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

<table>
<thead>
<tr>
<th>GP responsibilities</th>
<th>Consultant responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Prescribe dronedarone at the dose determined by the secondary care specialist</td>
<td>1. To confirm the patient has no contra-indications to treatment and consider the relevance of any cautions.</td>
</tr>
<tr>
<td>2. Refer to secondary care physician if the patient’s condition deteriorates.</td>
<td>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.</td>
</tr>
<tr>
<td>3. Perform monitoring tests as outlined in section VI.</td>
<td>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.</td>
</tr>
<tr>
<td>4. Primary care physician to report adverse events to the specialist and MHRA.</td>
<td>4. Perform monitoring tests as outlined in section VI.</td>
</tr>
<tr>
<td>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.</td>
<td>5. 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.</td>
</tr>
<tr>
<td>6. Stop treatment on the advice of the specialist or immediately if any urgent need to stop treatment arise.</td>
<td>6. 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).</td>
</tr>
<tr>
<td>7. To receive ECG monitoring results from the specialist.</td>
<td>7. To ensure that arrangements are in place for GPs to obtain advice and support where needed.</td>
</tr>
<tr>
<td>8. Report any adverse effects to the referring specialist and the MHRA yellow card scheme</td>
<td>8. To communicate promptly with the GP the results of any monitoring undertaken in secondary care and any changes to treatment made by the specialist.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Hospital contact: Derby Teaching Hospital Foundation Trust</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant/nurse via switchboard: 01332 340131</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chesterfield Royal Hospital Foundation Trust</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant via switchboard: 01246 277271</td>
</tr>
</tbody>
</table>

ii. out of hours contact and procedures:

- Pharmacy, DTHFT, ask for on-call pharmacist via switchboard: 01332 340131
- Cardiology, DTHFT, 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 (assuming 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 (assuming 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)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver function tests</td>
<td>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.</td>
</tr>
<tr>
<td>U&amp;E’s specifically Plasma creatinine (Cr)</td>
<td>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.</td>
</tr>
<tr>
<td>ECG</td>
<td>If QTc interval ≥ 500 milliseconds (Consultant responsible)</td>
</tr>
<tr>
<td>To be aware of the potential for persistent (rather than paroxysmal) AF to develop.</td>
<td>Referred back to secondary care for a further adjustment of their medication or formulation of new management plan.</td>
</tr>
<tr>
<td>Pulmonary toxicity</td>
<td>If suspected the patient should be referred back to the specialist for relevant lung examinations and treatment discontinued.</td>
</tr>
<tr>
<td>Heart failure symptoms</td>
<td>Discontinue treatment</td>
</tr>
</tbody>
</table>

#### 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**

Given the limited clinical data available with dronedarone, co-administration with rivaroxaban should be avoided.

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](http://www.medicines.org.uk).

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### 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 Derby Teaching Hospitals NHS Foundation Trust
Dr Rob McIntosh, Consultant Cardiologist Derby Teaching Hospitals NHS Foundation Trust: Royal Derby hospital

This does not replace the SPC, which should be read in conjunction with it.

**Date Prepared:** November 2017  **Review Date:** October 2019
Sample transfer letter

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.

<table>
<thead>
<tr>
<th>Dose Regimen</th>
<th>Date {Insert medicine name} started</th>
<th>Date for GP to start prescribing {Insert medicine name} from</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The baseline test results are (if applicable):

I confirm I have explained to the patient: the risks and benefits of treatment, the baseline tests conducted the need for monitoring, how monitoring will be arranged, and the roles of the consultant / nurse specialist, GP and the patient in shared care. I confirm the patient has understood and is satisfied with this shared care arrangement at this time.

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)

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.

<table>
<thead>
<tr>
<th>Patient:</th>
<th>NHS No:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant:</td>
<td>Medicine requested for shared care:</td>
</tr>
</tbody>
</table>

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:

Yours sincerely

{GP name}
{Surgery}

**Please send a copy of this response to:**

1. The specialist/consultant requesting shared care
2. **AN ANONYMISED COPY OF THIS FORM ONLY** to the Medicines Management Clinical Effectiveness Team, 1st Floor East Point, Cardinal Square, 10 Nottingham Road, Derby, DE1 3QT or E-MAIL: sderccg.derbyshiremedicinesmanagement@nhs.net

(Sending a copy of this form to the Clinical Effectiveness Team will help to identify any inappropriate requests for shared care e.g. indication not covered, hospital monitoring requirements not fulfilled. It will also help to inform the CCG prescribing group of the reasons shared care is not being undertaken allowing for changes to be made in future updates to improve patient care).