**SHARED CARE ARRANGEMENT AND PRESCRIBING INFORMATION FOR DRONEDARONE (adults only)**

NHS Grampian

**N.B.** This document should be read in conjunction with the current Summary of Product Characteristics (SmPC).

Patient safety is paramount. The clinician who signs the prescription legally assumes clinical responsibility for the medicine and the consequences of its use.

## GENERIC NAME (formulation and strength)

Name: Dronedarone (as hydrochloride); Trade name Multaq® prescribe generically.
Formulation: film-coated tablets
Strength: 400mg

## STATUS OF MEDICINE

Licence status: POM; licensed for requested condition.

Formulary status: Amber 1

Risk minimisation materials: https://www.medicines.org.uk/emc/product/497/rmms

## CONDITION(S) TO BE TREATED

Dronedarone is licensed for the maintenance of sinus rhythm after successful cardioversion in adult clinically stable patients with paroxysmal or persistent atrial fibrillation (AF).

Due to its safety profile dronedarone should only be prescribed after alternative treatment options have been considered.

Dronedarone must not be given to patients with left ventricular systolic dysfunction or to patients with current or previous episodes of heart failure.

| TYPICAL DOSAGE REGIME | |
|---|---|
| Licensed dose | The recommended dose is 400mg twice daily in adults.<br>It should be taken as one tablet with the morning meal and one tablet with the evening meal. If a dose is missed, patients should take the next dose at the regular scheduled time and should not double the dose. |
| Route of administration | Oral. Tablets should not be split/halved and should be swallowed whole with a drink of water during a meal. |
| Recommended starting dose | As directed by specialist |
| Titration dose/increment | N/A |
| Maximum dose | 400mg twice daily |
| Situations requiring dose adjustment | See Table 1 |
| Duration of treatment | As directed by specialist. **Note:** Not recommended to be continued if the patient develops permanent AF with a duration of >6 months. |

## RESPONSIBILITY OF ACUTE CARE/SPECIALIST SERVICE

Also see Multaq® Prescriber Guide https://www.medicines.org.uk/emc/product/497/rmms

Undertake baseline investigations/monitoring and initiate treatment.

- Baseline monitoring:
  - U&Es, LFTs
  - ECG
- Confirm absence of contraindications or significant drug interactions, and assess risk/benefit of treatment.
- Monitor the condition, response to the treatment and need to continue. Advise the GP of the need to discontinue treatment and how (if necessary).
- Advise patient not to take St. John's Wort and avoid grapefruit juice.
- Advise the patient to contact a healthcare professional immediately if they experience any signs/symptoms of potential liver injury (such as new onset abdominal pain, anorexia, nausea, vomiting, fever, malaise, fatigue, jaundice, dark urine or itching) or of new cardiac or pulmonary symptoms or signs.
- Inform the GP of patients who fail to attend clinic review appointments.
- Counsel female patients regarding taking adequate contraceptive precautions during treatment where appropriate.
- Be available for advice if the patient presents to the GP with new cardiac or pulmonary symptoms or signs, signs of hepatic impairment or reverts back to AF.
- Review the patient regularly in clinic. If the patient has reverted back to AF, consideration should be given to stopping the treatment, and treatment should be stopped if permanent atrial fibrillation occurs.
- Report any adverse effects detected to the MHRA using the Yellow Card System and GP (as necessary).
- Ensure the patient receives a dronedarone alert card, which details the requirements for U&Es, LFTs and ECGs.

## ADMINISTRATIVE RESPONSIBILITIES OF PRIMARY CARE

A practice agreeing to prescribe dronedarone should:

- Ensure that the relevant monitoring requirements are undertaken at the correct frequency.
- Ensure that the test results are checked for any abnormality as soon as the results are available.
- Ensure abnormal results are acted upon.
- Contact the GP or acute care/specialist service in the event of a drug reaction or monitoring abnormality or if you are concerned in any way regarding the current treatment regime.

## CLINICAL CARE WHICH IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN

Also see Multaq® Prescriber Guide https://www.medicines.org.uk/emc/product/497/rmms

- Prescribe medication under guidance of acute care/specialist service.
- Check before prescribing each instalment of medication that the monitoring is up to date and that results are within the normal range.

- Evaluate the patient every 6 months including ECG and evaluation of symptoms of heart failure, liver and pulmonary toxicity. Remind patient of signs and symptoms to report. Contact acute care/specialist service for advice regarding any signs/symptoms which suggest toxicity or cause concern, if AF recurs or permanent AF develops.
- Conduct recommended laboratory tests and contact acute care/specialist service to advise if results are outwith range (see over).
  - LFTs at 7 days, 1 month, monthly for 6 months, and at 9 and 12 months post initiation. LFTs should then be monitored annually unless there are concerns or slightly raised levels, where 3 monthly monitoring is recommended. Continued monitoring of LFTs and close observation of patients may be required if treatment requires to be stopped until LFTs normalise.
  - Creatinine at day 7, with a recheck at day 14 if a raised creatinine levels is seen on day 7. Consideration should be made for discontinuation if creatinine continues to rise and should be discussed with the acute care/specialist service. Creatinine should be monitored periodically, suggested at least 6 monthly, thereafter.
- Ensure no interacting medications are prescribed in primary care.
- Monitor for concordance with therapy.
- Report any adverse events to acute care/specialist service and the MHRA using the Yellow Card System.

When writing laboratory request forms always include details of the patient's relevant medication.

**Note:** In addition to absolute values for haematological or biochemical indices a rapid change or a consistent upward/downward trend in any value should prompt caution and extra vigilance.

If something unexpected occurs contact consultant.

Notify the acute care/specialist service if the drug is stopped.

**Table 1: Abnormal monitoring results**

| Abnormal Monitoring Results | Action To Be Taken |
|---|---|
| • ALT ≥3 times upper limit of normal on a single blood test | Repeat blood test within 48-72 hours. |
| • ALT ≥3 times upper limit of normal on 2 tests, taken within 48-72 hours of each other | Contact acute care/specialist service **urgently** to inform of need for treatment withdrawal, and arrange any appropriate investigations. |
| • Symptoms of dyspnoea or non-productive cough | Contact acute care/specialist service **urgently** for relevant lung examinations for suspected pulmonary toxicity and inform of need to withdraw treatment. |
| • Symptoms and signs of heart failure | Contact acute care/specialist service **urgently** for investigation and inform of need to withdraw treatment. |
| • Continued increase in creatinine | Refer to acute care/specialist service for consideration of withdrawal of treatment. Discuss **urgently** if CrCl <30mL/min. |

| Abnormal Monitoring Results | Action To Be Taken |
|---|---|
| Recurrence of AF or development of permanent AF>6 months | Refer to acute care/specialist service for consideration of withdrawal of treatment. |
| • QTc ≥500milliseconds | Contact acute care/specialist service **urgently** to inform of need for treatment withdrawal. |
| • Heart rate <50bpm | Refer to acute care/specialist service and review concurrent medications as appropriate. |
| • Low potassium or magnesium | Correct with supplementation and review concurrent medication for causes as appropriate as abnormal electrolytes have implications for rhythm control. **Note**: Magnesium should be checked if other electrolyte abnormalities are detected, or if the clinical condition of the patient requires, and corrected as appropriate. |

## RESPONSIBILITY OF OTHER HEALTHCARE PROFESSIONALS

N/A

## RESPONSIBILITY OF THE PATIENT

- Take medication regularly as directed by the specialist/doctor.
- Attend hospital and GP clinic appointments as requested by specialist/GP practice. Failure to attend appointments may result in medication being reviewed/stopped.
- Report any adverse effects/illness to the specialist/GP and present rapidly to specialist/GP should their condition significantly worsen.
- Avoid St John's Wort and grapefruit juice whilst taking dronedarone.

## PRESCRIBING INFORMATION

**For specific product information consult the current Summary of Product Characteristics (http://emc.medicines.org.uk/), the BNF/BNF for Children (https://www.medicinescomplete.com/mc/index.htm)**

## CONTRAINDICATIONS

- Left ventricular systolic dysfunction or patients with current or previous episodes of heart failure.
- Permanent AF (duration >6 months or unknown) and attempts to restore sinus rhythm no longer considered.
- Severe renal or liver impairment.
- Liver or lung toxicity related to previous amiodarone use.
- 2nd or 3rd degree atrioventricular (AV) block or sick sinus syndrome (unless permanent pacemaker in situ).
- Bradycardia (<50bpm).

- Co-administration of potent CYP450 inhibitors such as ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, nefasazone and ritonavir.
- Co-administration with other medicine which may induce torsades de pointes such as phenothiazines, tricyclic antidepressants, terfenadine, oral macrolides, Class I and III antiarrythmics.
- Co-administration with dabigatran (also see interaction section for DOACs).
- Potassium and magnesium deficiency.
- QTc >500 milliseconds.
- Hypersensitivity to active substance or excipients.

## PREGNANCY

Not recommended. Adequate contraception is required during and for one month after stopping treatment.

## BREAST-FEEDING

Not known. Advise to avoid.

## COMMON SIDE EFFECTS AND THEIR MANAGEMENT

The most common adverse events include diarrhoea, nausea, vomiting, fatigue and asthenia. Congestive heart failure and bradycardia are also commonly seen. See SmPC for full list.

## COMMON DRUG INTERACTIONS (for a full list see SmPC)

Also see Multaq® Prescriber Guide
https://www.medicines.org.uk/emc/product/497/rmms

Please also refer to Contraindications (above).

- Grapefruit juice: Patient should be advised to avoid grapefruit juice.
- Digoxin: Dose should be halved with concurrent dronedarone prescription. Clinical, ECG and biological monitoring is recommended for this combination.
- Statins: Should be used with caution, and lower starting and maintenance doses be considered, monitoring closely for signs of muscle toxicity.
- Warfarin: INR should be monitored closely. INR may increase significantly within one week after starting dronedarone.
- Rivaroxaban: Due to lack of clinical data, co-prescribing is advised to be avoided by UK rivaroxaban manufacturer. All other DOACs are advised to only be used with caution.
- Potent CYP3A4 inducers such as rifampicin, phenobarbital, carbamazepine, phenytoin or St John's Wort are not recommended.
- MAO inhibitors might decrease the clearance of the active metabolite of dronedarone and should therefore be used with caution.
- Dronedarone could increase plasma concentrations of immunosupressants (tacrolimus, sirolimus, everolimus and cyclosporine). Plasma serum concentration monitoring is recommended.

- Other sinus node or AV node depressants (e.g. beta blockers, rate limiting calcium antagonists) may predispose to bradycardia.

## ADVERSE DRUG REPORTING

If an adverse reaction does occurs inform relevant medical practitioner as soon as possible.

Report to the MHRA using the Yellow Card System https://yellowcard.mhra.gov.uk/

## REFERENCES

electronic Medicines Compendium (eMC), 2014. Multaq 400mg tablets. [Online]
Available at: https://www.medicines.org.uk/emc/product/497
[Last updated 01 January 2021; Accessed April 2021].

## ACUTE CARE/SPECIALIST SERVICE CONTACT INFORMATION

In the event of concern being raised, the primary care practitioner should contact the referring consultant via the hospital switchboard, via their secretary, by e-mail or letter, whichever is more appropriate. If the concern is urgent, and out of hours advice is required, the on call cardiologist may be contacted via switchboard.

<table>
<tr><td>Publish:<br>Public</td><td>Applies to:<br>NHS Grampian</td><td>Version: 2</td></tr>
<tr><td>Prepared by:<br>Lynne Davidson</td><td rowspan="2">Authorised for issue by:<br>NHSG Medicine Guidelines and Policies Group</td><td>Document no:<br>NHSG/SCA/Dronedarone/MGPG1180</td></tr>
<tr><td>Job title:<br>Highly Specialist Clinical Pharmacist - Cardiology</td><td>Effective date: August 2021<br><br>Review Date: April 2024</td></tr>
<tr><td>Signature:<br>Lynne Davidson<br>Date: August 2021</td><td>Signature:<br>Lesley Coyle<br>Date: August 2021</td><td>Supersedes:<br>NHSG/SCA/Dronedarone/MGPG881</td></tr>
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