bradycardia was more frequently observed when dronedarone was given in combination with beta-blockers. These medicinal products should be initiated at low dose and up titration should be done only after ECG assessment. In patients already on calcium antagonists or beta blockers at time of dronedarone initiation, an ECG should be performed and the dose should be adjusted if needed. Dabigatran: Dronedarone slightly increases the exposure to dabigatran and therefore it is advised to avoid concomitant use. Digoxin: Administration of dronedarone to patients receiving digoxin will bring about an increase in the plasma digoxin concentration and thus precipitate symptoms and signs associated with digoxin toxicity. Clinical, ECG and biological monitoring is recommended, and digoxin dose should be halved. A synergistic effect on heart rate and atrioventricular conduction is also possible. The digoxin dose should be reduced by approximately 50%, serum levels of digoxin should be closely monitored and clinical and ECG monitoring is recommended. Grapefruit juice: Patients should be warned to avoid grapefruit juice beverages while taking dronedarone. Immunosupressants: Dronedarone could increase plasma concentrations of immunosupressants (tacrolimus, sirolimus, everolimus and cyclosporine). Monitoring of their plasma concentrations and appropriate dose adjustment is recommended in case of co-administration with dronedarone. Lactose: This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption, should not take this medicinal product. MAO Inhibitors: Although there is evidence from a study that MAO contributed to the metabolism of the active metabolite of dronedarone, the clinical relevance is of this is unknown. Potent CYP3A4 inducers: Potent CYP3A4 inducers such as rifampicin, phenobarbital, carbamazepine, phenytoin or St John's Wort are not recommended as they decrease dronedarone exposure. Statins: Statins should be used with caution with concomitant use. Lower starting dose and maintenance doses of statins should be considered and patients monitored for clinical signs of muscular toxicity. Warfarin and other Vitamin K antagonists: Patients should be appropriately anti-coagulated as per clinical AF guidelines. Clinically significant INR elevations (≥5) usually within 1 week after starting dronedarone were reported in patients taking oral anticoagulants. International Normalised Ratio (INR) should be closely monitored after initiating dronedarone in patients taking vitamin K antagonists as per their label. Those mentioned below in contra-indications have not been duplicated in this section. Refer to the SPC for more detailed information on the interactions.			
(h) Contra-indications	• Hypersensitivity to the active substance or to any of the excipients listed in the SPC • 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 Caution: Coronary artery disease; correct hypokalaemia and hypomagnesaemia before starting and during treatment
This information does not replace the SPC, this should be read in conjunction with this document available from: https://www.medicines.org.uk/emc	