This SCP has been written to enable the safe and appropriate continuation of care for patients initiated on amiodarone in hospital. Amiodarone is always started in secondary care.

Although the SCP is aimed at new patients initiated on amiodarone, practices should review existing patients against this SCP to ensure they are being adequately monitored.

The SCP acknowledges that amiodarone is a useful medication but has potentially serious side effects and also that some patients are already prescribed amiodarone in primary care after initial specialist prescription.

Responsibilities of the secondary care clinician

i. **To initiate amiodarone in appropriate patients** (see indications)
ii. To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent.
iii. To issue the patient hand held book
iv. To ensure patients are commenced on an appropriate loading and then maintenance dose prior to shared care
v. To prescribe the first month's supply or a sufficient prescription until the maintenance dose is reached by the patient
vi. To contact patient's GP to request prescribing under shared care using the amiodarone **Transfer of Care (ToC) form** and send a link to or copy of the SCP
vii. To make the baseline test results available to the GP continuing care
viii. To advise the GP regarding the duration of treatment
ix. To address any concerns with the GP regarding the patient's treatment

Responsibilities of the primary care clinician

i. To refer appropriate patients to secondary care for assessment
ii. If appropriate, to agree to prescribe amiodarone in accordance with the SCP by returning the amiodarone ToC form to the referring consultant
iii. In the event that the GP is not able to prescribe, or where the SCP is agreed but the consultant is still prescribing certain items e.g. hospital only product, the GP will provide the consultant with full details of existing therapy promptly by fax on request
iv. Where the GP does not prescribe, amiodarone will be added to the practice prescribing system as a hospital only drug
v. To report any adverse reaction to the Commission on Human Medicines (CHM) and the referring consultant
vi. To continue to prescribe for the patient as advised by the consultant
vii. To undertake monitoring as per SCP
viii. To inform the consultant if the patient discontinues treatment for any reason
ix. To seek the advice of the consultant if any concerns with the patient's treatment
x. To conduct a six monthly face to face medication review (or more frequent if required)

Indications Oral amiodarone is indicated only for the treatment of severe rhythm disorders **not** responding to other therapies or when other treatments **cannot** be used:

- As an adjunctive short-term treatment prior to DC cardioversion of atrial flutter/fibrillation

(unlicensed indication)
- 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

Dose: **Only secondary care specialist should initiate** loading with amiodarone and an oral or intravenous route may be used, according to the clinical situation and indication.

The loading dose by mouth is: 200mg 3 times daily for 1 week reduced to 200mg twice daily for a further week. The loading dose should be prescribed by secondary care and GPs only asked to prescribe amiodarone at the maintenance dose.

Maintenance usually 200mg daily or the minimum required to control the arrhythmia. Maintenance doses above 200mg daily should be managed by secondary care and are **not** part of the SCP.

Monitoring: Monitoring should take place during the loading of amiodarone, and then every 6 months whilst treatment continues. See table below;

Ensure that "Patient on Amiodarone" is marked on every lab test form.

- **Monitoring at baseline and during loading is the responsibility of secondary care**
- **Further monitoring is the responsibility of primary care**

	Baseline	Loading	6 months & every 6 months thereafter unless otherwise stated
History & examination (H&E)	♦		Continue annually
Side-Effects	♦	♦	♦
Heart rate and ECG	♦	♦	Continue annually
TFTs*[1]	♦		♦
U & Es	♦		♦
LFTs (ALT)	♦	♦	♦
Digoxin level (if on digoxin)	♦	♦	Assess serum digoxin levels if dose increased or toxicity is suspected
INR (if on warfarin)	♦	♦	Monitor INR levels. Adjust warfarin dose accordingly
CXR*[2] PFTs inc DLCO	♦ ♦	If suspected pulmonary toxicity	
Eye examination	Assess if new or worsening visual symptoms occur		

*1 - An increase of up to 40% above the baseline T4 is a normal effect of amiodarone. This occurs approximately 2 months after initiation of therapy and does not require discontinuation.
The development of **thyrotoxicosis** is much less easy to predict than hypothyroidism - it is suggested if the TSH is low, which can occur quite rapidly (i.e. between tests), such patients should be referred to an endocrinologist.

*2 - Ask about breathlessness and non-productive cough, relating to possible pulmonary toxicity, at each review visit. Clinician's should have a low threshold for suspecting amiodarone induced pulmonary toxicity

ABNORMAL RESULTS: contact the cardiologist to discuss how to manage and the need for involvement of endocrinology or respiratory specialist or ophthalmology.

Contra-indications

For full details on contraindications, side effects and interactions see SPC available at; http://www.medicines.org.uk/emc/ & BNF available at http://www.bnf.org/bnf/index.htm

Common Side-Effects

Adverse effect	Frequency %	Investigation & Diagnosis	Treatment
Pulmonary toxicity (suggested by new or worsening cough and/or shortness of breath)	2 to 17	CXR and ECG to exclude alternative diagnoses	If pulmonary toxicity is suspected: refer urgently to initiating cardiologist or respiratory physician. Specialist to request PFTs including DLCO* and HRCT** chest scan
Hyperthyroidism	2	Free T4, TSH	Refer urgently to initiating cardiologist or endocrinology
Hypothyroidism	6	Free T4, TSH	Consider starting thyroxine
Liver toxicity	1	LFT	Refer urgently to initiating cardiologist
Optic neuropathy	0.13	Ophthalmologic examination	If optic neuropathy/neuritis is suspected, refer urgently to ophthalmology and discuss the possibility of stopping amiodarone & alternative antiarrhythmic therapy with patient's cardiologist
Pro-arrhythmia	<1	ECG	Stop amiodarone
Tremor Peripheral Neuropathy Myopathy	<10 <1	History and clinical examination	Reduce dosage or withdraw if possible Usually reversible on withdrawal of the drug
Bradycardia	2-4	Examination, ECG	If severe, discuss with cardiologist whether to stop amiodarone or insert pacemaker
Nausea, anorexia	30	History + examination	Reduce dosage
Corneal micro-deposits	>90	Slit-lamp examination	None
Photosensitivity	4-9	History, examination	Use sunblock
Blue discolouration of skin	<9	Examination	Reduce dosage if possible

*DCLO is Diffusing Capacity of Lung for carbon monOxide.
**HCRT is High Resolution Computed Tomography

Key Drug Interactions

Be aware that amiodarone has a long half-life (25–100 days); thus, interactions may occur for some time after drug withdrawal

Digoxin: Amiodarone may increase plasma levels of digoxin because of reduced renal digoxin clearance. If concurrent use is indicated, prescribe half the recommended dose of digoxin, and monitor the person closely in view of potential toxicity.

Warfarin: For patients taking warfarin prior to starting amiodarone the warfarin dose should be reduced by approximately one-third when amiodarone is started. INRs should then be checked weekly for 4-6 weeks and until INR stable. If / when amiodarone is stopped the interacting effect may persist for up 6 weeks or more, so again INR should be checked weekly until stable. Note that amiodarone-induced hyperthyroidism will increase warfarin dose requirements.

Beta-blockers: Only specialists should co-prescribe a beta-blocker and amiodarone. Hypotension, bradycardia, ventricular fibrillation, and asystole have been seen in a few people given amiodarone with propranolol, metoprolol, or sotalol.

Calcium-channel blockers: Avoid concurrent treatment with amiodarone, or use with caution. Cardiac depression can occur with concurrent treatment.

Colestyramine: Colestyramine appears to reduce amiodarone levels by about 50%. If colestyramine is started, monitor the person for decreased amiodarone effects. If necessary, seek specialist advice about adjusting the amiodarone dose, or consider prescribing an alternative to colestyramine.

Centrally acting anticholinesterases: The risk of adverse effects, including bradycardia, may be increased if amiodarone is given with a centrally acting anticholinesterase (such as galantamine, donepezil, or rivastigmine).

Drugs that prolong the QT interval: Only specialists should co-prescribe amiodarone and drugs that prolong the QT interval. This is because of the risk of additive effects, which may lead to serious and potentially life-threatening torsades de pointes arrhythmias. Examples of drugs that are known to have a high risk of causing QT prolongation include:

- Antiarrhythmics, such as sotalol, disopyramide, and quinidine.
- Antihistamines, such as astemizole and terfenadine.
- Antipsychotics, such as amisulpride, haloperidol, and droperidol.
- Antibiotics, such as erythromycin and clarithromycin.
- Antidepressants, such as citalopram, escitalopram, clomipramine, amitriptyline
- Lithium

Drugs that affect the liver enzyme cytochrome P450 isoenzyme 3A4

- Drugs that *inhibit* CYP 3A4 may increase serum concentration of amiodarone with the potential for toxicity. Examples include erythromycin, azole antifungals, and protease inhibitors. Grapefruit juice should also be avoided.
- Drugs that *induce* CYP 3A4 may decrease serum concentrations of amiodarone with the potential for loss of efficacy. Examples include carbamazepine, rifampicin, midazolam, lidocaine, fentanyl, sildenafil, St John's wort, and phenytoin. Amiodarone may also inhibit the hepatic metabolism of phenytoin resulting in an increase in phenytoin plasma levels.

Hepatitis C drugs: Concomitant use of amiodarone and some drugs used to treat hepatitis C (Harvoni® [sofosbuvir with ledipasvir] or a combination of Sovaldi® [sofosbuvir] and Daklinza® [daclatasvir]) may increase the risk of severe bradycardia or heart block .

Simvastatin: Rarely, myopathy and rhabdomyolysis have been reported in people taking amiodarone with high doses of simvastatin. The dose of simvastatin should not exceed 20 mg a day in people taking amiodarone unless the clinical benefit is likely to outweigh the increased risk of myopathy and rhabdomyolysis.

Stimulant laxatives: Concurrent use of amiodarone & a stimulant laxative (such as senna) may cause hypokalaemia, thus increasing the risk of torsades de pointes. Consider prescribing other types of laxatives (bulk forming [such as ispaghula husk] or osmotic laxatives [such as lactulose]).

REFERENCES

Full prescribing information is given in the amiodarone summary of product characteristics (SPC), available from www.emc.medicines.org.uk .

NICE CG36: Atrial fibrillation is available at http://guidance.nice.org.uk/CG36

Clinical Knowledge Summaries: Atrial fibrillation amiodarone initiation and monitoring
http://cks.nice.org.uk/atrial-fibrillation#!prescribinginfosub:18

Amiodarone Monitoring Protocol Derbyshire Joint Area Prescribing Committee Updated Nov 2012
http://www.derbyshiremedicinesmanagement.nhs.uk/images/content/files/Prescribing%20Guidelines/Amiodarone%20monitoring%20protocol%202012.pdf

Sheffield Area Prescribing Group (APG) Shared Care Protocol (SCP) for Amiodarone
http://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/Shared%20Care%20protocols/Amiodarone%20SCP%20January%202014.pdf

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