NHS
Shropshire
Clinical Commissioning Group

Essential Shared Care Agreement for Dronedarone

This local safety monitoring schedule supports clinicians providing shared care under the Local Enhanced Service for High Risk Drug Monitoring (formerly Near Patient Testing)
This shared care agreement outlines suggested ways in which the prescribing responsibilities can be shared between the specialist and GP. GPs are invited to participate. If the GP feels that undertaking the roles outlined in the shared care agreement is outside their area of expertise or have clinical concerns about the safe management of the drug in primary care, then he or she is under no obligation to do so. In such an event, clinical responsibility for the patient's health remains with the specialist. If a specialist asks the GP to prescribe, the GP should reply to this request as soon as practicable. Sharing of care assumes communication between specialist, GP and patient.

Consultant details	GP details	Patient details
Name:	Name:	Name:
Address:	Address:	NHS Number:
Email:	Email:	Date of birth:
Contact number:	Contact number:	Contact:

Signing indicates agreement with the responsibilities suggested in this document, and that the patient has been informed of the need to report any issues with their treatment to their doctor.

Specialist signature: **Date:**	**General Practitioner signature:** **Date:**

Introduction

Dronedarone is a multi-channel (sodium, potassium, calcium) blocker anti-arrhythmic drug for use in atrial fibrillation.[i]

Licensed indication:

Dronedarone is licensed for the maintenance of sinus rhythm after cardioversion in adults with paroxysmal or persistent atrial fibrillation (AF). It should **only** be initiated if alternatives are unsuitable. Dronedarone should not be given to patients with left ventricular systolic dysfunction or to patients with current or previous episodes of heart failure.

The licensed indication and MHRA guidance differ from NICE TAG197 Dronedarone (issued August 2010) for the treatment of nonpermanent atrial fibrillation.

Adult dosage and administration

The recommended dose is 400mg twice daily in adults, taken as:

- One tablet with the morning meal and
- One tablet with the evening meal

Dronedarone should **not** be taken together with grapefruit juice.

If a dose is missed, patients should take the next dose at the regular scheduled time and should **not** double the dose.

Treatment with Class I or III antiarrhythmics (flecainide, propafenone, quinidine, disopyramide, dofetilide, sotalol, amiodarone) **must be stopped** before starting dronedarone. For patients receiving amiodarone, a one month washout period is recommended before commencing dronedarone. **For patients receiving dronedarone who are to receive amiodarone, a two week washout period is recommended before commencement.**

Available as: Dronedarone 400mg tablets (MULTAQ®▼)

Specialist responsibilities

- Discuss with the patient options for treatment and suitability of dronedarone along with the potential benefits and side-effects of treatment.
- Provide patient/carer with relevant (preferably written) information on use, side-effects and need for monitoring of dronedarone.
- Ensure no clinically relevant drug interactions with patient's current medication
- Undertake baseline monitoring:[ii]
    - **LFTs** (baseline and at 7 days' treatment)
    - **Serum creatinine** (baseline and at 7 days' treatment)
    - **ECG**
    - **U&Es** (potassium and magnesium)
- Ensure patient receives further ongoing monitoring:
    - Regular cardiac examination including **ECG every 6 months**
    - **Annual PFTs**
- Arrange shared care with the patient's GP.
- Initiate treatment with dronedarone.
- Once patient stabilised, transfer prescribing and agreed monitoring to GP
- Review the patient at agreed specified intervals, sending a written summary to the GP when the patient is reviewed. Communicate promptly with the GP when treatment is changed
- Have a mechanism in place to receive a rapid referral of a patient from the GP in the event of deteriorating clinical condition and ensure that clear backup arrangements exist for GPs to obtain advice and support.
- Provide any other advice or information for the GP as required, including dose adjustment
- Report adverse events to the MHRA (via Yellow Card scheme)

Primary Care responsibilities

- Respond to the specialist's request for shared care.
- Prescribe dronedarone according to dose advised by specialist.
- Arrange and record ongoing monitoring as agreed with the specialist
    - **LFTs** every month until month 6, at month 9 and 12, and periodically thereafter
    - **Renal function** at agreed intervals (recommended annually)
    - Ensure patient receives **ECG every 6 months** and **PFT annually**
- Ensure no drug interactions with the patient's medication
- Contact the specialist and seek advice on any aspect of patient care that is of concern and may affect treatment
- Refer patient to consultant if patient's condition deteriorates especially if symptoms of heart failure or suspected pulmonary toxicity occur
- Stop treatment on the advice of the specialist
- Report adverse events to the consultant and MHRA (via Yellow Card)

Monitoring

Parameter	Frequency of monitoring	Result	Action
ECG	Monitor ECG for QTc (Bazett) interval prolongation. Baseline and at 6 monthly intervals (Specialist)	• ≤ 500 milliseconds • Reversion back to AF	Specialist
U&E	Creatinine at baseline and at 7 days (Specialist). Periodically afterwards (GP)	See below	See below
LFT	Prior to treatment and at 7 days (Specialist) Monthly for 6 months (GP) At 9 months (GP) At 12 months and periodically thereafter (GP)	ALT > 3xULN If still > 3xULN on retest (ULN, upper limit of normal)	Retest Withdraw dronedarone
Dyspnoea, cough, swelling of legs	Observe regularly for signs and symptoms of new or worsening heart failure (Specialist and GP)		Refer to Specialist

A ~10 micromol/L increased in plasma creatinine is commonly observed in healthy subjects and patients. If observed, re-test after a further 7 days. If no further increase, this result becomes the new baseline. If continues to rise, discontinuation of treatment should be considered. An increase in creatininaemia should not necessarily lead to discontinuation of treatment with ACE inhibitors or angiotensin II receptor antagonists.

Adverse effects, Precautions and Contra-indications

Adverse effects

Cardiac effects – congestive heart failure, bradycardia
Gastrointestinal effects – diarrhoea, vomiting, nausea, abdominal pain, dyspepsia
Respiratory – interstitial lung disease, including pneumonitis and pulmonary fibrosis (uncommon)
Skin – rashes, pruritis, photosensitivity (rare)
Others – fatigue, asthenia

Precautions

Dronedarone is not recommended for use during pregnancy and in women of childbearing potential not using contraception. For use during breastfeeding, the decision to discontinue breast-feeding or discontinue/abstain from dronedarone must be decided between the merits of either situation.

Contra-indications

Dronedarone is contra-indicated in patients with[iii]:

- Unstable haemodynamic conditions
- History of, or current, heart failure or left ventricular systolic dysfunction
- Permanent AF (i.e. duration ≥ 6 months or unknown, and attempts to restore sinus rhythm no longer considered by physician)
- Liver and lung toxicity related to previous use of amiodarone
- second- or third- degree AV block, complete bundle branch block, distal block, sinus node dysfunction, atrial conduction defects or sick sinus syndrome (except when used with a functioning pacemaker)
- bradycardia <50 beats per minute
- QTc Bazett interval 500 milliseconds
- severe hepatic impairment
- severe renal impairment (CrCl < 30 ml/min)
- Co-administration with **dabigatran**

Common Drug Interactions

Dronedarone is primarily metabolised by CYP3A4, therefore inhibitors and inducers have the potential to cause many drug interactions. **Consult the BNF and SPC before initiating any new drug therapy.**

- **Anti-arrhythmics**: increased risk of myocardial depression or ventricular arrhythmias with **amiodarone** or **disopyramide** – avoid concomitant use
- **Antibacterials and antifungals**: avoid use with **erythromycin**, **clarithromycin**, **telithromycin**, **rifampicin** , **ketoconazole**, **itraconazole**, **posaconazole**, **voriconazole** – all affect plasma concentrations
- **Antidepressants** : avoid use with **tricyclics** (risk of ventricular arrhythmias) and **St Johns Wort** (reduction in plasma concentration
- **Antiepileptics:** concentration of amiodarone reduced by **carbamazepine** and **phenytoin**
- **Antipsychotics:** avoid concomitant use with **phenothiazines**
- **Antivirals:** avoid use with **ritonavir**
- **Antihypertensives:** caution with **beta-blockers** and **calcium channel blockers**
- **Dabigatran:** co-administration greatly increases dabigatran plasma levels. Co-adminstration is contra-indicated.
- **Digoxin:** increases plasma concentration (dose should be halved)
- **Statins:** increased risk of myopathy with **simvastatin**, possibly increases plasma concentration of **rosuvastatin**

- **Drugs inducing torsades de pointes:** phenothiazines, cisapride, bepridil, tricyclic antidepressants, terfenadine and certain oral macrolides e.g. erythromycin, **Class I and III antiarrythmics (flecainide, propafenone, quinidine, disopyramide, dofetilide, sotalol, amiodarone).**

Communication

For any queries relating to this patient's treatment with dronedarone, please contact the consultant named at the top of this document.

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions Please refer to full prescribing data in the Summary of Product Characteristics (www.medicines.org.uk) or the British National Formulary (www.bnf.org)

[i] Multaq 400mg tablets – Summary of Product Characteristics. Available at www.medicines.org.uk/emc/medicine/22894.

[ii] Suggestions for Drug Monitoring in Adults in Primary Care. NHS UKMi, February 2014. Available at www.evidence.nhs.uk

[iii] Dronedarone (Multaq): cardiovascular, hepatic and pulmonary adverse events – new restrictions and monitoring requirements. MHRA October 2011