This guideline sets out details of the respective responsibilities of GPs and specialist services within shared care prescribing arrangements and is intended to provide sufficient information to enable GPs to prescribe dronedarone.

Currently there is no commissioned enhanced service to remunerate practices for additional work relating to this guideline.

This guideline has been approved to ensure that GP practices wishing to monitor and prescribe dronedarone for their patients are able to do so safely.

An electronic version of this document can also be viewed / downloaded from the North of Tyne and Gateshead Area Prescribing Committee Website at:


| Endorsed for use within North Tyneside, Northumberland, Newcastle and Gateshead by the North of Tyne and Gateshead APC September 2017 |
|---|---|
| Review date | Medicines Use and Guideline Group recommended review date: September 2019 |
| Membership of the guideline development group | The following were consulted on the review of the 2012 approved guidance: |
| | • Matthew Lowery, Formulary and Audit Pharmacist, NuTH |
| | • Stephen Murray, Consultant Cardiologist, NuTH |
Background

Dronedarone is included in the North of Tyne Formulary as an option for clinically stable adult patients, with paroxysmal or persistent atrial fibrillation for the maintenance of sinus rhythm after successful cardioversion. Due to its safety profile, it should only be prescribed after alternate treatment options have been considered.

Dronedarone is a multi-channel blocker, affecting potassium, sodium and calcium channels in myocytes. It prolongs the cardiac action potential and refractory period, giving it a broad anti-arrhythmic effect. The structure of dronedarone has several modifications compared to amiodarone, including removal of the iodine radical and the addition of a methane sulfonyl radical. This is believed to decrease its lipophilicity and explain its lack of thyroid complications. It has a short half life of 27-31 hours (the half life of amiodarone is of the order of 50 days).

Treatment with dronedarone should only be initiated by a cardiologist with experience of treating AF.

Referral criteria

Patients on dronedarone for the maintenance of sinus rhythm after cardioversion, once therapy has been stabilised.

Responsibilities of Hospital Specialist Team

- Initiation and provision of treatment with dronedarone until patient is stabilised on the licensed dose.
- Discussion with the patient/carer regarding the benefits, side effects and risks of treatment including the need for liver function test monitoring.
- To advise the patient to contact health care professionals immediately in case of signs or symptoms of liver injury (e.g. right subcostal pain, confusion, jaundice), or of new cardiac or pulmonary symptoms or signs.
- To monitor liver function tests which are required prior to treatment, at 7 days, monthly for 6 months, at 9 and 12 months and annually thereafter, and creatinine at initiation, at day 7 and 7 days after if rising, until such time as the general practitioner agrees to take over this responsibility.
- To ensure that, 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.
- To ensure INR is closely monitored after initiating dronedarone in patients taking vitamin K antagonists.
- Regular follow up of the patient until the patient is stabilised on treatment, and his dysrhythmia is controlled.
- To be available for advice if the patient’s condition changes, and review if new cardiac or pulmonary symptoms or signs of hepatic impairment develop.
- To assess patient 6 monthly including by ECG, evaluate for symptoms of...
heart failure and pulmonary toxicity.

- Prompt communication with the GP regarding the patient’s progress, and any reassessment and changes in treatment.
- To stop dronedarone if the patient develops any of the conditions which would lead to a contraindication.
- To discontinue dronedarone if permanent atrial fibrillation occurs, and consider discontinuation if atrial fibrillation reoccurs.
- Obtaining agreement of GP to participate in shared-care arrangement for dronedarone therapy.
- Report adverse events to the CSM.

**Responsibilities of General Practitioner:**

- Reply to request for shared care as soon as practical (within 28 days).
- Prescribe dronedarone in accordance with the specialist’s recommendations.
- To report to and seek advice from the specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- Subsequent to taking over prescribing ensure liver function tests have been monitored monthly for 6 months, at 9 and 12 months and annually thereafter.
- 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.
- To remind patients to contact health care professionals immediately in case of signs or symptoms of liver injury, or new cardiac or pulmonary symptoms or signs.
- Report adverse events to specialist and CSM.
**Prescribing Information Sheet**

**Dronedarone**  
*Shared Care Status: AMBER*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Information / Comments</th>
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| **Indication(s)**             | Dronedarone is licensed for use in adult, clinically stable patients, with paroxysmal or persistent atrial fibrillation for the maintenance of sinus rhythm after successful cardioversion.  
                                 | It should not be given to patients with left ventricular systolic dysfunction or to patients with current or previous episodes of heart failure.          |
| **Usual Initiation and Maintenance Dose** | The recommended dose is 400mg twice daily. It should be taken as one tablet with the morning meal and one tablet with the evening meal. Grapefruit juice should be avoided. |
| **Likely duration of treatment** | Indefinite, as long as treatment is considered appropriate by specialist.                                                                                |
| **Formulation available**     | 400 mg tablets                                                                                                                                         |
|                               | Dronedarone does not require any special storage conditions                                                                                           |
| **NHS Cost**                  | 400 mg twice daily - £63.00                                                                                                                             |
| **Potential Problem and its Management** | Cases of liver injury, including liver failure, requiring transplantation, have been reported. A less common side effect is interstitial lung disease including pneumonitis and pulmonary fibrosis. |
| **Other Adverse Effects**     | Very common side effects include changes in blood creatinine levels and congestive heart failure. Common side effects include bradycardia (<50 beats per minute), diarrhoea, nausea, vomiting and abdominal discomfort. Rashes and erythema may occur. |
### Contraindications

- Severe LV impairment
- Unstable haemodynamic condition
- Bradycardia, pulse rate < 50 bpm.
- History of, or current heart failure, or left ventricular systolic function.
- Permanent atrial fibrillation (atrial fibrillation duration > 6 months or unknown, and attempts to restore sinus rhythm no longer considered).
- Severe hepatic or renal impairment. Liver and lung toxicity related to the previous use of amiodarone.

### Special Precautions / Warnings

- There are no adequate data for the use of dronedarone in pregnant women, therefore it is not recommended during pregnancy. Adequate contraception is required during and for one month after stopping treatment.

  *Breast feeding* As it is not known whether dronedarone is excreted in human breast milk, it is best avoided in breast feeding women.

- As there is no experience in children and adolescents below 18 years of age, dronedarone is not recommended in this population.
- Due to the presence of lactose in dronedarone, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption, should not take dronedarone.

### Monitoring

- Regular cardiac examinations, including an ECG at least every 6 months.
- Evaluate for symptoms of heart failure.
- Consider pulmonary examination if dyspnoea or non-productive cough develops as interstitial lung disease has been reported.

For patients prescribed dronedarone, liver function tests should be performed:
- Prior to treatment and after seven days,
- On a monthly basis for six months,
- At months 9 and 12, and annually thereafter.
If alanine transaminase (ALT) levels are elevated to $\geq 3$ upper limit of normal (ULN), levels should be re-measured within 48 to 72 hours. If ALT levels are confirmed to be $\geq 3$ ULN after re-measurement, dronedarone treatment should be withdrawn.

Measure creatinine prior to and seven days after initiation, re-measuring after seven days if a rise is observed. Consider discontinuation if rising.

Patients should be advised to contact health care professionals immediately in case of occurrence of new cardiac or pulmonary symptoms or signs of hepatic impairment.

### Drug Interactions

Dronedarone is contraindicated with QT prolonging drugs e.g. phenothiazines and tricyclic antidepressants and potent cytochrome P450 3A4 inhibitors. Co-prescription of cytochrome P34A inducers, such as rifampicin, phenobarbital, carbamazepine or St John’s Wort is not recommended. Statins should be used with caution: lower starting dose and maintenance dose of statins should be considered and patients should be monitored for clinical signs of muscular toxicity.

Monitor INR closely after initiation in patients taking vitamin K antagonists.

Use of Dabigatran is contra-indicated with dronedarone. (MHRA July 2012). **Given the limited clinical data available with dronedarone, co-administration with rivaroxaban should be avoided.**
Shared Care Request/Confirmation

- Consultant/Specialist Nurse to complete first section of form and send to patient’s GP.
- GP to complete second section of form and return to hospital consultant within 28 days.

A copy of the full shared care guideline can be viewed at [www.northoftyneapc.nhs.uk](http://www.northoftyneapc.nhs.uk)

<table>
<thead>
<tr>
<th>Patient Details (use hospital label if preferred)</th>
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<tbody>
<tr>
<td>Consultant ........................................</td>
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<tr>
<td>Name ...............................................</td>
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<td>Department.......................................</td>
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Treatment Requested for Prescribing in Accordance with an Approved Shared Care Arrangement:

Drug Name........................................... Dose .......... Frequency ............

Other Information (if appropriate)

Signed (Hosp. Dr / Specialist Nurse)
Name (print) Date

To be completed by GP

I ACCEPT the proposed shared care arrangement for this patient
Or
I ACCEPT the proposed shared care arrangement with the caveats below
Or
I DO NOT ACCEPT the proposed shared care arrangement for this patient
My caveats / reason(s) for not accepting include:
Signed Name (print) Date
(Patients GP)

N.B. Participation in this shared care arrangement implies that prescribing responsibility is shared between the hospital consultant and the patient’s GP.