Name: Attach Banda Label here
Address:

Date of Birth:
NHS number:

Coventry & Warwickshire
Area Prescribing Committee

Dronedarone▼ (Multaq®)

SCA: DRONEDARONE for the treatment of non-permanent atrial fibrillation

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

Dronedarone has been approved by the Coventry & Warwickshire Area Prescribing Committee to be initiated by consultant cardiologists within its licensed indication and in accordance to NICE recommendation (NICE TA 197).

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of dronedarone for the management of non-permanent atrial fibrillation between secondary care specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with atrial fibrillation (AF) are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

Specialist responsibilities

1. General responsibility – initiate therapy and stabilise patient on treatment before requesting shared care
2. Assess patient suitability for treatment, ensure stable baseline creatinine and hepatic function
3. .Ask the GP if he/she is willing to participate in shared care
4. Discuss benefits, treatments and side-effects with the patient
5. Initiate treatment with dronedarone
6. After 7 days of treatment perform serum creatinine and liver function tests
7. Provide the GP with advice on any implications of co-prescribing with current medications, particular caution with:
   potent CYP 3A4 inducers e.g. rifampicin, phenobarbitone, carbamazepine, phenytoin or St John's Wort; potent CYP 3A4 inhibitors e.g. clarithromycin, ketoconazole, voriconazole;digoxin; β-blockers; statins; calcium antagonists; ACE inhibitors; sirolimus; tacrolimus
8. Assess potential adverse events and report these to the MHRA on a yellow card www.mhra/gov.uk/yellowcard, to GP and appropriate Medicines Management team
9. Ensure regular cardiac examinations, including an ECG **at least every 6 months**. Promptly inform the GP of any results of investigations and changes in treatment following hospital admission or out-patient consultation
10. Advise the GP on when and how to stop treatment
11. .Ensure clear arrangements for GP back up, advice, and support

General Practitioner responsibilities

1. Reply to the request for shared care as soon as practicable
2. Prescribe dronedarone following communication with specialist about the need for treatment
3. Adjust dose of any concomitant medication known to interact with dronedarone as advised by the specialist
4. Assess patient's clinical status prior to all dose changes
5. Provide adequate monitoring of response to treatment (see monitoring) *e.g.* renal function, hepatic function, BP, heart rate, weight. Seek specialist advice if necessary
6. Upon initiation, monitor liver function tests on a monthly basis for first 6 months, at month 9 and month 12 and periodically thereafter
7. Ensure that a cardiology assessment is carried out every 6 months
8. Refer back to specialist if condition deteriorates. Particular attention should be paid to symptoms of heart failure or pulmonary toxicity (onset of dyspnoea or non-productive cough)
9. Report adverse events to the MHRA, on a yellow card (www.mhra.gov.uk/yellowcard), specialist and appropriate Medicines Management team
10. Stop treatment on advice of specialist

Patient/carer's role

1. Report any adverse effects to the specialist or GP whilst taking dronedarone
2. Share any concerns in relation to treatment with dronedarone. Pay particular attention to any other medicines being taken whilst receiving dronedarone.
3. He/she must not take St John's Wort or drink grapefruit juice whilst receiving dronedarone
4. Report to the GP or specialist as soon as possible should his/her condition significantly worsen
5. Report to the specialist or GP if he/she does not have a clear understanding of the treatment
6. The patient must immediately notify the GP or specialist if he/she develops any of the following:
   increasing swelling of the feet or legs; wheezing; chest tightness or coughing up frothy sputum at rest, night time or after minor exertion; using more pillows to prop themselves up at night to ease breathing; weight gain of ≥2 – 3 kg (or 5 pounds) in a short period of time, difficulty in breathing or non-productive cough.
7. Report to the GP or specialist if he/she suffers symptoms of liver injury *e.g. abdominal pain or discomfort, loss of appetite, nausea and vomiting, darkening of urine, itching, yellowing of the skin & whites of the eye, fatigue*
8. The patient may also choose to report any adverse drug reaction direct to the MHRA on a Yellow Card , available at pharmacies, GP surgeries or from the Yellow Card hotline (freephone 0808 100 3352 during business hours). The form can also be downloaded from www.mhra.gov.uk/yellowcard.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist:				
Pharmacy Dept:				
Other:				

NICE Recommendation:

Dronedarone is recommended as an option for the treatment of non-permanent atrial fibrillation **ONLY** in those:

- whose AF is not controlled by first-line therapy (usually including β-blockers), that is, as a second-line treatment option, **and**
- who have at least one 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 ≥ 50mm
  - left ventricular ejection fraction (LVEF) < 40% *[note: SPC does not recommend in patients with LVEF < 35% due to limited experience]*
  - age 70 years or older, **and**
- who do not have unstable New York Heart Association (NYHA) class III or IV heart failure

SUPPORTING INFORMATION (see SPC for complete details/specific guidance http://emc.medicines.org.uk)

Licensed indications: Dronedarone is indicated in adult clinically stable patients with a history of, or current non-permanent AF to prevent recurrence of AF.

Dosage and administration: Recommended dose is 400mg twice daily in adults. It should be taken as one tablet with the morning meal and one tablet with the evening meal.

Monitoring:

- **Cardiovascular monitoring**
  Patients should receive regular cardiac examinations, including and ECG at least every 6 months, to identify those who revert to AF. Discontinuation of dronedarone should be considered for these patients.
  Discontinue treatment if patient develops permanent AF.
  Patients should be carefully evaluated for symptoms of heart failure during treatment.
  Patients should be appropriately anticoagulated as per clinical AF guidelines. INR should be closely monitored after initiating dronedarone in patients taking Vitamin K antagonists as per SPC.

Renal monitoring

- Check U & Es at baseline, and **7 days** after commencing dronedarone. Electrolyte imbalances (if found) should be corrected before initiation and during dronedarone therapy
  If an increase in creatinine is found after 7 days, serum creatinine should be re-measured after a further 7 days. If no further increase is observed, this value should be used as the new reference baseline.
  If serum creatinine continues to rise then consideration should be given to further investigation and discontinuing treatment.
  This initial creatinine rise should not necessarily lead to discontinuation of ACE inhibitor & Angiotensin-II receptor blocker.

Hepatic monitoring

- Check LFTs before starting treatment with dronedarone, after 1 week of treatment; monthly for 6 months, at month 9, at month 12 and periodically thereafter.
- **Pulmonary monitoring**
  Cases of interstitial lung disease, including pneumonitis and pulmonary fibrosis, have been reported in association with dronedarone. Onset of dyspnoea or non-productive cough may be related to pulmonary toxicity. If pulmonary toxicity is suspected during treatment, relevant lung examinations should be considered and treatment discontinued if confirmed.

Summary of assessments during treatment (as above)

- **Assessments for first 6 months**
- ECG, at least every 6 months
- Liver function tests: day 7, month 1, month 2, month 3, month 4, month 5, month 6
- Serum creatinine: day 7

Month 6 to year 1

- ECG at 12 months
- Liver function tests at month 9, month 12

Beyond year 1

- ECG at least every 6 months
- Periodic liver function tests
- Periodic renal function tests

Cautions:

- Avoid in patients with a recent history of moderate heart failure, or with a significantly reduced left ventricular function
- Correct hypokalaemia and hypomagnesaemia before starting and during treatment
- Measure serum creatinine 7 days after initiation

Contra-indications:

- Hypersensitivity to the active ingredient or to any of the excipients (including those with galactose intolerance)
- 2nd or 3rd degree atrio-ventricular block or sick sinus syndrome (except when used in conjunction with a functioning pacemaker)
- Bradycardia <50bpm
- Permanent AF with an AF duration ≥ 6months (or duration unknown) and attempts to restore sinus rhythm no longer considered by the physician
- Patients in unstable haemodynamic conditions
- History of, or current heart failure or left ventricular systolic dysfunction
- Co-administration with potent CYP 3A4 inhibitors *e.g.* ketoconazole, itraconazole, clarithromycin, ritonavir
- Co-administration of medicinal products that could induce *torsades de pointes e.g.* terfenadine, tricyclic antidepressants, Class I & III antiarrhythmics
- QTc Bazett interval ≥ 500msec
- Severe hepatic impairment
- Severe renal impairment (CrCl < 30ml/min)

Side effects:

Common side effects: GI disturbances (*e.g.* diarrhoea, nausea & vomiting, dyspepsia); fatigue; asthenia; bradycardia; rash; pruritus
Uncommon/rare side effects: erythematous rash ; eczema & dermatitis; photosensitivity reactions

Drug interactions (see also above under cautions):

Dronedarone is primarily metabolised by CYP 3A4. It is a moderate inhibitor of CYP 3A4, a mild inhibitor of CYP 2D6, and a potent-inhibitor of P-glycoproteins.

- *Statins:* Use lower starting dose and maintenance doses due to increase risk of statin-induced myopathy
- *Digoxin:* Increased risk of digoxin-toxicity. Reduce digoxin dose by 50%
- *Verapamil & Diltiazem:* Use with caution due to depressant effects on sinus and AV node
- *β-blockers:* Use with caution
- *Grapefruit juice & St. John's Wort*: Avoid with dronedarone
- *Macrolides & Antifungals*: Avoid with dronedarone

Cost: At current prices one year's treatment will cost £821 (dm+d May 2015)

References:

Sanofi-aventis: Summary of Product Characteristics (SPC) for dronedarone (Multaq®) October 2011
National Institute for Health and Clinical Excellence (NICE) technology appraisal guidance on dronedarone (TA 197) 25th August 2010
Effective shared care agreement toolkit for dronedarone. Keele University. www.esca-keele.co.uk/dronedarone/agreementsetup.php *<accessed 15th Sept 2010>*
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