Bedfordshire Clinical Commissioning Group

Luton Clinical Commissioning Group

Bedfordshire and Luton Shared care guideline for Amiodarone

PATIENT NAME:		
ADDRESS:		
NHS NUMBER:		
CONSULTANT NAME:		
TEL:	FAX:	EMAIL:
GP	NAME:	
TEL:	FAX:	EMAIL:
Other Health Care Professional contact details (if appropriate):		

The purpose of this template of principles for shared care is to provide a framework for the seamless transfer of care for a person from a hospital or specialist service setting to general practice, where this is appropriate and in their best interests.

What are key elements of the process to ensure good shared care arrangements are in place?

N.B. Shared care arrangements can involve the Specialist Service sharing care with GPs or other health care professionals e.g. Community Nursing Service administering medicines subject to close monitoring. The same shared care principles apply.

- The hospital clinician/specialist service should prescribe if the patient will be attending hospital/specialist service regularly for specialist monitoring, otherwise contact the GP/other health care professional to agree to share care. It will be assumed that the GP/other health care professional will accept shared care unless they advise the hospital clinician/specialist service to the contrary.
- Transfer of clinical responsibility to primary care should only be considered where the person's clinical condition is stable or predictable.

- Patients should be at the centre of any shared care arrangements. Individual patient information and a record of their preferences (including patient consent) should accompany shared care prescribing guidelines where appropriate.
- A copy of the shared care guideline should be provided by the specialist centre initiating the treatment to both the patient (where appropriate) and the clinician participating in the shared care. Failure to provide a copy of the shared care guideline could result in a delay in responsibility for prescribing/administration being accepted in primary care.
- Adhere to CCG policies.
- The GP/other health care professional should have sufficient information on the drug to either allow them to monitor the patient's response to therapy and adjust dosages as required or know in what circumstances they should refer the patient back to the hospital clinician
- Where the hospital clinician/specialist service retains responsibility for monitoring drug therapy or making dosage adjustments, the GP/other health care professional must be informed of any dose changes as soon as possible to avoid an incorrect dose being administered. Similarly if the GP/other health care professional changes the patient's medication then the hospital clinician/specialist service involved in the shared care agreement should be informed
- If a GP is unwilling to participate in a shared care agreement, the CCG medicines optimisation/management team should be asked for assistance in facilitating suitable prescribing arrangements for the patient.
- The patient should inform their usual community pharmacist that they will be starting the treatment to help ensure that supplies are available.

Therapeutic Summary and Key Responsibilities

Therapeutic Summary	Amiodarone has an important place in the treatment of severe cardiac rhythm disorders where other treatments either cannot be used or have failed. However it has potential major toxicity and its use requires monitoring both clinically and via laboratory settings. NICE clinical guideline on Atrial Fibrillation (AF) CG 180 puts greater emphasis on rate rather than rhythm control and has clarified the place of amiodarone in the treatment pathway: https://www.nice.org.uk/guidance/CG180. It may also be suitable in patients prior and post cardioversion or in specific patients who also have heart failure or left ventricular impairment. NICE have issued the following "Do not do" recommendation: **Do not offer amiodarone for long-term rate control.** Guidance from NHS England states that amiodarone should be initiated by a specialist and only continued in primary care under a shared care arrangements.
Patient Criteria for shared care	Oral amiodarone is indicated only for the treatment of severe rhythm disorders not responding to other therapies or when other treatments cannot be used: • Rhythm control of atrial fibrillation or flutter where other treatments cannot be used. • All types of tachyarrhythmias of paroxysmal nature including supraventricular, nodal and ventricular tachycardias, ventricular fibrillation, when other drugs cannot be used. • Tachyarrhythmias associated with Wolff-Parkinson-White Syndrome This protocol does not cover the short-term use of amiodarone prior to or following DC cardioversion or ablation for the management of atrial flutter/fibrillation (unlicensed indication).

Responsibilities of the specialist initiating treatment	• To assess the suitability of the patient for treatment • Initiate treatment • Undertake baseline monitoring as specified in this document (see baseline Monitoring) • Ensure that the patient/carer has received counselling and understands the therapy, its benefits, limitations, continued monitoring (where applicable), adverse effects, and is aware of actions to take if adverse effects are suspected • Inform the GP of the information provided to the patient • Monitor patient's initial reaction to and progress on the drug • 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 prescribing responsibility • Ensure the patient is taking a maintenance dose and has an adequate supply of medication until GP supply can be arranged • Continue to review the patient annually, sending a written summary to the GP whenever the patient is reviewed, or in individuals cases and after agreement with the relevant GP • Assess response to treatment and initiate any dose changes as clinically appropriate including discontinuation of treatment • Support and advise GPs as required
Responsibilities of other prescribers (GP):	• **GPs should never initiate therapy with amiodarone.** • Prescribe follow up prescriptions for amiodarone- ensure continued prescribing of amiodarone remains clinically appropriate at dose advised by initiating team • Carry out drug monitoring as listed – and communicate abnormal results to the Consultant Cardiologist • Ensure there are no drug interactions with any other medications initiated in primary care • Notify Consultant if treatment with amiodarone is discontinued (e.g. stopped by another specialist) • To stop treatment on the advice of the specialist • To refer back to the Specialist if the patient's condition deteriorates • To continue monitoring for up to 12 months following discontinuation of amiodarone • Identify adverse effects to amiodarone and report these to the Specialist and where appropriate to the Commission on Human Medicines/MHRA (Yellow card scheme)
Responsibilities of the Patient / Carer:	• Report any possible adverse reactions to the GP – in particular changes in vision, new respiratory problems • Attend hospital and GP clinical appointments, including those for routine blood tests/investigations • Failure to attend appointments will result in medication being stopped on specialist advice • Ensure they have an adequate supply of medication • Avoid exposure of skin to direct sunlight or sun lamps during treatment and for several months after stopping • Avoid grapefruit juice • If taking a statin and amiodarone report any signs of unexplained muscle pain, tenderness or weakness or dark coloured urin

Amiodarone (Drug Information Sheet)	
Licensed Indication	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
Contra-indications	• Patients with sinus bradycardia, and sino-atrial heart block. (Note it should be used only in conjunction with a pacemaker in patients with severe conduction disturbance or sinus node disease). • Patients with evidence or history of thyroid dysfunction or known hypersensitivity to iodine or amiodarone. • Combination with drugs that increase the risk of torsades de pointes. • Pregnancy (unless exceptional circumstances). • Breast feeding.
Typical Dosage Regimen	**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. **All dose adjustments will be done by secondary care unless directions have been specified in the medical letter to the GP.**
Drug Interactions	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 (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.** **Anticoagulants:** The anticoagulant effects of **warfarin** are increased by amiodarone. The onset of this interaction may be slow (up to 2 weeks), with the peak effect occurring about 7 weeks after warfarin treatment is started. Reduce the dose of warfarin 50% if amiodarone is added, and monitor the international normalized ratio (INR) once a week until INR is stable. Consider changing to a NOAC if clinically appropriate (never appropriate for patients with metal prosthetic heart valves). **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. **Beta blockers:** Hypotension, bradycardia, ventricular fibrillation, and asystole have been seen in a few people given amiodarone with propranolol, metoprolol, or sotalol. **Ciclosporin:** Amiodarone increases levels of ciclosporin. Reduced dose of ciclosporin is recommended. **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. **Diltiazem and verapamil:** Avoid concurrent treatment with amiodarone, or use with caution. Cardiac depression can occur with concurrent treatment. bradycardia and myocardial depression

<table>
<tr><td></td><td colspan="2">Flecainide: plasma concentration of flecainide is increased
Statins: the risk of muscular toxicity is increased with statins metabolised by CYP 3A4. Simvastatin- restrict dose to 20mg daily
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, and amitriptyline; and lithium.
For full list see BNF or SPC at www.medicines.org.uk/EMC</td></tr>
<tr><td>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</td><td colspan="2">Most serious toxicity is seen with long-term use and may therefore present first to GPs.</td></tr>
<tr><td></td><td>Adverse effect</td><td>Management</td></tr>
<tr><td></td><td>Respiratory: Pneumonitis and fibrosis may present as dyspnoea (which may be severe and unexplained by the current cardiac status), non-productive cough, and deterioration in general health (fatigue, weight loss, and fever).</td><td>CXR and ECG to exclude alternative diagnoses.
If pulmonary toxicity is suspected: refer urgently to initiating cardiologist or respiratory physician.</td></tr>
<tr><td></td><td>Cardiovascular: Severe bradycardia and conduction disturbances, are associated with high doses of amiodarone, especially in elderly people.</td><td>Seek Cardiology specialist advice. May require reduced dose or if severe treatment withdrawal. Due to long-half-life effect may persist despite treatment discontinuation.</td></tr>
<tr><td></td><td>Endocrine:
Hyperthyroidism (5% of patients): weight loss , asthenia, restlessness, increase in heart rate, onset of arrhythmia, angina, congestive heart failure

Hypothyroidism (20% of patients); weight gain, fatigue bradycardia.</td><td>Perform thyroid function tests. See section on drug monitoring.</td></tr>
<tr><td></td><td>Eyes: Corneal micro deposits (very common) occur almost always in patients on continuous therapy. They may be associated with coloured halos in dazzling light or blurred vision.

Optic neuropathy/neuritis that may progress to blindness (Very rare)</td><td>Corneal micro-deposits consist of complex lipid deposits and are reversible following discontinuation of treatment and do not require discontinuation of amiodarone.

Prompt ophthalmological examination including fundoscopy. Appearance of optic neuropathy and/or optic neuritis requires amiodarone withdrawal due to the potential progression to blindness Discuss urgently with Cardiology specialist.</td></tr>
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	Hepatobiliary: Asymptomatic increase in serum transaminases (very common) usually 1.5 to 3 times normal range. Acute liver disorders, with high transaminases and/or jaundice have been reported.			It may return to normal with dose reduction or spontaneously. If severe liver function abnormalities or clinical signs of liver disease (for example jaundice) develop, seek **specialist advice**	
	Neurological symptoms, such as tremor, ataxia, and (rarely) peripheral neuropathy, have been associated with amiodarone treatment.			Commonly occur with loading doses and improve when maintenance treatment is started.	
	Gastrointestinal : taste disturbance, nausea, vomiting (Very common)			Commonly occur with loading doses of amiodarone but resolve with dose reduction.	
	Skin: Blue-grey skin discolouration **Photosensitivity** May persist for months after treatment is stopped.			Reversible Patients should be cautioned to avoid exposure of skin to direct sunlight or sun lamps. A wide spectrum sunscreen should be used.	
Baseline Monitoring	**To be undertaken by Secondary Care:** • Thyroid function tests (T_3, T_4 & TSH) • Liver function tests. • Serum electrolyte and urea measurement. • Chest x-ray (or ensure in the last 12 months) • ECG				
Monitoring It is recommended that monitoring continued for 12 months following discontinuation of amiodarone		**Frequency**	**Results**		**Action**
	Clinical Review	Every 6 months	Patient is assessed twice per year: Clinical GP assessment alternates approximately 6 monthly with secondary care review. Assess for adverse effects & clinical effectiveness.		Both
	LFTs	Every 6 months	> 1.5x rise in ALT or jaundiced	**Seek advice from Cardiology Specialist.** At the beginning of therapy, elevation of serum transaminases which can be in isolation (1.5 to 3 times normal) may occur. These may return to normal with dose reduction, or even spontaneously.	Primary Care
	TFTs (TSH, FT_4)	Every 6 months	Normal	Euthyroid subjects taking amiodarone for more than three months frequently have increased T4, decreased T3 but normal TSH	Primary Care
		TSH > 4.5	TSH > 4.5IU/L & T_4 elevated	Repeat TFTs in 3 months. If TSH still elevated or rising and /or T_4 low contact **endocrinology advise & guidance.**	
		Hypothyroid	TSH > 10IU/L	**Seek advice form Endocrinology & Cardiology Specialist.** May require discontinuation or amiodarone on	

				concomitant treatment with levothyroxine.	
		Hyperthyroid	TSH < 0.1IU/L and T4 and T3 normal (may need to request T3)	**Refer to Endocrinology Specialist, seek advice from cardiology specialist**. The development of thyrotoxicosis is harder to predict than hypothyroidism - if the TSH is low, such patients should be referred to an endocrinologist.	
		Thyrotoxicosis	TSH < 0.1IU/L and raised T_4 or T_3 or clinically hyperthyroid.	**Discuss or refer urgently to Endocrinology Specialist, seek advice from cardiology specialist.**	
	U&Es	Every 6 months	Avoid hypokalaemia	Correct the cause of hypokalaemia	Primary care
	Eyes	Annually New or worsening visual symptoms occur	As recommend in product SPC. Arrange urgent ophthalmological assessment, including fundoscopy.	Patients should be encouraged to attend optician annually. **Discuss urgently with Ophthalmology specialist.** Appearance of optic neuropathy and/or optic neuritis requires amiodarone withdrawal due to the potential progression to blindness. **Contact cardiology Specialist Urgently if amiodarone requires withdrawal.**	Both

Contact Details:

Advice and Guidance (part of the E-RS booking system)

GPs can contact Consultant Specialists from Cardiology and a range of other Specialities for advice via the 'Advice & Guidance' facility in the E-RS booking system.

'Consultant Connect' is another facility that may be available (this varies across the geographical county)

Alternatively for urgent calls contact the Bedford Hospital cardiology department on 01234 792119

Or for Luton & Dunstable Hospital via switchboard on 01582 491166

References

Adapted from AWMSG: Shared Care Protocol – Amiodarone

- NHS England. Items which should not routinely be prescribed in primary care: Guidance for CCGs, version 2, June 2019. https://www.england.nhs.uk/wp-content/uploads/2019/08/items-which-should-not-routinely-be-prescribed-in-primary-care-v2.1.pdf
- NICE Clinical Knowledge Summarise. Atrial Fibrillation (update May 19). https://cks.nice.org.uk/atrial-fibrillation
- British National Formulary, Edition 78, September 19
- Amiodarone 100mg Tablets (Accord Healthcare) – Summary of Product Characteristics (updated May 17) https://www.medicines.org.uk/emc/product/6019/smpc
- Specialist Pharmacy Services. Suggestions for Therapeutic Drug Monitoring in Adults in Primary Care, December 2017. https://www.sps.nhs.uk/wp-content/uploads/2017/12/Drug-monitoring-2017.pdf