NHS
Shropshire
Clinical Commissioning Group

Effective Shared Care Agreement for Amiodarone

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

Amiodarone is an antiarrhythmic drug that increases the duration of ventricular and atrial muscle action by inhibiting Na^+-K^+-activated myocardial adenosine triphosphatase, resulting in decreased heart rate and vascular resistance.

Licensed indication:
Amiodarone's Summary of Product Characteristics and the British National Formulary state that it should be used for severe cardiac rhythm disorders **when other treatment is ineffective or contra-indicated:**

- 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.

Adult dosage and administration

Initial Stabilisation (in hospital): Treatment should be started with 200 mg, three times a day and may be continued for 1 week, to achieve adequate tissue levels rapidly. The dosage should then be reduced to 200 mg, twice daily for a further week.

Maintenance: After the initial period the dosage should be reduced to 200 mg daily, or less if appropriate. Rarely, the patient may require a higher maintenance dose. The scored 100 mg tablet should be used to titrate the minimum dosage required to maintain control of the arrhythmia. The maintenance dose should be regularly reviewed, especially where this exceeds 200 mg daily.

IMPORTANT: Amiodarone is strongly protein bound and has an average plasma half-life of 50 days (range 20 to 100 days). Sufficient time must be allowed for a new distribution equilibrium to be achieved between adjustments of dosage. In patients with potentially lethal arrhythmias, the long half-life is a valuable safeguard, as omission of occasional doses

does not significantly influence the overall therapeutic effect. It is important that the minimum effective dosage is used and the patient be monitored regularly to detect clinical features of excess amiodarone dosage, so therapy can be adjusted accordingly.

Dose reduction/withdrawal: Side-effects slowly disappear as tissue levels fall. Following drug withdrawal, residual tissue bound amiodarone may protect the patient for up to a month. However, the likelihood of arrhythmia during this period should be considered.

Available as: Amiodarone 100 mg and 200 mg tablets.

Specialist responsibilities

- It is the responsibility of the initiating specialist to ensure that a clear care plan, including indication, dose and duration of amiodarone therapy and hospital follow up, is sent to the patient's GP before expecting the GP to assume ongoing prescribining responsibility.
- If the initiating specialist is not a cardiologist, and there is not an end date for prescribing amiodarone, then the patient should be referred to a cardiologist for a long-term care plan.
- Arrange shared care with the patient's GP.
- Provide patient/carer with relevant (preferably written) information on use side-effects and need for monitoring of medication.
- Provide shared care monitoring record booklet or amiodarone monitoring card if required.
- Baseline tests:[i]
    - **LFTs, U&Es and creatinine, TFTs (T_3, T_4 and TSH)**
    - **Chest X-ray (ensure chest X-ray within the last 12 months)**
    - **Electrocardiogram (ECG) before initiating treatment and after 1 week**
    - **Pulmonary Function Tests (PFTs)**
- Review results of safety monitoring and request additional tests as required.
- Initiate treatment and adjust dose.
- Ensure the patient is taking a maintenance dose and has an adequate supply of medication until GP supply can be arranged.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Ensure ECG is performed at agreed intervals specified in patient's long-term care plan
- Ensure PFTs performed at agreed intervals specified in patient's long-term care plan
- Provide any other advice or information for the GP including dose adjustments, and advice on when to stop amiodarone.

Primary Care responsibilities

- **GPs should never initiate therapy with amiodarone.**
- Prescribe amiodarone according to dose advised by specialist.
- Arrange and record ongoing monitoring as agreed with specialist:
    - **LFTs**: every 6 months: isolated increase in serum transaminases, which is usually moderate (1.5 to 3 times normal range), commonly occurs at the beginning of therapy, it may return to normal with dose reduction or even spontaneously.
    - **U&Es:** every 6 months
    - **TFTs:** every 6 months (and for several months following discontinuation). Amiodarone may induce hypothyroidism or hyperthyroidism, particularly in patients with a personal history of thyroid disorders. If TFTs are borderline, repeat test in 6 weeks.[i]
    - **ECG and PFTs:** should be performed regularly as agreed in patient's long-term care plan with specialist. ECG performed at 6 months and then annually thereafter, PFTs performed annually.
- **Eye examination:** Unless blurred or decreased vision occurs, ophthalmological examination is recommended annually. If blurred or decreased vision occurs, complete ophthalmologic examination including fundoscopy should be promptly performed. Appearance of optic neuropathy and/or optic neuritis requires amiodarone withdrawal due to the potential progression to blindness.

- **Onset of dyspnoea or non-productive cough** may be related to pulmonary toxicity, contact the specialist who reviews the patient in secondary care for advice.
- Ensure that monitoring and dosage record is kept up to date.
- Report the adverse drug reactions to specialist and usual bodies (e.g MHRA).
- Ensure no drug interactions with other medicines.
- Symptoms or results are appropriate actioned, recorded and communicate to secondary care when necessary.

Adverse effects, Precautions and Contra-indications [ii, iii]

Most serious toxicity is seen with long-term use and may therefore present first to GPs.

- Very common side effects (≥ 10%) include: Corneal micro-deposits – coloured halos in dazzling light or blurred vision (reversible on discontinuation, considered essentially benign and do not require discontinuation of amiodarone); increase in serum transaminases; taste disturbance, nausea and vomiting
- Common side effects (≥ 1% and < 10%) include: **bradycardia (seek specialist advice)**; blue-grey skin discolouration (reversible); **thyroid disorders**; **pulmonary toxicity**; extrapyramidal tremor (regression usually occurs after dose reduction or withdrawal), nightmares and sleep disturbances.
- Uncommon side effects (≥ 0.1% and < 1%) include: worsening of arrhythmias and peripheral sensorimotor neuropathy and/or myopathy (usually reversible on withdrawal of the drug). Full details of adverse effects can be found in the SPC.

If you suspect an adverse reaction has occurred, please contact the specialist department. The patient should be advised to report any of the following signs or symptoms without delay:

- Increased breathlessness, dyspnoea or non-productive cough
- Altered vision
- Loss of appetite/weight loss
- Sleep disturbance/nightmares
- Tremor/loss of co-ordination

Precautions

Amiodarone can cause photosensitivity which may persist for months after treatment is stopped, so **patients should be cautioned to avoid exposure of skin to direct sunlight or sun lamps**. A wide spectrum sunscreen should be used.

Contraindications

Hypersensitivity to iodine or amiodarone or any excipients*;* evidence or history of hyperthyroidism; uncorrected hypothyroidism; sinus bradycardia and sino-atrial heart block, combined use with drugs that may induce torsades de pointes (see Drug Interactions below), pregnancy (except in exceptional circumstances) and breast feeding. In patients with severe conduction disturbances or sinus node disease, amiodarone should be used only in conjunction with a pacemaker.

Common Drug Interactions

Amiodarone is metabolised by the cytochrome P450 system and therefore has the potential to cause many drug interactions. **The SPC or BNF should be consulted before initiating any new drug therapy.**[iii]
Amiodarone has an average plasma half-life of 50 days (range 20-100 days). **There is potential for drug interactions to occur several weeks or months after stopping treatment and the onset of drug interactions may be slow after initiating amiodarone.**

Amiodarone, being highly protein bound, raises the plasma concentrations of other highly protein bound drugs.

- **Anticoagulants:** Amiodarone can increase anticoagulant effect. Consider **warfarin** dose reduction. Patients should be monitored closely and the dose of anticoagulant altered accordingly, remembering that amiodarone levels take several weeks to stabilise.
- **Antiepileptics:** Amiodarone can increase plasma concentration of **phenytoin**, phenytoin dose should be reduced. Note that small changes in phenytoin dose can result in large changes in phenytoin levels. Monitor patient closely and counsel on signs of toxicity.
- **Digoxin:** increases plasma digoxin level and can precipitate symptoms and signs associated with high digoxin levels. Clinical, ECG and biological monitoring is recommended, digoxin dose should be halved when amiodarone is started.

Drugs that prolong the QT interval: Concurrent therapy is contra-indicated due to the increased risk of torsades de pointes:

- **Antiarrhythmics**: e.g. quinidine, procainamide, disopyramide, sotalol.
- **Antipsychotics**: e.g. phenothiazines, haloperidol, amisulpiride.
- **Antihistamines**: e.g. mizolastine and terfenadine.
- **Antimalarials**: e.g. chloroquine, hydroxychloroquine, mefloquine, quinine, artemether with lumefantrine
- **Lithium, tricyclic antidepressants, citalopram, escitalopram**
- **Others**: IV co-trimoxazole, IV erythromycin, pentamidine, some antivirals, moxifloxacin
- Avoid concomitant use with **fluoroquinolones** due to risk of QTc interval prolongation, with or without torsades de pointes (note moxifloxacin above is contra-indicated)

Drugs metabolized by cytochrome P450 system:

- **Statins:** Increased risk of myopathy by inhibition of CYP 3A4. **Simvastatin- restrict dose to 20mg daily**. Other statins: counsel patients to report any muscle pain or weakness immediately.
- **Ciclosporin:** Amiodarone increases levels of ciclosporin by as much as two-fold. Reduced dose of ciclosporin is recommended to maintain plasma concentration in therapeutic range
- **Flecainide**: Amiodarone increases levels of flecainide through CYP 2D6 inhibition - reduce flecainide dose by 50% and monitor the patient for adverse effects. The manufacturer recommends to monitor plasma flecainide levels.

Combined therapy not recommended:

- **Beta blockers:** increased risk of bradycardia, AV block and myocardial depression. **Sotalol- avoid concomitant use.**
- **Calcium channel blockers** (diltiazem and verapamil)**:** increased risk of bradycardia, AV block and myocardial depression.
- **Dabigatran:** Amiodarone increases levels of dabigatran. Close clinical surveillance is recommended especially in renal impairment.
- **Diuretics:** increased risk of cardiotoxicity if hypokalaemia occurs.
- **Stimulant laxatives:** caution with use as potential to cause hypokalaemia. Other laxatives recommended.

Communication

For any queries relating to this patient's treatment with amiodarone, 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] Suggestions for Drug Monitoring in Adults in Primary Care. NHS UKMi, February 2014. Available at www.evidence.nhs.uk

[ii] British National Formulary, Edition 68, Section 2.3.2, Amiodarone hydrochloride

[iii] Cordarone X 100mg Tablets – Summary of Product Characteristics. Available at www.medicines.org.uk/emc/medicine/27062