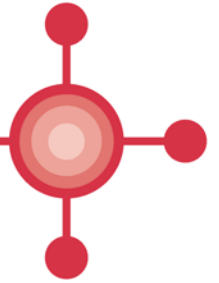


All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan



# Prescribing of Amiodarone for Atrial Fibrillation and Atrial Flutter in Wales

August 2010

(Reviewed and updated September 2016)

This document has been prepared by a multiprofessional collaborative group, with support from the All Wales Prescribing Advisory Group (AWPAG) and the All Wales Therapeutics and Toxicology Centre (AWTTC), and has subsequently been endorsed by the All Wales Medicines Strategy Group (AWMSG).

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This document should be cited as:

All Wales Medicines Strategy Group. Prescribing of Amiodarone for Atrial Fibrillation and Atrial Flutter in Wales. September 2016.



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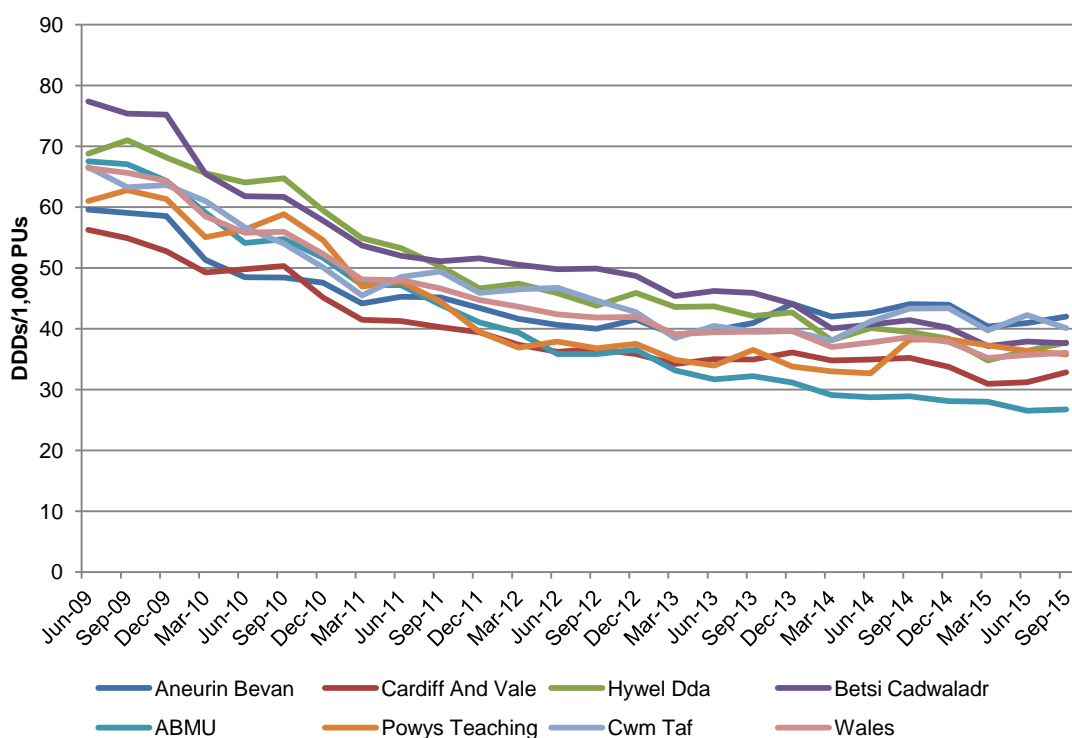
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## SUMMARY

Amiodarone has a limited place in the treatment of severe cardiac rhythm disorders where other treatments either cannot be used or have failed<sup>1-3</sup>. Historically widely prescribed as a treatment for acute atrial fibrillation (AF), it may have been started intravenously to treat an acute episode and then continued as long-term oral therapy; however, its use requires regular monitoring due to potential major toxicity<sup>4</sup>. National Institute for Health and Care Excellence (NICE) *Clinical Guideline (CG) 180 Atrial fibrillation: management*, published in 2014, states that amiodarone should not be offered for long-term rate control<sup>3</sup>. Therapeutic monitoring of a basket of drugs is covered by a National Enhanced Service for Near Patient Testing, but this does not currently include amiodarone, although some health boards have made local arrangements for amiodarone monitoring. A 2009 audit and review of patients taking amiodarone revealed poor counselling of patients and inconsistent monitoring. Both primary and secondary care clinicians recognised that it would be beneficial to review all patients taking amiodarone in Wales to establish the need for ongoing treatment. The enclosed documentation has been developed to assist this process. Please see Appendix 1 for Amiodarone Audit Sheet.

## 1.0 BACKGROUND

**Figure 1. Amiodarone prescribing in NHS Wales primary care – DDDs per 1,000 PUs**



AWMSG approved a shared care agreement for amiodarone in June 2008 (updated in September 2016), in which there are recommendations for treatment initiation and therapeutic monitoring by specialists and GPs (see Appendix 2 for Amiodarone Shared Care Protocol). Welsh cardiologists endorse this shared care agreement in the following circumstances:

*Patients receiving amiodarone for life-threatening arrhythmias will normally be reviewed (annually) by cardiologists. For remaining indications where lifelong treatment is appropriate, but hospital review is practically difficult, consultants may in individual cases, after agreement with the relevant GP, decide to discharge a patient to primary care monitoring, with urgent access to advice and/or review from the initiating department<sup>4</sup>.*

Several localities have developed guidance to review patients initiated on amiodarone prior to the AWMSG guidance including Bridgend Local Health Board (LHB) (now Abertawe Bro Morgannwg University Health Board) and Gwent LHBs (now Aneurin Bevan University Health Board).

Wrexham and Ynys Mon (Betsi Cadwaladr University Health Board) completed systematic reviews of patients taking amiodarone in 2009. The Wrexham review of 222 patients followed concerns raised by the local cardiologists as a result of a death of a patient from pulmonary fibrosis attributable to amiodarone treatment.

Prescribing support teams and cardiologists agreed the criteria for reviewing patients and the basis for switching treatment. Pharmacists completed a review of all the GP clinical records of patients taking amiodarone, collecting the relevant data and subsequently agreeing a management plan with the patient's GP, with cardiologists available to offer advice as necessary.

An audit of 57 patients completed in Wrexham revealed:

- 54% of amiodarone was initiated by cardiologists;
- 68% of amiodarone was prescribed for AF;
- 16% (nine patients) had no recorded indication;
- the mean age of patients was 76 years (range 44–97);
- average duration of treatment was 5.4 years (range 1 month–17 years);
- 14% of the records had documented evidence of patients receiving verbal information;
- biannual tests for thyroid function test (TFT) (28%), liver function test (LFT) (30%), and urea and electrolytes (U&E) (28%);
- three patients had annual pulmonary review;
- one patient had annual ophthalmic follow-up.

In Ynys Mon a separate audit was conducted (163 patients):

- 91% of amiodarone was initiated by cardiologists;
- 58% of amiodarone was prescribed for AF;
- 54% had taken amiodarone for > 5 years (one patient had taken it for 27 years);
- 47% were under regular cardiology review;
- biannual tests for TFT (54%) and LFT (63%).

Following the review, many patients had their amiodarone treatment stopped and where necessary alternative treatment started, following the guidance below.

### **Aims:**

All patients prescribed amiodarone:

- are identified and their records reviewed;
- have a clear indication and duration for treatment (seek expert advice if necessary);
- have a documented record that they have been fully informed of the risks and benefits of treatment;
- are systematically assessed to establish the appropriateness of continued treatment;
- are switched to alternative treatment where safe and appropriate;
- are monitored clinically and via laboratory testing according to national guidance<sup>4</sup>.

Target audience: GPs, hospital clinicians and prescribing support pharmacists.

### 1.1 Place of amiodarone in the treatment of rhythm disorders

The use of amiodarone in the treatment of severe cardiac rhythm disorders requires monitoring both clinically and via laboratory testing due to potential major toxicity<sup>4</sup>. For example, the incidence of potentially fatal pulmonary side effects, such as hypersensitivity pneumonitis, alveolar/interstitial pneumonitis or fibrosis, pleuritis and bronchiolitis obliterans organising pneumonia (BOOP), are listed in the Summary of Product Characteristics (SPC) as common ( $\geq 1\%$  and  $< 10\%$ )<sup>2</sup>.

A systematic review on the safety of amiodarone gave numbers needed to treat (NNTs) and numbers needed to harm (NNHs) (see Table 1)<sup>5</sup>.

**Table 1. Amiodarone NNTs and NNHs<sup>5</sup>**

Indication	NNT	Adverse effects	NNH
Acute conversion of AF (11 trials)	4 at 24 h ( $p = 0.003$ )	Bradycardia, hypotension, nausea or phlebitis	4 (pooled) ( $p < 0.001$ )
Prevention of postoperative AF (18 trials)	8 ( $p < 0.001$ )		
Maintenance of sinus rhythm	3 (pooled) ( $p < 0.001$ )	Thyroid toxicity, gastrointestinal discomfort, skin toxicity or eye toxicity	11 (pooled) ( $p < 0.001$ )
Prophylaxis of sudden cardiac death (15 trials)	38 ( $p < 0.001$ )	Thyroid toxicity, hepatic toxicity, pulmonary toxicity or bradycardia	14 ( $p < 0.001$ )

NICE *CG180 Atrial fibrillation: management*, puts a greater emphasis on rate rather than rhythm control and has clarified the place of amiodarone for persistent AF<sup>3</sup>.

A rhythm control strategy, which may involve cardioversion, may be preferable in patients who are:

- symptomatic
- younger
- presenting with lone AF
- secondary to a treated or corrected precipitant with congestive heart failure.

A rate-control strategy (beta-blocker therapy or rate-limiting calcium antagonist) should be the preferred initial option in the following patients with persistent AF<sup>3</sup>:

- over 65
- with coronary artery disease
- with contraindications to anti-arrhythmic drugs
- unsuitable for cardioversion

In both cases amiodarone is relegated to situations where treatment with other strategies has failed. Primary and secondary care clinicians have therefore recognised that it would be beneficial to review all patients on long-term amiodarone.

## 2.0 RECOMMENDED PROCESS

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### 2.1 Identify all patients taking amiodarone

For each patient, the data collection sheet should be completed to establish:

- the original indication and place of initiation
- evidence of routine monitoring
- management options.

Where the initial indication for treatment has been clearly identified, a switch from amiodarone could be considered in primary care, without referral to secondary care, in patients for whom<sup>6</sup>:

- Amiodarone was initiated first line for persistent/permanent AF.
- Amiodarone was initiated for paroxysmal AF but the patient is now in permanent AF as documented in out-patient letters or a current electrocardiogram (ECG).
- Amiodarone has been recommended for three months following coronary artery bypass graft (CABG)<sup>7</sup> or twelve months following cardioversion<sup>3</sup>. This can be inadvertently continued. GPs may need to confirm with the initiating department that this is the only reason for amiodarone initiation.

If after careful review of the patient's medical records, the indication for initiating or continuing amiodarone long term remains unclear or the GP is uncertain whether a switch from amiodarone is indicated, a cardiologist should be contacted for advice. Where the initiating department was outside the health board and the patient is no longer under follow-up, advice should be sought locally from cardiology.

### 2.2 Consider initiating an alternative therapy

#### 2.2.1 Decide whether to use a washout period

Interaction through the co-administration of beta-blockers and amiodarone can cause symptomatic bradycardia and sinus arrest. Amiodarone should be used with caution in patients receiving beta-blockers, particularly if there is suspicion of underlying dysfunction of the sinus node such as bradycardia or sick sinus syndrome, or if there is partial atrioventricular block. Adverse effects of concomitant beta-blocker and amiodarone use include hypotension, bradycardia and cardiac arrest.

Amiodarone has a very long elimination half-life (average 50 days, range 20–100 days) and therefore has the potential to interact with the substituted therapy for several months or more. In some instances amiodarone will be stopped and the patient's heart rate remains normal and therefore no alternative therapy is needed. Some practitioners therefore prefer to allow a washout period before initiating alternative treatment with a beta-blocker or rate-limiting calcium-channel blocker. However, there is no national guidance. Some cardiologists do not wait for a washout period. A reasonable empirical approach would be to review the need for alternative treatment within a month of stopping amiodarone.

#### 2.2.2 Establish current heart rhythm with an ECG

A proportion of patients in sinus rhythm switched to a beta-blocker will relapse into AF. This is not always predictable and the patients should be advised of this prior to conversion. It is therefore advisable that the opinion of a specialist is sought before any changes in therapy are undertaken if the current ECG confirms sinus rhythm.

#### 2.2.3 Consider patients bradycardic on amiodarone

If a patient is considered suitable for switching, but is bradycardic on amiodarone (heart rate less than 60/min), stop amiodarone and reassess approximately 7 days later. Heart rate should be greater than 60/min before initiating a beta-blocker or rate-limiting calcium-channel blocker.

See NICE guidance<sup>3</sup> and flow charts (reproduced in Figures 2 and 3) for guidance on rate and rhythm control.

Figure 2. Rate control for persistent and permanent AF

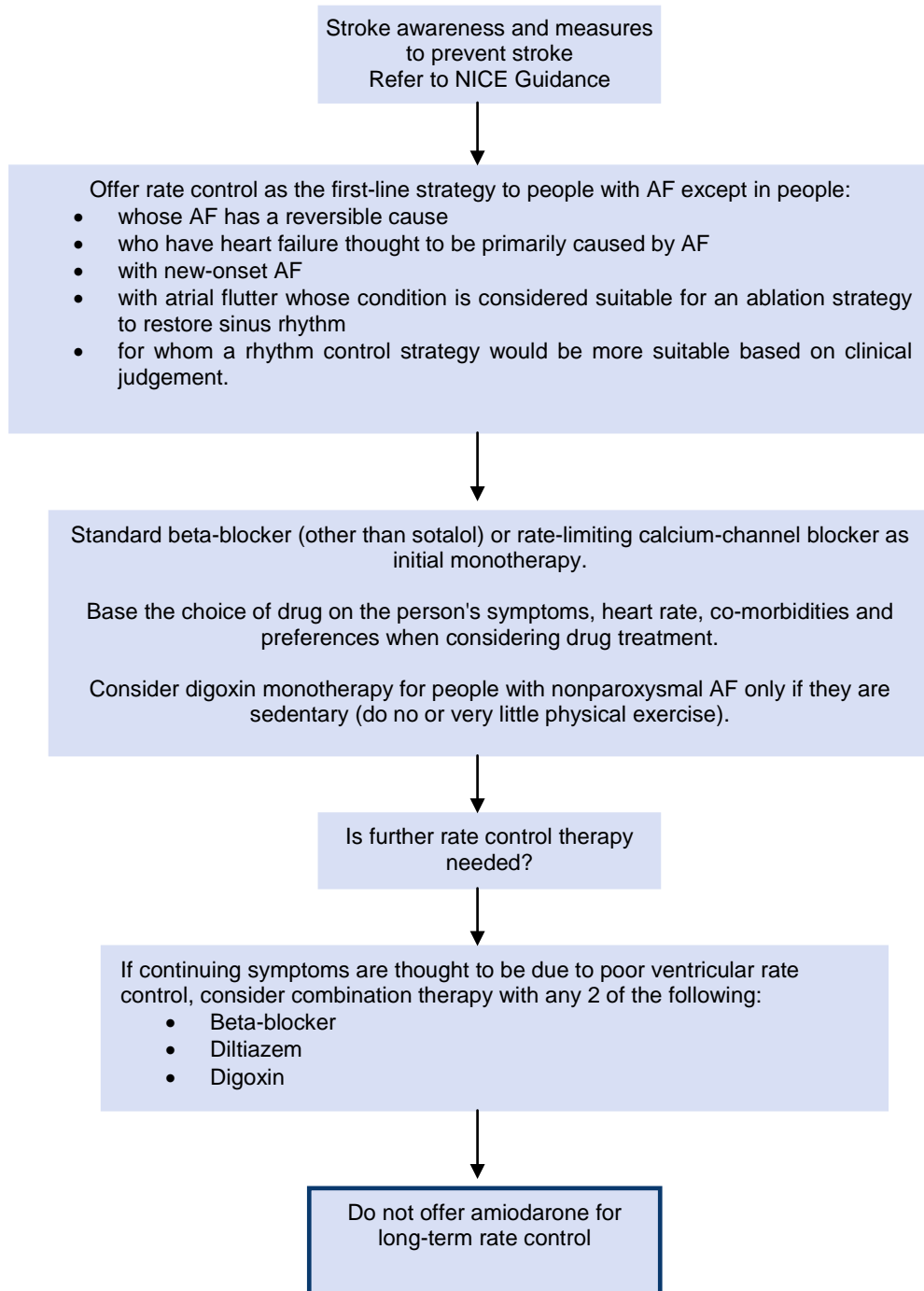
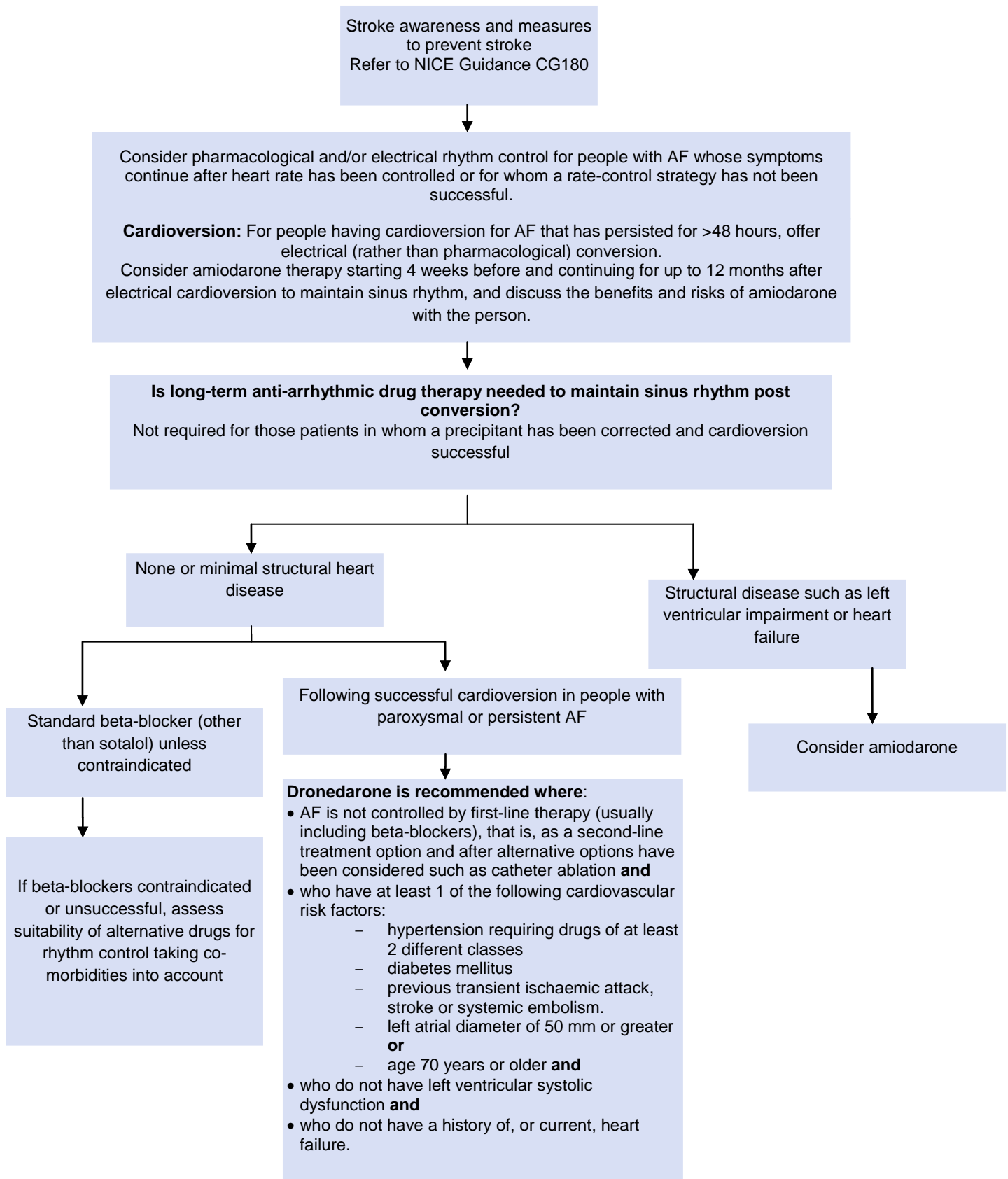




Figure 3. Rhythm control for persistent AF, including cardioversion



### 2.3 Decide which beta-blocker will be used

Beta-blockers act as anti-arrhythmic drugs principally by attenuating the effects of the sympathetic system on automaticity and conductivity within the heart. They can be used in conjunction with digoxin to control the ventricular response in AF.

The choice of beta-blocker will usually depend on the person's comorbidities, local recommendations, and cost<sup>8,9</sup>. It is recommended that the choice of beta-blocker be made in conjunction with cardiologists and Medicines and Therapeutics Committees.

### 2.4 Give advice to patients

Patients must be informed of any potential side effects and asked to contact the surgery if they experience any of the symptoms listed in Table 2.

**Table 2. Symptoms that should prompt patients to contact surgery**

Symptom	Probable side effect
<ul style="list-style-type: none"> <li>wheezing or trouble breathing; weight loss; fever</li> </ul>	Pulmonary fibrosis
<ul style="list-style-type: none"> <li>fatigue, lethargy, bradycardia, dyspnoea, cold intolerance, dry skin, weight gain, constipation, and reduced appetite;</li> <li>agitation, weight loss, increased sweating</li> </ul>	Hypo or hyperthyroidism
<ul style="list-style-type: none"> <li>yellow eyes or skin, unusual bleeding or bruising;</li> <li>appetite loss</li> </ul>	Cirrhosis, liver
<ul style="list-style-type: none"> <li>swelling of feet or ankles;</li> <li>chest pain (may be related to disease and not a side effect);</li> <li>giddiness on getting up/symptoms of postural hypotension;</li> <li>slow, fast, or irregular heartbeat;</li> <li>fainting or severe dizziness</li> </ul>	Cardiovascular including congestive heart failure
<ul style="list-style-type: none"> <li>visual halos, blurred vision, corneal opacities;</li> <li>sore, tender eyes</li> </ul>	Corneal microdeposits; optic neuropathy

Patients in sinus rhythm should continue on warfarin.

### 2.5 Assess response

Stop amiodarone and start beta-blocker treatment according to British National Formulary (BNF) directions. Check symptoms, pulse and blood pressure one week after each dose titration to assess response to treatment and potential side effects.

If pulse is less than 60/min or blood pressure is low, consider stopping beta-blocker treatment.

It is recommended that a patient who has successfully switched from amiodarone to alternative therapy should be reviewed in general practice at one, three and six months to ensure that their condition remains stable. Some side effects may not appear for up to two years after amiodarone has been discontinued.

Cardiologists/specialist nurses tend to review patients soon after cardioversion at which time a longer term management strategy will be decided.

### 2.6 Assess the likely effect of amiodarone withdrawal on drug interactions

For example, patients on anticoagulants will need more frequent monitoring for several months as the blood levels of amiodarone drop.

## 2.7 Monitor

Patients remaining on, or newly initiated onto, amiodarone require regular clinical and laboratory monitoring in accordance with the AWMSG Amiodarone Shared Care Protocol. Clinicians monitoring amiodarone may wish to consider the following:

- Do you have a register?
- Do you have a safe recall system?
- How do you identify non-attenders?
- How do you ensure that abnormal results are always followed-up?
- Have all patients had a face to face annual review documenting details relating to amiodarone?

It is recommended that where amiodarone is included in General Medical Services (GMS) Near Patient Testing Local Enhanced Service schedules, its monitoring is funded for 2 years following discontinuation.

## 3.0 ACKNOWLEDGEMENTS

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This documentation was based on work undertaken in Bridgend and Gwent and subsequently Wrexham Local Health Boards. The draft documentation was circulated for comment to the Cardiac Networks, Welsh Cardiovascular Society and Society of Physicians in Wales. The document was reviewed and updated in 2016.

AWPAG consultation leads for 2016 update: Mrs L Howard-Baker and Dr Khalid Khan

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### Further Reading:

Welsh Medicines Resource Centre (WeMeReC). Things to Know... about amiodarone. November 2008. Available at: [www.wemerec.org/Documents/Things2Know/T2KAmiodarone2008.pdf](http://www.wemerec.org/Documents/Things2Know/T2KAmiodarone2008.pdf).

**APPENDIX 1: AMIODARONE AUDIT SHEET**

DATA COLLECTION					
Patient name		Date of birth		NHS number	
Who initiated the amiodarone?					
Date of amiodarone initiation					
If no date, has the patient been taking the amiodarone for > 5 years/> 10 years (from repeat prescription)?					
Is there an indication? Tick in corresponding box	AF		Ventricular tachycardia (VT) or ventricular fibrillation (VF)		
	Atrial flutter		Other; specify		
	Maintenance of sinus rhythm post electrical cardioversion (12 months)				
	Supraventricular tachycardia (SVT)		None		
<b>If no accurate indication, write to initiating physician and request details of the original indication and expected duration of treatment.</b>					
MONITORING					
Is there any evidence of regular monitoring?					
SYSTEM	MONITORING	Y/N	SYSTEM	MONITORING	Y/N
Cardiac	Baseline ECG		Hepatic	<sup>6/</sup> <sub>12</sub> AST or ALT	
Pulmonary	Baseline chest X-ray		Neurological	Examination if symptomatic	
Pulmonary	Documented absence of respiratory symptoms. Lung function test if symptomatic		Ophthalmic	Annual eye examination or if symptomatic	
Endocrine	<sup>6/</sup> <sub>12</sub> Thyroid function tests		Dermatological	Examination if symptomatic	
ACTION					
<b>FOR AF AND ATRIAL FLUTTER INDICATIONS (For other indications, seek advice)</b>					
<b>Confirm heart rhythm by ECG</b>					
Is the patient still in AF? Has the patient had amiodarone for more than 12 months post electrical cardioversion?					
YES	Stop amiodarone If patient is still symptomatic, seek advice for further management				
NO	For decision on whether to discontinue amiodarone and initiate alternative treatment, use algorithm overleaf and refer to the accompanying guidance document.  Assess response at 1, 3 and 6 months to ensure condition remains stable				
Plan:					

Figure 2. Rate control for persistent and permanent AF

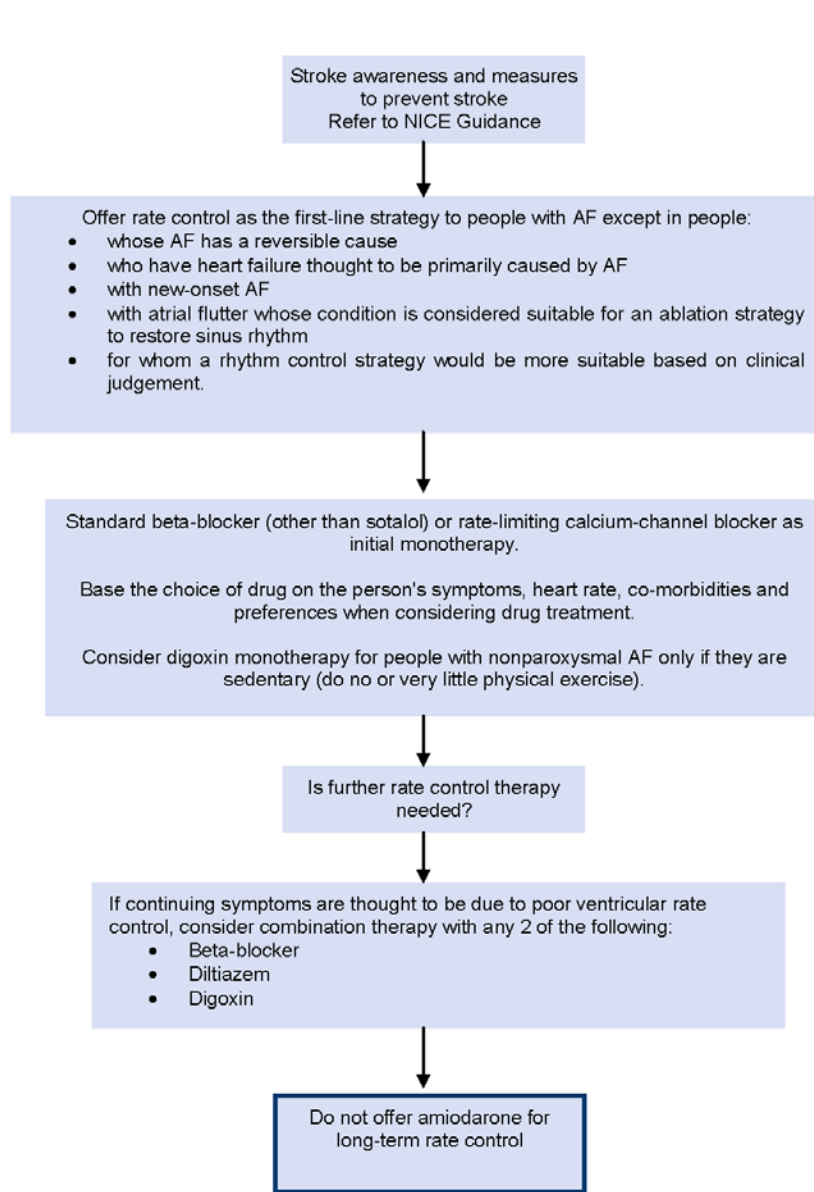
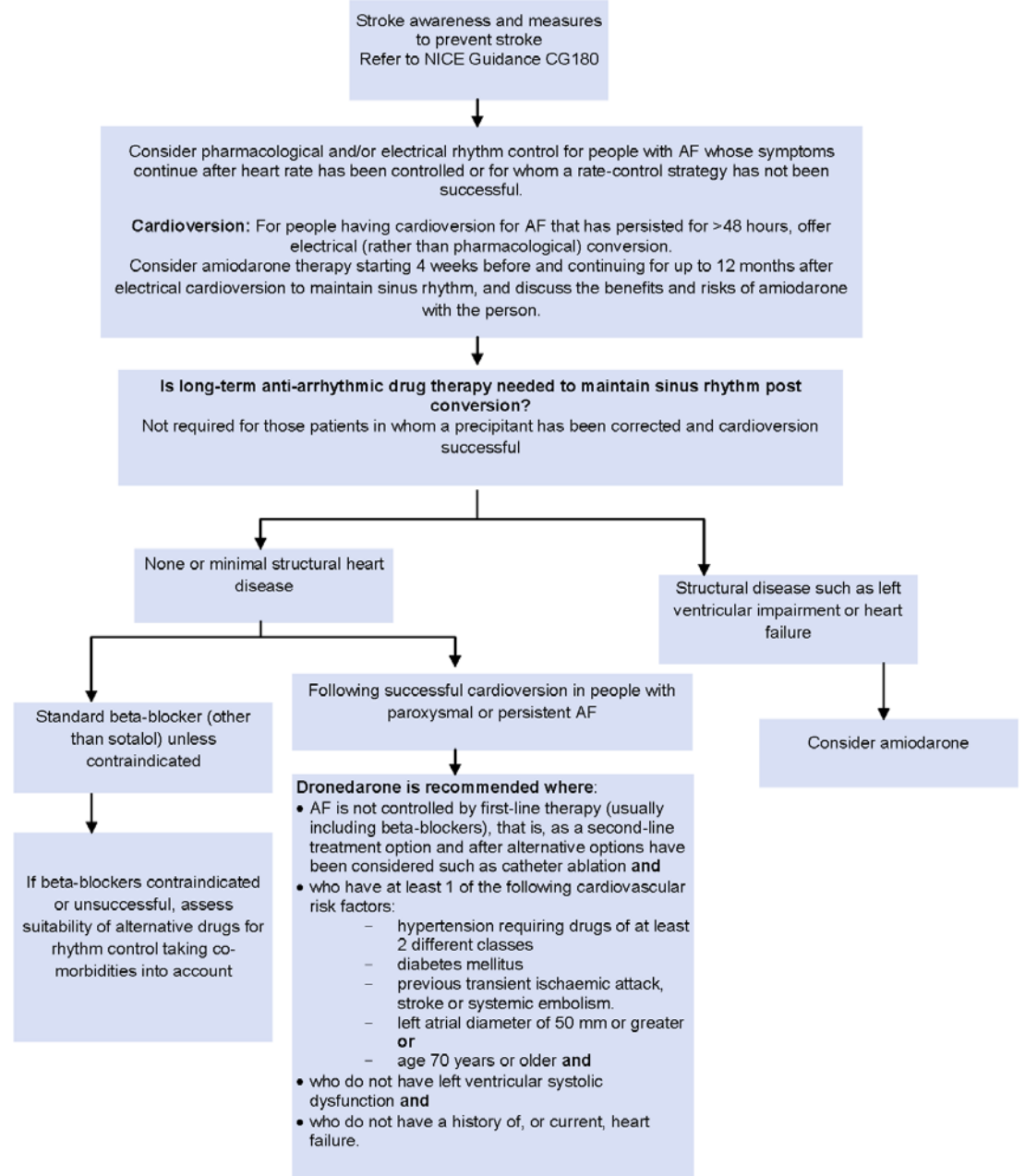


Figure 3. Rhythm control for persistent AF, including cardioversion



## **APPENDIX 2: AMIODARONE SHARED CARE PROTOCOL**

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**AWMSG recommends that shared care arrangements are suitable for patients newly initiated on amiodarone.**

**Initiation doses of amiodarone should be prescribed by specialists; GPs should only prescribe maintenance doses.**

**The shared care template has been endorsed by the Wales Council of the British Geriatric Society. The consultation process has included Local Medical Committees and Welsh Medicines & Therapeutics Committees.**

A proportion of patients currently taking amiodarone will have been discharged or lost to follow-up. The place of amiodarone in therapy has altered in recent years. The indication for treatment and therefore the most appropriate management will be dependent upon local historical patterns of prescribing. It is therefore recommended that local agreement is reached for patients started on amiodarone historically. Guidance on Atrial fibrillation: management has been issued by NICE in [CG180](#) (2014) and [Clinical Knowledge Summaries](#).

**Welsh cardiologists endorse this shared care agreement in the following circumstances:**

Welsh Cardiovascular Society meeting 1.5.08

Patients receiving amiodarone for life-threatening arrhythmias will normally be reviewed (annually) by cardiologists. For remaining indications where lifelong treatment is appropriate, but hospital review practically difficult, consultants may in individual cases, after agreement with the relevant GP, decide to discharge a patient to primary care monitoring, with urgent access to advice and/or review from the initiating department.

## PROTOCOL: AMIODARONE

*This document should be read in conjunction with the current SPC: [www.medicines.org.uk/](http://www.medicines.org.uk/)*

<b>1. Licensed Indications</b>	Amiodarone is licensed for the treatment of severe cardiac rhythm disorders where other treatments either cannot be used or have failed.
<b>2. Therapeutic use and background</b>	<b>AWMSG 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 arrhythmias) and the Wales Council of the British Geriatric Society. The consultation process has included Local Medical Committees and Welsh Drugs &amp; Therapeutics Committees.</b> 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 AF or who have converted from, or relapsed into AF following cardioversion. It is also used before heart surgery to help prevent AF. Amiodarone has been used for prevention of ventricular arrhythmias.
<b>3. Contraindications</b>	Hypersensitivity to iodine or amiodarone or any excipients, evidence or history of thyroid dysfunction, 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.
<b>4. Typical dosage regimen (adults)</b>	<b>A loading regimen is necessary and will be prescribed by secondary care.</b> <b>Loading:</b> 200 mg three times daily for one week, then 200 mg twice daily for one week, then a further reduction to 200 mg daily. <b>Maintenance</b> dose is usually 200 mg daily; however, 100 mg daily may be sufficient in elderly patients. The minimum dose to control arrhythmia is used. In rare cases a maintenance dose of above 200 mg daily may be required. Maintenance doses above 200 mg daily should be reviewed regularly. <b>All dose adjustments will be done by secondary care unless directions have been specified in the medical letter to the GP.</b>
<b>5. Drug interactions</b> For a comprehensive list consult the BNF or SPC	Amiodarone is metabolised by the cytochrome P450 system and therefore has the potential to cause many drug interactions. The SPC 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). <b>There is potential for drug interactions to occur several months after stopping treatment and the onset of drug interactions may be slow after initiating amiodarone. Some interactions may not become evident until two years after stopping treatment</b> <b>Statins:</b> Increased risk of myopathy. <b>Simvastatin – restrict dose to 20 mg daily.</b> Other statins: counsel patients to report any muscle pain or weakness immediately. <b>Anticoagulants:</b> Amiodarone can increase anticoagulant effect. Consider <b>warfarin</b> dose reduction. Patients should be monitored closely and the dose of anticoagulant altered accordingly, remembering that amiodarone levels take several weeks to stabilise. <b>Antiepileptics:</b> 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. <b>Beta-blockers:</b> Increased risk of bradycardia, AV block and myocardial depression. Sotalol – avoid concomitant use. <b>Calcium-channel blockers</b> (diltiazem and verapamil): increased risk of bradycardia, AV block and myocardial depression. <b>Ciclosporin:</b> Amiodarone increases levels of ciclosporin. Reduced dose of ciclosporin is recommended. <b>Digoxin:</b> dose should be halved when amiodarone is started. <b>Diuretics:</b> increased risk of cardiotoxicity if hypokalaemia occurs. <b>Drugs that prolong the QT interval:</b> Concurrent therapy is contra-indicated due to the increased risk of torsades de pointes: <ul style="list-style-type: none"> <li>• <b>Anti-arrhythmics:</b> e.g. quinidine, procainamide, disopyramide, sotalol.</li> <li>• <b>Antipsychotics:</b> e.g. phenothiazines, haloperidol, amisulpride, sertindole</li> <li>• <b>Antihistamines:</b> e.g. mizolastine and terfenadine.</li> <li>• <b>Antimalarials:</b> e.g. chloroquine, hydroxychloroquine, mefloquine, quinine</li> <li>• Lithium and tricyclic antidepressants.</li> <li>• <b>Others:</b> co-trimoxazole IV erythromycin, moxifloxacin, pentamidine, some antivirals</li> <li>• <b>Hepatitis C drugs:</b> cases of severe, potentially life-threatening bradycardia and heart block have been observed in combination with sofosbuvir in combination with other DAAs. Refer to SPC where concomitant use cannot be avoided.</li> <li>• <b>Concomitant use with fluoroquinolones</b> should be avoided.</li> </ul>



<p><b>6. Adverse drug reactions</b> Some adverse events can occur up to two years after treatment has been discontinued.</p> <p>For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult SPC or BNF</p>	<p><b>Most serious toxicity is seen with long-term use and may therefore present first to GPs.</b> Adverse reaction frequency are classified using the following convention: Very common ( ≥ 10%), common ( ≥ 1% and &lt;10%); uncommon ( ≥ 0.1% and &lt;1%).</p>	
	<b>Clinical condition</b>	<b>Management</b>
	<p><b>Lung:</b> Onset of <b>DYSPNOEA</b> or non-productive <b>COUGH</b> may be related to pulmonary toxicity – pneumonitis, diffuse alveolitis and pulmonary fibrosis (common). Sometimes fatal.</p>	<p>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</p>
	<p><b>Heart:</b> Dose dependent sinus <b>BRADYCARDIA</b> (common). Worsening of arrhythmia (uncommon). May present as <b>BLACKOUTS</b></p>	<p>Seek specialist advice</p>
	<p><b>Thyroid disorders</b> (common): Hyperthyroidism: <b>WEIGHT LOSS</b>, asthenia, restlessness, increase in heart rate, onset of arrhythmia, angina, congestive heart failure. Sometimes fatal</p>	<p>Perform thyroid function tests Action: See section 8 Monitoring</p>
	<p>Hypothyroidism (common)</p>	
	<p><b>Eyes:</b> Corneal microdeposits – coloured halos in dazzling light or blurred vision (very common)</p>	<p>Corneal microdeposits are reversible and amiodarone can be continued.</p>
	<p>Optic neuropathy/neuritis that may progress to blindness (Very rare): <b>BLURRED OR REDUCED VISION</b></p>	<p>Prompt ophthalmological examination including fundoscopy. Appearance of optic neuropathy and/or optic neuritis requires amiodarone withdrawal due to the potential progression to blindness.</p>
	<p><b>Liver:</b> Increase in serum transaminases (Very common) usually 1.5 to 3 times normal range.</p>	<p>It may return to normal with dose reduction or even spontaneously.</p>
	<p>Acute liver disorders (common) with high serum transaminases and/or jaundice, including hepatic failure. Sometimes fatal</p>	<p>Seek specialist advice</p>
	<p><b>Nervous system:</b> extrapyramidal tremor, nightmares, sleep disorders (Common)</p>	<p>Tremor: regression usually occurs after reduction of dose or withdrawal</p>
	<p>Peripheral sensorimotor neuropathy and/or myopathy (Uncommon)</p>	<p>Both these conditions may be severe, although recovery usually occurs within several months after amiodarone withdrawal, but may sometimes be incomplete.</p>
	<p><b>Gastrointestinal:</b> taste disturbance, nausea, vomiting (Very common)</p>	<p>Usually occurring with loading dosage and resolve with dose reduction</p>
	<p><b>Skin:</b> Blue-grey skin discolouration (common)</p>	<p>Reversible</p>
<p><b>Photosensitivity (very common):</b> May persist for months after treatment is stopped.</p>	<p>Patients should be cautioned to avoid exposure of skin to direct sunlight or sun lamps. A wide spectrum sunscreen should be used.</p>	
<p><b>IF YOU SUSPECT AN ADVERSE REACTION HAS OCCURRED, PLEASE CONTACT THE SPECIALIST DEPARTMENT.</b> All serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. <b>The patient should be advised to report any of the following signs or symptoms without delay:</b></p> <ul style="list-style-type: none"> <li>- Increasing breathlessness, dyspnoea or non-productive cough</li> <li>- Altered vision</li> <li>- Loss of appetite/weight loss</li> <li>- Sleep disturbance/nightmares</li> <li>- Tremor/loss of coordination</li> </ul>		
<p><b>7. Baseline investigations</b></p>	<p><b>To be undertaken by secondary care</b> Chest X-ray (ensure CXR within the last 12 months), TFT (ultrasensitive TSH) LFTs, urea &amp; electrolytes and creatinine, ECG. Consideration could be given to lung function tests and examination of skin, eyes, and neurological systems</p>	

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8. Monitoring	Monitoring	Frequency	Results		Action and responsibility
<p>It is essential to have a recall system to identify patients who do not attend, especially following abnormal results</p> <p>It is recommended that monitoring continues for two years following discontinuation of amiodarone treatment.</p> <p><sup>(i)</sup> Adapted from Amiodarone and the thyroid, Basaria S, Cooper D, The American Journal of Medicine</p>	Clinical adverse effects	Every 6 months*	Assess for adverse effects detailed in section 6		Both: Patients who have had life-threatening arrhythmias
	Clinical effectiveness	Every 6 months*	Assess patient remains in sinus rhythm and heart rate is satisfactory  *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 : usTSH(i)	us TSH If normal repeat every 6 months	Normal	It is not unusual for patients on amiodarone to have slight elevations of TSH and T4	
	TSH > 4.5	TSH > 4.5, fT4 elevated and duration less than 3 months	Observe Repeat in 3 months		
	Sub clinical hypothyroidism	TSH > 10, fT4 normal persisting for over 6 months	Consider treating with levothyroxine or repeat in 3 months		
	Hypothyroid	TSH > 4.5, fT4 low	May be treated with levothyroxine if amiodarone is considered essential		
	Thyrotoxicosis	TSH < 0.1mU/l T3 & T4 normal or minimally increased	Repeat in 2-4 weeks		
		TSH < 0.1mU/l & T4 elevated, T3 elevated or 50% greater than baseline	Discuss urgently with specialist who may advise amiodarone withdrawal. Arrange TSH-receptor antibodies and TPO antibodies		
	<b>Electrolyte</b>	Every 6 months in patients taking diuretics	Avoid hypokalaemia	Correct the cause of hypokalaemia	Primary care
<b>Eyes</b>	Annual	Ophthalmological examination recommended in data sheet	Patient should be encouraged to attend optician annually.	Both	
	If blurred or decreased vision	Arrange urgent ophthalmological assessment	Discuss urgently with Specialist	Both	
<b>9. Pharmaceutical aspects</b>	<b>No special considerations</b>				

**Prescribing of Amiodarone for Atrial Fibrillation and Atrial Flutter in Wales**

<b>10. Secondary care contact information</b>	<p><b>If stopping medication or needing advice please contact:</b>  <b>Dr</b>  .....  <b>Contact number</b>  .....  <b>Hospital:</b></p>	
<b>11. Criteria for shared care</b>	<p>Prescribing responsibility will only be transferred when</p> <ul style="list-style-type: none"> <li>• Treatment is for a specified indication and duration.</li> <li>• Treatment has been initiated and established by the secondary care specialist.</li> <li>• The patient's initial reaction to and progress on the drug is satisfactory.</li> <li>• The GP has agreed in writing in each individual case that shared care is appropriate.</li> <li>• The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements.</li> </ul>	
<b>12. Responsibilities of initiating consultant</b>	<ul style="list-style-type: none"> <li>• Initiate treatment.</li> <li>• Undertake baseline monitoring.</li> <li>• Dose adjustments.</li> <li>• Monitor patient's initial reaction to and progress on the drug.</li> <li>• Ensure that the patient is taking a maintenance dose and has an adequate supply of medication until GP supply can be arranged.</li> <li>• 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</li> <li>• For remaining indications where lifelong treatment is appropriate, but hospital review practically difficult, consultants may in individual cases, after agreement with the relevant GP, decide to discharge a patient to primary care monitoring, with urgent access to advice and/or review from the initiating department.</li> <li>• Provide GP with: <ul style="list-style-type: none"> <li>– Diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review.</li> <li>– 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</li> <li>– Advice on when to stop amiodarone</li> <li>– Provide patient with relevant drug information to enable</li> <li>– Informed consent to therapy,</li> <li>– Understanding of potential side effects and appropriate action</li> <li>– Understanding of the role of monitoring.</li> </ul> </li> </ul>	
<b>13. Responsibilities of primary care</b>	<ul style="list-style-type: none"> <li>• To monitor and prescribe in collaboration with the specialist according to this protocol.</li> <li>• To continue monitoring for two years after discontinuation of amiodarone.</li> <li>• To ensure that the monitoring and dosage record is kept up to date.</li> <li>• Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary.</li> <li>• Provision of shared care is in accordance with Local Enhanced Scheme, where available</li> </ul>	
<b>14. Responsibilities of patients</b>	<ul style="list-style-type: none"> <li>• To attend hospital and GP clinic appointments, bring monitoring booklet (if issued)</li> <li>• Failure to attend will result in medication being stopped on specialist advice.</li> <li>• To report adverse effects to their specialist or GP.</li> <li>• To attend optician annually and inform optician that they are taking amiodarone</li> </ul>	
<b>15. Responsibilities of all prescribers</b>	<p>Any serious reaction to an established drug should be reported to the MHRA via the Yellow Card scheme.</p>	
<b>16. Supporting documentation</b>	<p>Include patient information leaflet if available e.g. Treatment Notes produced by the Consumers' Association</p>	
<b>17. Patient monitoring book</b>	<p>Not needed</p>	
<b>18. GP letter</b>	<p>Attached below</p>	
<b>19. Guideline date.</b>	<p>Production date: May 2008</p>	<p>Updated: September 2016</p>
<b>20. Guideline review date</b>		

**Sample Amiodarone Shared Care Agreement Form**

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

Baseline assessment		Notes
<b>Indication (please tick box)</b>	1. Paroxysmal AF. 2. Persistent AF. 3. Other SVT. 4. Post CABG. 5. Pre/Post Cardioversion. 6. VT or previous VF.	
<b>Start date</b>		
<b>Dose</b> -Initiation dose will be prescribed by hospital -Maintenance dose usually 200 mg daily or less	200 mg daily	
<b>Duration of therapy</b>	.....months*. .....Long term	*Short-term therapy (3 months or less) does not require specific monitoring
<b>CXR</b> - within the last 12 months -- Date if not undertaken during this admission/outpatient visit	Normal/abnormal	
<b>T<sub>3</sub>, T<sub>4</sub> &amp; TSH</b>	Normal/abnormal	
<b>LFTs, urea &amp; electrolytes and creatinine</b>	Normal/abnormal	
<b>ECG</b>		
<b>Next appointment</b>	.....months	

This drug has been accepted for Shared Care by AWMSG and [*insert local Trust/formulary committee where appropriate*]. The protocol is available at [www.awmsg.org/docs/awmsg/medman/Shared%20Care%20Template%20-%20Amiodarone.doc](http://www.awmsg.org/docs/awmsg/medman/Shared%20Care%20Template%20-%20Amiodarone.doc) or [*local formulary link*].

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 .....

**Please contact the department immediately (phone numbers: *insert* ) if you are unable to undertake the prescribing and monitoring of amiodarone for this patient.**