NHS South West Yorkshire Partnership NHS Foundation Trust

NHS Barnsley Hospital NHS Foundation Trust

NHS South Yorkshire Integrated Care Board

Amiodarone Shared Care Guideline

Introduction

Amiodarone is a useful medication but has potentially serious side effects, some of which can be life-threatening.

This Shared Care Guidance has been written to enable the safe and appropriate continuation of care for patients initiated on amiodarone in hospital. Although aimed at new patients on amiodarone, practices are urged to audit existing patients to ensure they are being adequately monitored (see section on monitoring).

Indication/Licensing information

Treatment should be initiated by specialists only

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.

Other indications fall outside this guidance and the patient should be referred back to the original prescriber.

Pharmacology

Amiodarone is structurally similar to thyroxine. It exhibits all four of the classic Vaughan Williams mechanisms of action, namely sodium and potassium channel blockade, a mild antisympathetic action and some calcium channel blockade, but it is usually classified as a Class III antiarrhythmic drug. It prolongs the refractory period in all cardiac tissues.

After oral administration, amiodarone only has a bioavailability of 30%. It also has a half-life of approximately 50 days, so it can take weeks for therapeutic effects to appear.

Dosage and administration

A 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 dose is usually 200mg daily or the minimum required to control the arrhythmia

Maintenance doses above 200mg daily should be managed by secondary care.

Available as Amiodarone 100mg and 200mg tablets.

Responsibilities of the specialist initiating treatment

Summary

- To assess the suitability of the patient for treatment (including confirming the patient has no contra-indications to treatment and considering the relevance of any cautions, including interactions).
- To discuss the benefits and side effects of treatment with the patient/carer and the need for long term monitoring if applicable.
- To perform baseline tests and monitoring during loading until the patient is stable on the maintenance dose (see the monitoring section).
- To prescribe for the first 12 weeks of treatment.
- To provide the patient with an Amiodarone Patient Alert Card. This card includes important information on the most serious and potentially life-threatening side-effects (and their symptoms) that may occur during treatment with amiodarone and also reminds patients of the potential for drug to drug interactions.
- To ask the GP whether they are willing to participate in shared care.
- To provide the GP with a summary of information relating to the individual patient to support the GP in undertaking shared care (See Shared care request form in Appendix A).
- To advise the GP of any dosage adjustments required, monitoring required, when to refer back, and when and how to stop treatment (if appropriate).
- To advise the GP when the patient will next be reviewed by the specialist.
- To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow card scheme).
- To provide the GP with contact details in case of queries.

Baseline Tests
See Monitoring section

Routine Tests
See Monitoring section

Responsibilities of other prescribers

Acceptance of Responsibility by the Primary Care Clinician
It is optional for GPs to participate in taking on responsibility for shared care for the patient. GPs will take on shared care only if they are willing and able.

Summary

- To reply to the request for shared care as soon as possible.
- To prescribe for the patient as recommended by the specialist.
- To ensure there are no interactions with any other medications initiated in primary care (refer to the interaction section below).
- To continue monitoring as agreed with secondary care (see monitoring section).
- To conduct a six monthly face to face medication review or more frequent if required; enquiring specifically about adverse effects and considering possible interacting drugs (see monitoring section).
- To refer back to the specialist if any concerns with the patient's treatment. For example:
  - Patient or general practitioner is **not** comfortable to continue with the existing regime due to either change in condition or drug side effects.
  - Advice in respect of concordance.
  - Special situations, (e.g. Pregnancy).
- To inform the consultant if the patient discontinues treatment for any reason.
- Discontinue the drug as directed by the specialist if required.
- To identify adverse events if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse events to the specialist and where appropriate the Commission on Human Medicines/MHRA (Yellow card scheme).

The list below is not exhaustive. Please see the full Summary of Product Characteristics (http://www.medicines.org.uk/emc/) and the BNF (http://www.bnf.org/bnf/index.htm) for more information.

<table>
<tr><td>BNF therapeutic class</td><td>Antiarrhythmics: Class III</td></tr>
<tr><td>Cautions</td><td>Acute porphyrias, conduction disturbances (in excessive dosage), elderly, heart failure, hypokalaemia, severe bradycardia (in excessive dosage).</td></tr>
<tr><td>Contraindications</td><td>Sinus bradycardia, sino-atrial heart block, severe conduction disturbances or sinus node disease (unless pacemaker fitted), thyroid dysfunction, iodine sensitivity, pregnancy (except in exceptional circumstances), lactation.

The combination of amiodarone with drugs which may induce Torsades de Pointes is contra-indicated.</td></tr>
<tr><td>Monitoring</td><td>Monitoring should take place during the loading of amiodarone, and then every 6 months whilst treatment continues. See table below. Please 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.

<table>
<tr><th></th><th>Baseline</th><th>Loading</th><th>At 6 months and every 6 months thereafter unless otherwise stated</th></tr>
<tr><td>History & examination (H&E)</td><td>✓</td><td></td><td>Continue annually</td></tr>
<tr><td>H&E relating to adverse effects[1]</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>Heart rate and ECG</td><td>✓</td><td>✓</td><td>Continue annually</td></tr>
<tr><td>TFTs</td><td>✓</td><td></td><td>✓ [2]</td></tr>
<tr><td>U & Es</td><td>✓</td><td></td><td>✓</td></tr>
<tr><td>LFTs (ALT)</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>Digoxin level (if on digoxin)</td><td>✓</td><td>✓</td><td>Assess serum digoxin levels if dose increased or toxicity is suspected</td></tr>
<tr><td>INR (if on warfarin)</td><td>✓</td><td>✓</td><td>Monitor INR levels. Adjust warfarin dose accordingly</td></tr>
<tr><td>CXR</td><td>✓</td><td colspan="2">If suspected pulmonary toxicity</td></tr>
<tr><td>PFTs inc DLCO</td><td>✓</td><td colspan="2">If suspected pulmonary toxicity</td></tr>
<tr><td>CT scan[3]</td><td colspan="3">Consider if suspected pulmonary toxicity</td></tr>
<tr><td>Eye examination</td><td colspan="3">Assess if new or worsening visual symptoms occur</td></tr>
</table>

NB. 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, can occur quite rapidly (i.e. between tests) and such patients should be referred to an endocrinologist.

[1] Ask about breathlessness, non-productive cough, and general health deterioration (fatigue, weight loss and fever) relating to possible pulmonary toxicity, at each review visit.
[2] and for up to 12 months after discontinuation of amiodarone as hyperthyroidism may occur up to several months after discontinuation
[3] CT (computerised tomography) scans are more specific than X-rays and therefore may be therefore more helpful in confirming a suspected diagnosis of lung toxicity.</td></tr>
</table>

	Note: Healthcare providers should have a low threshold for suspecting amiodarone induced pulmonary toxicity.
Interactions	Amiodarone has a long half-life; there is a potential for drug interactions to occur for several weeks (or even months) after treatment with it has been stopped. Amiodarone has the potential to interact with many different drugs. Please refer to the BNF and SPC for further guidance: https://www.medicinescomplete.com/mc/bnf/current/interactions-of-amiodarone.htm http://www.medicines.org.uk/emc/ The combination of amiodarone with drugs which may induce Torsades de Pointes is contra-indicated. See SPC for full list of drugs. Use extreme caution or avoid concomitant use of drugs that prolong the QT interval (such as clarithromycin). Concomitant use of amiodarone with fluoroquinolones should be avoided (concomitant use with moxifloxacin is contra-indicated).There have been rare reports of QT interval prolongation, with or without torsades de pointes. Concomitant use of amiodarone is not recommended with the following drugs: beta-blockers, heart rate lowering calcium channel inhibitors (verapamil, diltiazem) and stimulant laxative agents which may cause hypokalaemia. **Simvastatin** Amiodarone increases the risk of rhabdomyolysis when given with simvastatin. The dose of simvastatin should not exceed 20mg daily. MHRA December 2014: https://www.gov.uk/drug-safety-update/simvastatin-updated-advice-on-drug-interactions **Digoxin** Administration of amiodarone to a patient already receiving digoxin will bring about an increase in the plasma digoxin concentration. 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 to two-thirds when amiodarone is started. INRs should then be checked weekly for 7 weeks and until INR stable. If / when amiodarone is stopped the interacting effect may persist for up to 6 weeks or more, so again INR should be checked weekly until stable. Note that amiodarone-induced hyperthyroidism will increase warfarin dose requirements. **Drugs which may cause hypokalaemia/hypomagnesaemia** Caution should be exercised over combined therapy with the following drugs which may cause hypokalaemia and/or hypomagnesaemia, e.g. diuretics, systemic corticosteroids, tetracosactide and intravenous amphotericin. **Phenytoin** Plasma level of phenytoin increased with amiodarone. Phenytoin dosage should be reduced if signs of overdosage appear (resulting in neurological signs), and plasma levels may be measured. **MHRA advice** Coadministration of amiodarone with sofosbuvir in combination with another hepatitis C virus direct acting antiviral (such as daclatasvir, simeprevir, or ledipasvir) is not

	recommended as it may lead to serious symptomatic bradycardia. https://www.gov.uk/drug-safety-update/simeprevir-with-sofosbuvir-risk-of-severe-bradycardia-and-heart-block-when-taken-with-amiodarone https://www.gov.uk/drug-safety-update/sofosbuvir-with-daclatasvir-sofosbuvir-and-ledipasvir-risks-of-severe-bradycardia-and-heart-block-when-taken-with-amiodarone

Table of amiodarone adverse effects

Adverse effects	**Frequency %**	**Investigation & Diagnosis**	**Treatment**
Pulmonary toxicity, including pneumonitis and fibrosis (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 (see advice under monitoring)
Hyperthyroidism	2	Free T4, TSH	See algorithm Appendix B
Hypothyroidism	6	Free T4, TSH	See algorithm Appendix B
Liver toxicity	1	LFTs	See algorithm Appendix C
Optic neuropathy/neuritis which may progress to blindness	0.13	Ophthalmologic examination	If optic neuropathy/neuritis is suspected (blurred or decreased vision), refer urgently to ophthalmology and discuss the possibility of stopping amiodarone & prescribing alternative antiarrhythmic therapy with patient's cardiologist
Pro-arrhythmia (onset or worsening of arrhythmia)	<1	ECG	Stop amiodarone
Extrapyramidal tremor	<10	History and clinical examination	Usually reversible on withdrawal of the drug
Peripheral neuropathy, Myopathy	<1	History and clinical examination	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, vomiting, taste disturbance, anorexia	30	History + examination	Reduce dosage (usually occur with loading dose and resolve with dose reduction)
Reversible corneal micro-deposits	>90	Slit-lamp examination	None – the deposits are considered essentially benign and do not require discontinuation of amiodarone
Photosensitivity	4-9	History, examination	Avoid exposure to sun and use sunblock
Blue discolouration of light-exposed skin, particularly the face	<9	Examination	Reduce dosage if possible

*DCLO is Diffusing Capacity of Lung for carbon monoxide.
**HCRT is High Resolution Computed Tomography
Adapted from: Siddoway LA. Amiodarone: guidelines for use and monitoring. American family physician. 2003 Dec 1;68(11): 2189-96.

Communication

Specialist to GP
The specialist will inform the GP when they have initiated amiodarone. When the patient is near completing the satisfactory initiation period, the specialist will write to the GP to request they take over prescribing and where possible give an indication as to the expected length of treatment. The Specialist will also send a Shared care request form to support the GP in undertaking shared care. (Appendix A)

GP to specialist
If the GP has concerns over the prescribing of amiodarone, they will contact the specialist as soon as possible.

Contact names and details

Contact Details	Telephone number	Email
Dr Naeem Tahir Consultant Cardiologist	01226 730000	naeem.tahir@nhs.net
Dr Deoraj Zamvar Consultant Cardiologist	01226 730000	deoraj.zamvar@nhs.net
Dr Abdul Qadeer Negahban Consultant Physician specialising in Cardiology	01226 730000	a.negahban@nhs.net
Dr David Robson Consultant Cardiologist	01226 730000	d.robson1@nhs.net
Dr U Velupandian Consultant Cardiologist	01226 730000	uma.velupandian@nhs.net
Daniel Kaye Cardiology Clinical Nurse Specialist	01226 730000	danielkaye@nhs.net
Mark Balchin Cardiology Clinical Nurse Specialist	01226 730000	markbalchin1@nhs.net
Specialist Cardiac nurses Apollo Court Medical Practice	01226 209881	
Gillian Turrell Medicines Information Pharmacist	01226 432857	gilliansmith2@nhs.net

References

- British National Formulary. Available at: www.medicinescomplete.com/mc/bnf/current/
- Summary of Product Characteristics. Available at: http://www.medicines.org.uk/emc/
- MHRA. Available at: https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency
- Suggestions for Therapeutic Drug Monitoring in Adults in Primary Care. December 2017. Available at https://www.sps.nhs.uk
- NPS Medicinewise Aust Prescr 2005;28:150-4.Available at https://www.nps.org.au/australian-prescriber/articles/amiodarone
- Siddoway LA. Amiodarone: guidelines for use and monitoring. American family physician. 2003 Dec 1;68(11): 2189-96
- NHS Clinical Knowledge Summaries. Atrial Fibrillation. May 2019. Available at: https://cks.nice.org.uk/atrial-fibrillation
- MHRA March 2022 Amiodarone (Cordarone X): reminder of risks of treatment and need for patient monitoring and supervision. Available at: Amiodarone (Cordarone X): reminder of risks of treatment and need for patient monitoring and supervision - GOV.UK (www.gov.uk) Accessed 28.6.22

Acknowledgement: This guideline document has been adapted from the Sheffield and Derbyshire shared care protocols for amiodarone
http://www.derbyshiremedicinesmanagement.nhs.uk/assets/Clinical_Guidelines/Formulary_by_BNF_chapter_prescribing_guidelines/BNF_chapter_2/Amiodarone_monitoring.pdf (please copy and paste link)

Shared Care Protocol –remains open to review in light of any new evidence
***Amber** = To be initiated and titrated to a stable dose in secondary care with follow up prescribing and monitoring by primary care.*

https://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/Shared%20Care%20protocols/Amiodarone_SCG%20.pdf?UNLID=346006162019103010231 2

Development Process

This guidance has been produced by following an AMBER classification status of amiodarone by the Barnsley Area Prescribing Committee. This information has been subject to consultation by the Cardiologists in Barnsley and was ratified by the Area Prescribing Committee on 12th February 2020 (Minor amendment September 2022).

Appendix A – Amiodarone Shared Care request form (Amber)

- Specialist to complete when requesting GP to enter a shared care arrangement.
- GP to return signed copy of form.
- Both parties should retain a signed copy of the form in the patient's record.

From (**Specialist**): _____ **To** (**GP**): _____

Patient details

Name: _____ ID Number: _____

Address: _____ DOB: _____

Diagnosed condition: _____

Amber Drug details

Drug name: _____ Dose and frequency: _____

Date of initiation: _____ Length of treatment: _____

The patient will be reviewed by the Consultant on: _____

The patient should be reviewed by the GP by: _____

Monitoring

The following monitoring should be undertaken by the GP:

Parameter	Date next test due	Frequency

Communication

Consultant
Telephone number: _____ Fax number:_____

Email address: _____

Specialist Nurse
Telephone number_____ Fax number: _____

Email address: _____

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____

Specialist (Doctor/Nurse) signature: _____ Date: _____

I, Dr ……., can confirm I :

☐ accept the request to participate in shared care for the patient named above.

☐ reject the request to participate in shared care for the patient named above. The reason for this being ……..

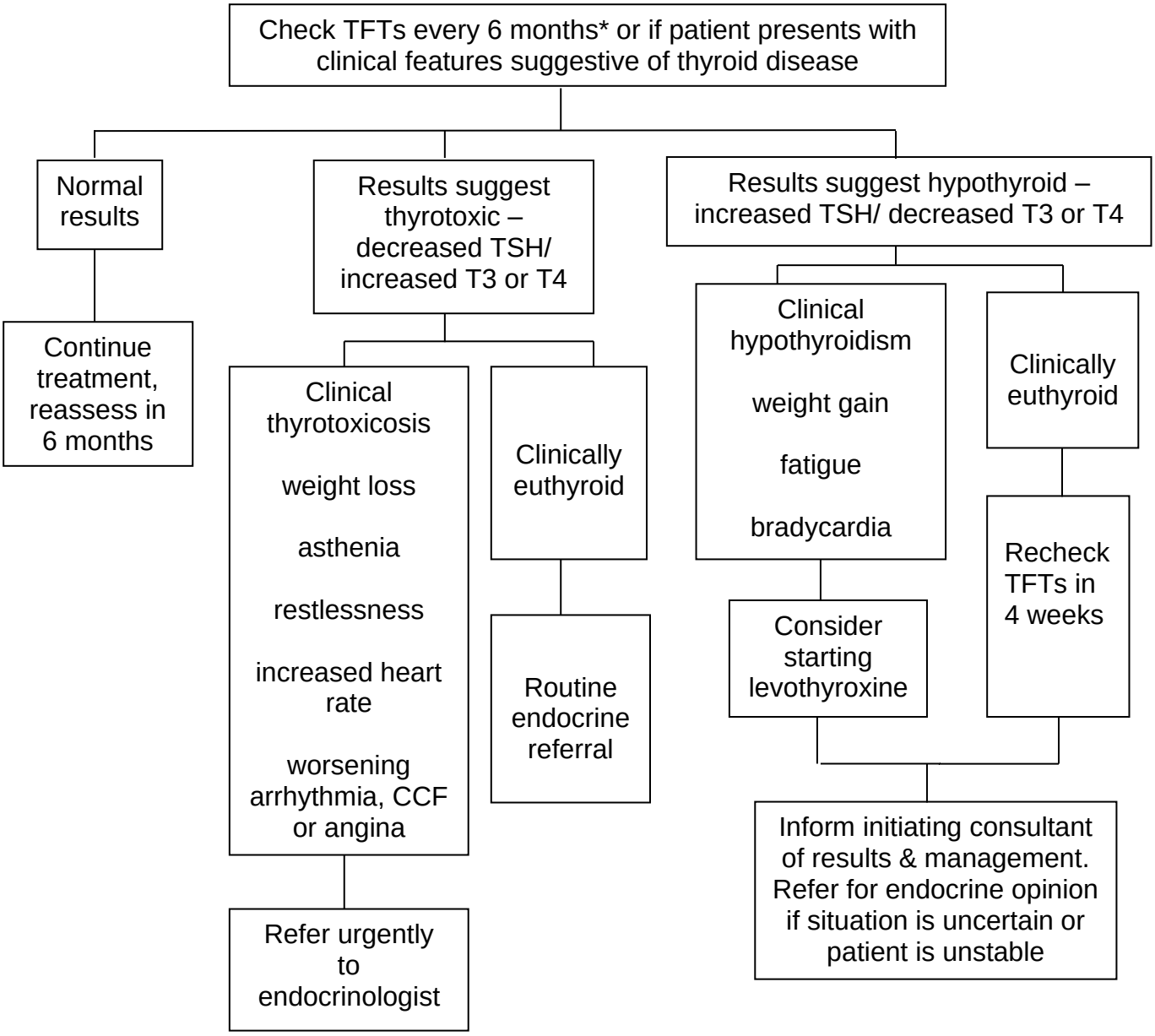
GP signature: _____ Date: _____

To save resources you have been sent Appendix A of the shared care document.

The full document (Amiodarone Shared Care Guideline, *date approved February 2020)* can be accessed on the Barnsley BEST website at the following link:
http://best.barnsleyccg.nhs.uk/clinical-support/medicines/shared-care-guidelines/

Or via the Barnsley Area Formulary www.barnsleyformulary.nhs.uk

Appendix B: Thyroid Function - TFTs every 6 months



*and for up to 12 months after discontinuation of amiodarone as hyperthyroidism may occur up to several months after discontinuation

Appendix C: Liver Function – LFTs every 6 months

Patients taking amiodarone may have co-morbidities that affect LFTs; these should be considered when interpreting LFTs.