PROTOCOL: CV 44 AMIODARONE

This document should be read in conjunction with the current Summary of Product Characteristics
http://www.medicines.org.uk/

1. Licensed Indications	Amiodarone is licensed for the treatment of severe cardiac rhythm disorders where other treatments either cannot be used or have failed.
2. Therapeutic use & Background	**The All Wales Medicines Strategy Group recommends that shared care arrangements are suitable for patients newly initiated on amiodarone. This protocol has been endorsed by the Welsh Cardiovascular Society (for patients with life-threatening arrythmias) and the Wales Council of the British Geriatric Society. The consultation process has included Local Medical Committees and Welsh Drugs & Therapeutics Committees.** This protocol does not cover the use of oral amiodarone in short term treatment prior to cardioversion. Amiodarone is commonly used to maintain sinus rhythm in patients with atrial fibrillation or who have converted from, or relapsed into atrial fibrillation following cardioversion. It is also used before heart surgery to help prevent atrial fibrillation. Amiodarone has been used for prevention of ventricular arrhythmias.
3. 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) & breast feeding. In patients with severe conduction disturbances or sinus node disease, amiodarone should be used only in conjunction with a pacemaker.
4. Typical Dosage Regimen (Adults)	***A loading regimen is necessary and will be prescribed by secondary care.*** **Loading**: 200mg three times daily for one week, then 200mg twice daily for one week, then a further reduction to 200mg daily. **Maintenance** dose is usually 200mg daily; however 100mg daily may be sufficient in elderly patients. The minimum dose to control arrhythmia is used. In rare cases a maintenance dose of above 200mg daily may be required. **All dose adjustments will be done by secondary care unless directions have been specified in the medical letter to the GP.**
5. Drug Interactions **For a comprehensive list consult the BNF(Appendix 1) or Summary of Product Characteristics**	Amiodarone is metabolised by the cytochrome P450 system and therefore has the potential to cause many drug interactions. The Summary of Product Characteristics or BNF (Appendix 1) should be consulted before initiating any new drug therapy. 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.** **Statins:** Increased risk of myopathy. **Simvastatin- restrict dose to 20mg daily**. Other statins: counsel patients to report any muscle pain or weakness immediately. **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. **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. **Ciclosporin:** Amiodarone increases levels of ciclosporin. Reduced dose of ciclosporin is recommended. **Digoxin** dose should be halved when amiodarone is started. **Diuretics** increased risk of cardiotoxicity if hypokalaemia occurs **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

	• Lithium and tricyclic antidepressants. • **Others**: co-trimoxazole IV erythromycin, moxifloxacin, pentamidine, some antivirals

6. Adverse drug reactions

For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF

Most serious toxicity is seen with long-term use and may therefore present first to GPs. Adverse reaction frequency are classified using the following convention:
Very common (≥ 10%), common (≥ 1% and < 10%); uncommon (≥ 0.1% and < 1%).

Clinical condition	**Management**
Lung Onset of **DYSPNOEA** or non-productive **COUGH** may be related to pulmonary toxicity- pneumonitis, diffuse alveolitis and pulmonary fibrosis (common). Sometimes fatal.	Diagnosis based on clinical and radiological findings and exclusion of other causes. Damage is usually reversible if amiodarone is withdrawn early. Consider CXR. Seek specialist advice
Heart Dose dependent sinus **BRADYCARDIA** (common). Worsening of arrhythmia (uncommon). May present as **BLACKOUTS**	Seek specialist advice
Thyroid disorders (common): Hyperthyroidism: **WEIGHT LOSS,** asthenia, restlessness, increase in heart rate, onset of arrhythmia, angina, congestive heart failure. Sometimes fatal	Perform thyroid function tests Action: See section 8 Monitoring
Hypothyroidism (common)	
Eyes: Corneal microdeposits – coloured halos in dazzling light or blurred vision (very common)	Corneal microdeposits are reversible and amiodarone can be continued.
Optic neuropathy/neuritis that may progress to blindness (Very rare): **BLURRED OR REDUCED VISION**	Prompt opthalmological examination including fundoscopy. Appearance of optic neuropathy and/or optic neuritis requires amiodarone withdrawal due to the potential progression to blindness.
Liver: Increase in serum transaminases (Very common) usually 1.5 to 3 times normal range.	It may return to normal with dose reduction or even spontaneously.
Acute liver disorders (common) with high serum transaminases and/or jaundice, including hepatic failure. Sometimes fatal	Seek specialist advice
Nervous system extrapyramidal tremor, nightmares, sleep disorders (Common)	Tremor: regression usually occurs after reduction of dose or withdrawal
Peripheral sensorimotor neuropathy and/or myopathy (Uncommon)	Both these conditions may be severe, although recovery usually occurs within several months after amiodarone withdrawal, but may sometimes be incomplete.
Gastrointestinal : taste disturbance, nausea, vomiting (Very common)	Usually occurring with loading dosage and resolve with dose reduction
Skin Blue-grey skin discolouration (common)	Reversible
Photosensitivity (very common) May persist for months after treatment is stopped.	Patients should be cautioned to avoid exposure of skin to direct sunlight or sun lamps. A wide spectrum sunscreen should be used.

IF YOU SUSPECT AN ADVERSE REACTION HAS OCCURRED, PLEASE CONTACT THE SPECIALIST DEPARTMENT.
All serious adverse reactions should be reported to the CHM via the "Yellow Card" scheme.
The patient should be advised to report any of the following signs or symptoms without delay: - Increasing breathlessness, dyspnoea or non-productive cough
- Altered vision
- Loss of appetite/ Weight loss
- Sleep disturbance /nightmares
- Tremor / Loss of coordination

7. Baseline investigations	**To be undertaken by secondary care** Chest X-ray (ensure CXR within the last 12 months), TFT (T_3, T_4 & TSH) LFTs, electrolytes and creatinine, ECG. Consideration could be given to lung function tests and examination of skin, eyes, and neurological systems

8. Monitoring

It is essential to have a recall system to identify patients who do not attend, especially following abnormal results

(i) Adapted from Amiodarone and the thyroid, Basaria S, Cooper D, The American Journal of Medicine

Monitoring	Frequency	Results	Action & Responsibility	
Clinical adverse effects	**Every 6 months***	Assess for adverse effects detailed in section 6 Assess patient remains in sinus rhythm and heart rate is satisfactory		Both: **Patients who have had life-threatening arryhthmias**
Clinical effective-ness	**Every 6 months***	***Patient is assessed twice per year: Clinical GP assessment *Alternates approximately 6 monthly with* Clinical/ ECG assessment, secondary care unless otherwise stated.(See section 12 & shared care agreement form)		
LFT	**Every 6 months**	>1.5 fold rise in AST or ALT, or signs of jaundice	Discuss with specialist who may advise amiodarone withdrawal	Primary Care
TFT : T_3,T_4&TSH (i)	T_3, T_4 & TSH If normal repeat **every 6 months**	Normal	It is not unusual for patients on amiodarone to have slight elevations of TSH and T_4	
	TSH > 4.5	TSH > 4.5, fT_4 elevated and duration less than 3 months	Observe Repeat in 3 months	
	Sub clinical hypothyroidism	TSH > 10, fT_4 normal persisting for over 6 months	Consider treating with levothyroxine or repeat in 3 months	
	Hypothyroid	TSH > 4.5, fT_4 low	May be treated with levothyroxine if amiodarone is considered essential	
	Thyrotoxicosis	TSH < 0.1mU/l T_3 & T_4 normal or minimally increased	Repeat in 2-4 weeks	
		TSH < 0.1mU/l & T_4 elevated, T_3 elevated or 50% greater than baseline	Discuss urgently with specialist who may advise amiodarone withdrawal. Arrange TSH-receptor antibodies and TPO antibodies	
Electrolytes	**Every 6 months** in patients taking diuretics	Avoid hypokalaemia	Correct the cause of hypokalaemia	Primary Care
Eyes	**Annual**	Opthalmological examination recommended in data sheet	Patient should be encouraged to attend optician annually.	Both
	If blurred or decreased vision	Arrange urgent opthalmological assessment	Discuss urgently with Specialist	Both

9. Pharmaceutical aspects	**No special considerations**

10. Secondary care contact information	**If stopping medication or needing advice please contact:** **Dr** **……..** **Contact number** **……** **Hospital:**			
11. Criteria for shared care	Prescribing responsibility will only be transferred when ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated and established by the secondary care specialist. ▪ The patient's initial reaction to and progress on the drug is satisfactory. ▪ The GP has agreed in writing in each individual case that shared care is appropriate. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements.			
12. Responsibilities of initiating consultant	• Initiate treatment. • Undertake baseline monitoring. • Dose adjustments. • Monitor patient's initial reaction to and progress on the drug. • Ensure that the patient is taking a maintenance dose and has an adequate supply of medication until GP supply can be arranged. • For patients initiated following life-threatening arrhythmia, continue to monitor and supervise the patient annually according to this protocol, while the patient remains on amiodarone • For remaining indications where lifelong treatment is appropriate, but hospital review practically difficult, consultants may in individual cases, after agreement with the relevant general practitioner, decide to discharge a patient to primary care monitoring, with urgent access to advice and /or review from the initiating department . Provide GP with • Diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. • Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient does not attend appointment • Advice on when to stop amiodarone • Provide patient with relevant drug information to enable • Informed consent to therapy, • Understanding of potential side effects and appropriate action • Understanding of the role of monitoring.			
13. Responsibilities of primary care	• To monitor and prescribe in collaboration with the specialist according to this protocol. • To ensure that the monitoring and dosage record is kept up to date. • Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. Provision of shared care is in accordance with Local Enhanced Scheme, where available			
14. Responsibilities of patients	• To attend hospital and GP clinic appointments, bring monitoring booklet (if issued) • Failure to attend will result in medication being stopped on specialist advice. • To report adverse effects to their specialist or GP. To attend optician annually and inform optician that they are taking amiodarone			
15. Responsibilities of all prescribers	Any serious reaction to an established drug should be reported to CHM via the "yellow card scheme."			
16. Supporting documentation	Include patient information leaflet if available e.g. Treatment Notes produced by the Consumers' Association			
17. Patient monitoring book	Not needed			
18.GP letter	Attached below			
19. Guideline date.	Production date	May 2008	20. Guideline review date	

Amiodarone Shared Care Agreement Form

To be added at end of outpatient letter when a patient is initiated /discharged on amiodarone

Name of Patient (attach addressograph)

Baseline assessment		**Notes**
Indication (please tick box)	1. Paroxysmal AF. 2. Persistent AF. 3. Other SVT. 4. Post CABG. 5. Pre/Post Cardioversion. 4. VT or previous VF.	
Start date		
Dose ***-****Initiation dose will be prescribed by hospital* *-Maintenance dose usually 200mg daily or less*	200mg daily	
Duration of therapy	…….months* . .....Longterm	*Short term therapy (3 months or less) does not require specific monitoring
CXR - within the last 12 months -- Date if not undertaken during this admission/outpatient visit	Normal / abnormal	
T_3, T_4 & TSH	Normal / abnormal	
LFTs, urea & electrolytes and creatinine	Normal / abnormal	
ECG		
Next appointment	……. months	

A) The patient **has further follow up planned** as above but we would be grateful if you could ensure appropriate monitoring as per protocol.

B) This patient was not started on amiodarone for a life-threatening arrhythmia.
Routine follow-up is not planned
Life-long treatment is likely to be appropriate, there are no other ongoing medical problems that require input in secondary/tertiary care and/or hospital follow-up is practically difficult for the patient. Please continue to monitor them closely in primary care according to this protocol.

The medical staff of the department are available to give you advice at any time whether or not the patient is under active follow up and can be contacted on ……. or by e-mail ……

GP RESPONSE Please tick as appropriate

A. I am willing to undertake
Shared care/NPT ☐ as set out in SCP No--- for this patient
Shared care ☐
B. I wish to discuss this request with you ☐

C. I am unable to undertake shared care for this patient ☐ - *please tick reason(s) below*

Practice does not participate in Shared Care ☐ Training issues ☐

Unwilling to take responsibility for prescribing this drug ☐ Time issues ☐

Patient currently not stabilised on drug ☐ Other-please state ----------
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G.P. signature_____ Date _____

Practice Address/Stamp _____

(Please return whole completed form or a photocopy to the consultant requesting shared care prescribing within one week).