Shared-Care Guideline

Drug: amiodarone and dronedarone
Indication: treatment of arrythmias – see individual preparations

Introduction

Amiodarone hydrochloride is used in the treatment of arrhythmias, particularly when other drugs are ineffective or contraindicated. It can be used for paroxysmal supraventricular, nodal and ventricular tachycardias, atrial fibrillation and flutter, and ventricular fibrillation. It can also be used for tachyarrhythmias associated with Wolff-Parkinson- White syndrome.

Dronedarone may be considered in paroxysmal or persistent atrial fibrillation.

Dose & Administration

Drug	Licensed Indication/s	Dose
Amiodarone	Treatment should be initiated and normally monitored only under hospital or specialist supervision. Oral amiodarone is indicated only for the treatment of severe rhythm disorders not responding to other therapies or when other treatment cannot be used. Tachyarrhythmias associated with Wolff-Parkinson-White syndrome. Atrial flutter and fibrillation when other drugs cannot be used. All types of tachyarrhythmias of paroxysmal nature including: supraventricular, nodal and ventricular tachycardias. ventricular fibrillation; when other drugs cannot be used.	**Initial stabilisation:** Treatment should be started with 200mg, 3 times a day and may be continued for 1 week. The dosage should then be reduced to 200mg twice daily for a further week. **Maintenance:** After the initial period the dosage should be reduced to 200mg daily, or less if appropriate. Rarely, the patient may require a higher maintenance dose.
Dronedarone	Dronedarone is indicated 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. **NICE TA 197 (Dronedarone for the treatment of non-permanent atrial fibrillation [updated December 2012]):** Dronedarone is an option for the maintenance of sinus rhythm after successful cardioversion in paroxysmal or persistent atrial fibrillation which is not controlled by first-line therapy (usually including beta-blockers), and after alternative options have been considered in patients: 1. who have at least 1 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 50 mm or greater, or age 70 years or older, and 2. who do not have left ventricular systolic dysfunction nor a history of, or current, heart failure.	The recommended dose is 400 mg twice daily in adults. It should be taken as one tablet with the morning meal and one tablet with the evening meal.

Secondary Care Responsibilities	1. To confirm the diagnosis 2. Ensure that the decision to commence amiodarone or dronedarone will be made jointly by the patient and clinician, with due consideration to the principles in the relevant NICE clinical guidelines (NICE CG 180 and NICE TA 197), following an informed discussion of: a. likely benefits, b. side effects, c. licensed indications 3. Initiate and provide the patient with an initial supply of no less than one month's duration. Secondary care will be responsible for the physical monitoring of the patient during the initial period of supply. 4. Make contact with the patient's GP requesting them to prescribe under a shared care agreement as soon as practicably possibly after the initial supply has been provided to the patient. **Please note** secondary care retains responsibility for monitoring and supply until the GP has agreed to prescribe under this shared care agreement. 5. Share the results of any blood monitoring with primary care. 6. Reassess the patient after 3 months for amiodarone or 6 months for dronedarone for clinical response. 7. Prior to entering into a shared-care agreement, secondary care will advise the GP on frequency of monitoring, management of any dose adjustments and when to stop treatment. 8. Secondary care should ensure that clear backup arrangements exist for GPs to obtain advice if required. Once the GP has agreed to participate in the shared prescribing arrangements a record will be made in the patient's clinical record and the patient will be informed that their next supply of medication will be obtained from their GP.
Primary Care Responsibilities	**Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.** 1. To consider requests to prescribe under shared care arrangements and reply in a timely manner by completing, signing and returning Part 2 of the Shared Care Agreement Form or responding to an equivalent request. 2. To provide continuation prescriptions or identify any concerns about the request to the prescriber in the specialist team. It is expected that primary care prescribers will not make changes to the dose unless it is in consultation with the specialist team. 3. To monitor the patient as outlined in the following sections of this document and contact the specialist team if results give rise to concern. Any further monitoring requirements for individual patients discharged from secondary care will be identified by the specialist service as part of the discharge information to the GP. 4. To contact specialists within the team where concerns arise about a patient's presentation or when advice is needed. 5. To refer to secondary care if withdrawal of treatment might be indicated. **Circumstances for discontinuation of treatment in Primary Care** 1. As a joint decision with the specialist team providing specific advice in case of an adverse effect. 2. As a joint decision with the specialist team providing specific advice in case of the recurrence of arrythmia.

<table>
<tr><td>Monitoring Required in Primary Care</td><td colspan="3">Amiodarone

Thyroid function tests should be performed every 6 months.

Liver function tests every 6 months.

Perform ECG every 6 months

Dronedarone

Monitor for signs of heart failure.

Perform ECG at least every 6 months—consider discontinuation if atrial fibrillation reoccurs.

Monitor liver function every 3 months for 6 months and every 6 months thereafter.

Monitor renal function every 6 months</td></tr>
<tr><td rowspan="2">Adverse Effects & contraindications</td><td><u>Drug</u></td><td><u>Common side effects</u></td><td><u>Contraindications</u></td></tr>
<tr><td>Amiodarone</td><td>Arrhythmias; hepatic disorders; hyperthyroidism; nausea; respiratory disorders; skin reactions. Constipation; corneal deposits; hypothyroidism; movement disorders; photosensitivity reaction; sleep disorders; taste altered; vomiting

Because of the possibility of phototoxic reactions, patients should be advised to shield the skin from light during treatment and for several months after discontinuing amiodarone; a wide-spectrum sunscreen to protect against both long-wave ultraviolet and visible light should be used.

Further important information

Corneal microdeposits
Patients taking amiodarone may develop corneal microdeposits (reversible on withdrawal of treatment). However, if vision is impaired or if optic neuritis or optic neuropathy occur, amiodarone must be stopped to prevent blindness and expert advice sought.

Thyroid function
Amiodarone contains iodine and can cause disorders of thyroid function; both hypothyroidism and hyperthyroidism can occur. Hypothyroidism can be treated with replacement therapy without withdrawing amiodarone if it is essential; careful supervision is required.

Hepatotoxicity
Amiodarone is also associated with hepatotoxicity and treatment should be discontinued if severe liver function abnormalities or clinical signs of liver disease develop.

Pulmonary toxicity
Pneumonitis should always be suspected if new or progressive shortness of breath or cough develops in a patient taking amiodarone.</td><td>Sinus bradycardia and sino-atrial heart block: In patients with severe conduction disturbances (high grade AV block, bifascicular or trifascicular block) or sinus node disease, amiodarone should be used only in conjunction with a pacemaker.

Evidence of history of thyroid dysfunction: Thyroid function tests should be performed prior to therapy in all patients.

Known hypersensitivity to iodine or to amiodarone (one 100mg tablet contains approximately 37.5mg iodine), or to any of the excipients.

The combination of amiodarone with drugs which may induce Torsades de Pointes is contra-indicated.

Pregnancy and lactation.</td></tr>
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	Dronedarone	Asthenia; bradycardia; congestive heart failure; diarrhoea; gastrointestinal discomfort; nausea; QT interval prolongation; skin reactions; vomiting. **Further important information** **Liver injury** Liver injury including life-threatening acute liver failure reported rarely; discontinue treatment if 2 consecutive alanine aminotransferase concentrations exceed 3 times upper limit of normal. **Patients or their carers should be told how to recognise signs of liver disorder and advised to seek prompt medical attention** if symptoms such as abdominal pain, anorexia, nausea, vomiting, fever, malaise, itching, dark urine, or jaundice develop. **Heart failure** New onset or worsening heart failure reported. If heart failure or left ventricular systolic dysfunction develops, discontinue treatment. **Patients or their carers should be told how to recognise signs of heart failure and advised to seek prompt medical attention** if symptoms such as weight gain, dependent oedema, or dyspnoea develop or worsen. **Pulmonary toxicity** Interstitial lung disease, pneumonitis and pulmonary fibrosis reported. Investigate if symptoms such as dyspnoea or dry cough develop and discontinue if confirmed.	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

Drug Interactions	**Amiodarone** **MHRA/CHM advice: Sofosbuvir with daclatasvir; sofosbuvir and ledipasvir (May 2015); simeprevir with sofosbuvir (August 2015): risk of severe bradycardia and heart block when taken with amiodarone.** Avoid concomitant use unless other antiarrhythmics cannot be given. Coadministration of the following should be avoided: drugs inducing Torsade de Pointes or prolonging QT; drugs lowering heart rate or causing automaticity or conduction disorders; agents which may induce hypokalaemia. Amiodarone and/or its metabolite, desethylamiodarone, inhibit CYP1A1, CYP1A2, CYP3A4, CYP2C9, CYP2D6 and P-glycoprotein and may increase exposure of their substrates. **Dronedarone** Dronedarone has the potential to interact on medicinal products substrates of P-glycoproteins, CYP 3A4 or CYP 2D6. Concomitant use of ketoconazole as well as other potent CYP 3A4 inhibitors such as itraconazole, voriconazole, posaconazole, ritonavir, telithromycin, clarithromycin or nefazodone is contraindicated. Medicinal products inducing torsades de pointes such as phenothiazines, cisapride, bepridil, tricyclic antidepressants, certain oral macrolides (such as erythromycin), terfenadine and Class I and III antiarrhythmics are contraindicated because of the potential risk of proarrhythmia. Caution should also be taken with co-administration with beta-blockers or digoxin. The co-administration of dabigatran and dronedarone is contraindicated. Patients should be warned to avoid grapefruit juice beverages while taking dronedarone.

This guidance does not replace the SPC's, which should be read in conjunction with this guidance.

Bibliography

1. Royal Pharmaceutical Society. British National Formulary. Online. Accessed via: www.evidence.nhs.uk. [Accessed online: 22nd January 2020].
2. Summary of Product Characteristics. Multaq 400mg film-coated tablets. Sanofi. Updated: 09/10/2019. Accessed via: https://www.medicines.org.uk/emc/product/497/smpc [Accessed online: 22nd January 2020].
3. Summary of Product Characteristics. Cordarone X 200 mg Tablets. Zentiva. Updated: 08/08/2018. Accessed via: https://www.medicines.org.uk/emc/product/2823/smpc [Accessed online: 22nd January 2020].

Appendix 1: Monitoring Requirements

Drug	Time Period	Responsibility	Monitoring Required
Amiodarone **(Also see 'Adverse Effects & Contraindications')**	Baseline	**Secondary care**	Thyroid function tests should be performed before treatment Liver function tests required before treatment Serum potassium concentration should be measured before treatment. Chest x-ray required before treatment.
	From 3 months post-initiation	**Primary care**	Liver function test at 6 months post-initiation and 6 monthly ongoing Thyroid functions test at 6 months and 6 monthly ongoing Perform ECG every 6 months
Dronedarone **(Also see 'Adverse Effects & Contraindications')**	Baseline to 6 months post-initiation	**Secondary care**	Measure serum creatinine before treatment and 7 days after initiation—if raised, measure again after a further 7 days and consider discontinuation if creatinine continues to rise. Monitor liver function before treatment, 1 week and 1 month after initiation of treatment, then monthly for 6 months.
	From 6 months post-initiation	**Primary care**	Monitor liver function every 3 months for 6 months and 6 monthly thereafter. Monitor renal function every 6 months. Perform ECG at least every 6 months—consider discontinuation if atrial fibrillation reoccurs – discuss with specialist. Monitor for signs of heart failure.

Optional Shared Care Agreement form

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

PLEASE NOTE: The use of this form is not compulsory, but the same information must be communicated between the specialist service and primary care in advance of entering into a shared-care agreement.

Part 1 - To be signed by Consultant / Associate Specialist / Speciality Trainee or Specialist Nurse (who must be a prescriber)

Dear Doctor:	Click or tap here to enter text.
Name of Patient:	Click or tap here to enter text.
Address:	Click or tap here to enter text.
	Click or tap here to enter text.
	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Patient NHS Number:	Click or tap here to enter text.
Patient Hospital Number:	Click or tap here to enter text.
Diagnosed Condition:	Click or tap here to enter text.

I request that you prescribe:

(1) Click or tap here to enter text.
(2) Click or tap here to enter text.
(3) Click or tap here to enter text.
(4) Click or tap here to enter text.

for the above patient in accordance with the LSCMMG shared care guideline(s) (Available on the LSCMMG website).

Last Prescription Issued:	Click or tap to enter a date.
Next Supply Due:	Click or tap to enter a date.
Date of last blood test (if applicable):	Click or tap to enter a date.
Date of next blood test (if applicable:	Click or tap to enter a date.
Frequency of blood test (if applicable:	Click or tap here to enter text.

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care guideline.

If this is a Shared Care Agreement for a drug indication which is unlicensed or off label, I confirm that informed consent has been received from the patient.

I will accept referral for reassessment at your request. The medical staff of the department are available if required to give you advice.

Details of Specialist Clinicians

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Position:	Choose an item.
Signature:	Click or tap here to enter text.

(An email from the specialist clinician will be taken as the authorised signature)
In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a Specialist Nurse, it is the supervising consultant who takes medicolegal responsibility for the agreement.

Consultant	Click or tap here to enter text.

Contact Details

Telephone Number	Click or tap here to enter text.
Extension	Click or tap here to enter text.
Email Address	Click or tap here to enter text.

Part 2 - To be completed by Primary Care Clinician (GP)

I agree to prescribe and monitor Click or tap here to enter text. for the above patient in accordance with the LSCMMG shared care guideline(s) commencing from the date of next supply / monitoring (as stated in Part 1 of the agreement form).

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Signature:	Click or tap here to enter text.

*Please sign and return a copy **within 14 calendar days** to the address above* **OR**

If you **do not** agree to prescribe, please sign below and provide any supporting information as appropriate:

I **DO NOT** agree to enter in to a shared care agreement on this occasion.

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Signature:	Click or tap here to enter text.
Further information:	Click or tap here to enter text.