Therapeutics Advisory Group

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Norfolk and Waveney Integrated Care System

NORFOLK AND WAVENEY STP THERAPEUTICS ADVISORY GROUP (TAG)

SHARED CARE AGREEMENT FRAMEWORK

Shared care guidelines for Use of Amiodarone in Adult Services
Monitoring level 2 - Prescribe the drug and perform a more intense level of monitoring, e.g. quarterly

Generic and Proprietary/Brand Name	
Amiodarone / Cordarone X®	
Indications for shared care	
• Tachyarrhythmias associated with Wolff-Parkinson-White Syndrome. • Atrial flutter fibrillation / atrial fibrillation when other drugs cannot be used. • All types of tachyarrhythmias of paroxysmal nature including: supraventricular, nodal and ventricular tachycardias and ventricular fibrillation when other drugs cannot be used	
Specialist Prescribing and Monitoring Responsibilities	**GP / Community Team - Primary Care Prescribing and Monitoring Responsibilities**
• Assess the patient, provide diagnosis and communicate to primary care. • Discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling to enable the patient to reach an informed decision. • Provide an appropriate patient information leaflet. • Assess for contraindications, cautions and interactions • Conduct required baseline investigations and initial monitoring • Initiate and optimise treatment. Prescribe the maintenance treatment for at least 4 weeks and until optimised. • Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information • Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care. • Conduct the required reviews and monitoring and communicate the results to primary care. • After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring remains appropriate. • Reassume prescribing responsibilities if a patient becomes or wishes to become pregnant. • Provide advice to primary care on the management of adverse effects if required.	• Accept shared care agreement and prescribe ongoing treatment as detailed in the request, taking into any account potential drug • Adjust the dose of amiodarone prescribed as advised by the specialist. • Conduct the required monitoring • Communicate any abnormal results to the specialist. • Manage adverse effects as detailed and discuss with specialist team when required. • Stop amiodarone and make an urgent referral to the specialist if hyperthyroidism, thyrotoxicosis, new or worsening arrhythmia or heart block, ophthalmological effects, hepatotoxicity, pulmonary toxicity or bullous skin reactions are suspected. • Refer the management back to the specialist if the patient becomes or plans to become pregnant. • Stop treatment as advised by the specialist.

Patient Information

- Take amiodarone as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
- Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms listed below
- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of amiodarone with their pharmacist before purchasing any OTC medicines.
- Avoid grapefruit juice while taking amiodarone and for several months after discontinuation.
- Moderate their alcohol intake to no more than 14 units per week to reduce the risk of hepatotoxicity.
- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:

- Breathlessness, non-productive cough or deterioration in general health (e.g. fatigue, weight loss, fever)
- New or worsening visual disturbances
- Progressive skin rash +/- blisters or mucosal lesions
- Signs and symptoms of bradycardia or heart block, e.g. dizziness, fatigue, fainting, shortness of breath, chest pain or palpitations, confusion or trouble concentrating

The patient should be advised to use appropriate self-care against the possibility of phototoxic reactions: e.g. sun avoidance, protective clothing, avoiding tanning (including tanning beds) and to purchase and use a broad spectrum sunscreen (at least SPF30). These measures to be continued for the duration of therapy and for several months after discontinuation.

If taking a statin and amiodarone, to report any signs of unexplained muscle pain, tenderness, weakness or dark coloured urine.

Avoid grapefruit and grapefruit juice while taking amiodarone and for several months after discontinuation. Although there have been no case reports on enhanced hepatoxicity with alcohol, patients should be advised to moderate their alcohol intake to no more than 14 units per week while taking amiodarone.

Specialist Contact Details

Contact the initiating consultant via hospital switchboards:

- NNUH: 01603 286286
- JPUH: 01493 452452
- QEH: 01553 613613

GENERAL PRINCIPLES FOR SHARED CARE PRESCRIBING

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- GPs are **invited** to participate. If GPs are not confident to undertake these roles, they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.
- **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable if they are unwilling to do so.**
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and when the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- **The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

Background to Treatment

Amiodarone is used in the treatment of arrhythmias. It has an important place in the treatment of severe cardiac rhythm disorders where other treatments either cannot be used or have failed. Amiodarone has potentially serious adverse effects and use requires regular monitoring.
Due to the significant safety concerns, NHS England (NHSE) and NHS Clinical Commissioners' (NHSCC) guidance advises that prescribers should not initiate amiodarone in primary care for any new patients. In exceptional circumstances, if there is a clinical need for amiodarone to be prescribed, this must be initiated by a specialist and only continued under a shared care arrangement in line with NICE clinical guidance Atrial fibrillation: NG 196. NICE defines the place in therapy of amiodarone in NG196 and has made a "Do not do" recommendation: "**Do not offer amiodarone for long-term rate control**". Amiodarone may also be suitable in patients prior and post cardioversion or in specific patients who have heart failure or left ventricular impairment.
Where there is an existing cohort of patients taking amiodarone who are not currently under shared care, it is recommended that these patients be reviewed to ensure that prescribing remains safe and appropriate and a shared care arrangement is introduced.

This document applies to adults aged 18 and over.

Licenced use and agreed local off-label use

Licensed indications:

- Tachyarrhythmias associated with Wolff-Parkinson-White Syndrome.
- Atrial flutter fibrillation / atrial fibrillation when other drugs cannot be used.
- All types of tachyarrhythmias of paroxysmal nature including supraventricular, nodal and ventricular tachycardias and ventricular fibrillation when other drugs cannot be used.

As per RMOC, there are no appropriate off-label indications

Criteria for Patient Selection

Treatment should be initiated 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.

Clear information must be provided by the hospital specialist to the GP regarding the indication for use, the recommended dosage to be prescribed by the GP, the anticipated duration of treatment, and any recommendations on when and how the treatment should be reviewed, and by whom.

Form and strength of preparation

Oral tablets - 100mg and 200mg

Side Effects and Management

Link to BNF

Link to SPC

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard	
As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.	
The most serious toxicity with amiodarone is seen with long-term use and patients may therefore present first to primary care. Due to the long half-life of amiodarone there is potential for adverse effects to occur for several weeks/months after treatment has been discontinued.	
Result	**Action for primary care**
Electrolyte deficiency: hypokalaemia / hypomagnesaemia	Continue amiodarone. Correct deficiency as per local guidelines. Review other medicines that may be contributing to a deficiency
Cardiovascular effects: Bradycardia: • Heart rate 50 - 60bpm without symptoms	Continue amiodarone. Repeat monitoring. No action required unless symptoms develop or heart rate decreases further.
Heart rate ≤ 50bpm, or ≤ 60bpm with symptoms	Discuss with specialist team; dose reduction may be required
Worsening of arrhythmia, new arrhythmia, or heart block	**Stop amiodarone.** Urgent referral to initiating specialist.
Thyroid dysfunction: Borderline results according to local reference range	Continue amiodarone. Repeat test after 6 weeks.
Hyperthyroidism / thyrotoxicity: high T4, normal/high T3, low TSH	**Stop amiodarone.** Urgent referral to initiating specialist and endocrinologist.
Hypothyroidism: low/normal T4, low/normal T3, high TSH	Continue amiodarone. Inform initiating specialist. Consider starting levothyroxine based on initiating specialist's advice. Monitor levothyroxine according to local pathways.
Subclinical hypothyroidism normal T4, raised TSH; clinical features not overtly manifest	Contact specialist team for advice, which may include input from endocrinology services. Anticipate the need for additional monitoring, investigations and potentially thyroid hormone replacement based on specialist recommendations.
Ophthalmological effects: Optic neuropathy/neuritis; blurred or decreased vision	**Stop amiodarone.** Urgent referral to initiating specialist and ophthalmology.

Corneal micro-deposits: blueish halos when looking at bright lights, with no blurred or decreased vision	Continue amiodarone; reversible on discontinuation. The deposits are considered essentially benign and do not require discontinuation of amiodarone.
GI disturbance: nausea, anorexia, vomiting, taste disturbance	Continue amiodarone. May require dose reduction; discuss with specialist if persistent.
Hepatotoxicity: abnormal LFTs +/- symptoms of hepatic injury (e.g. hepatomegaly, weakness, ascites, jaundice)	If serum transaminases elevated >3xULN but no symptoms of hepatic injury continue amiodarone and – repeat LFTs in 2 weeks. If still elevated may require dose reduction; discuss with specialist. If serum transaminases >5xULN or any symptoms of hepatic injury- **stop amiodarone**. Urgent referral to initiating specialist and hepatologist.
Neurological symptoms: Extrapyramidal tremor, ataxia, peripheral neuropathy, myopathy	Continue amiodarone. May require dose reduction; discuss with specialist.
Pulmonary toxicity: including pneumonitis or fibrosis new/worsening cough, shortness of breath or deterioration in general health (e.g. fatigue, weight loss, fever)	**Stop amiodarone.** Urgent referral to initiating specialist and respiratory specialist. Admission may be required.
Bullous skin reactions: life threatening or even fatal cutaneous reactions Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN)	**Stop amiodarone.** Urgent referral to dermatology, inform initiating specialist.
Photosensitivity	Continue amiodarone. Reinforce appropriate self-care e.g. sun avoidance and purchasing of a broad spectrum sunscreen (at least SPF30).
Skin discolouration (blue/grey): occurs in unprotected, light exposed skin	Continue amiodarone. May require dose reduction; discuss with specialist. Reinforce self-care measures (as for photosensitivity above). Pigmentation slowly disappears following treatment discontinuation

Drug Interactions

Link to BNF

Link to SPC

Cautions and Contraindications

Link to BNF

Link to SPC

Initiation of therapy and ongoing dose regimen

- Transfer of monitoring and prescribing to primary care is normally after at least 12 weeks, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:
200mg three times per day for one week, then reduce to 200mg twice per day for one week.
Amiodarone is initiated with a loading dose in order to achieve adequate tissue levels rapidly.
Rarely, the specialist team may use an alternative loading regimen.
The loading period must be prescribed by the initiating specialist.

Maintenance dose (following initial stabilisation):
200mg per day, or less if appropriate. The minimum dose required to control the arrhythmia should be used.
Rarely, a higher maintenance dose may be required. The maintenance dose should be reviewed regularly, particularly if it exceeds 200mg per day.
The initial maintenance dose must be prescribed by the initiating specialist.

Conditions requiring dose adjustment:
Although there is no evidence that dose requirements for elderly patients are lower, they may be more susceptible to bradycardia and conduction defects if too high a dose is prescribed. The minimum effective dose should be used. Particular attention should be paid to monitoring thyroid function.

Administration Information

For oral administration.

Maintenance dose can be given once daily, however doses >200 mg daily (including loading period) may be given as split doses to minimise nausea.

If necessary, tablets may be crushed and dispersed in water, but have a bitter taste (unlicensed). Different brands of may disperse in water at notably different rates. The solution for injection is irritant and should not be given orally.

The half-life of amiodarone is very long, with an average of 50 days (range 20-100 days). Side effects slowly disappear as tissue levels fall. Following drug withdrawal, residual tissue bound amiodarone may protect the patient for up to a month. However, the likelihood of recurrence of arrhythmia during this period should be considered.

Grapefruit juice should be avoided during treatment with oral amiodarone and for several months after discontinuation

Duration of therapy / How the treatment will be reviewed and if appropriate, stopped

The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.

Baseline assessment and ongoing monitoring – by Specialist

Baseline investigations:
- Thyroid function tests (free T4, free T3 and TSH)
- Liver function tests (LFTs, particularly transaminases)
- Urea and electrolytes (U&Es, including magnesium and potassium)
- Electrocardiogram (ECG)
- Chest X-ray

- For patients taking warfarin: monitor international normalised ratio (INR) at baseline and during dose stabilisation period
- For patients taking digoxin: clinical monitoring is recommended and the digoxin dose should be halved. Digoxin levels should be monitored appropriately.

Ongoing monitoring:
- ECG (at least annually – see below regarding primary care availability)
- Chest X-ray and pulmonary function tests, if respiratory symptoms or toxicity suspected

After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether ongoing monitoring remains appropriate.

GP / Community Team or other Primary Care monitoring responsibilities

Monitoring and advice	Frequency
• Thyroid function tests (free T4, free T3 and TSH) • LFTs (particularly transaminases) • U&Es (including magnesium and potassium)	Perform all tests every 6 months during treatment, and 6 months after discontinuation. Thyroid function should continue to be monitored for up to 12 months after discontinuation, with frequency determined clinically.
ECG (monitoring may be conducted in primary care where this service is available)	At least annually

Consultant / Specialist prescribing responsibilities

- Assess the patient, provide diagnosis and communicate to primary care.
- Discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling to enable the patient to reach an informed decision.
- Provide an appropriate patient information leaflet.
- Assess for contraindications, cautions and interactions
- Conduct required baseline investigations and initial monitoring
- Initiate and optimise treatment. Prescribe the maintenance treatment for at least 4 weeks and until optimised.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the required reviews and monitoring and communicate the results to primary care.
- After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring remains appropriate.
- Reassume prescribing responsibilities if a patient becomes or wishes to become pregnant.
- Provide advice to primary care on the management of adverse effects if required.

GP prescribing responsibilities

- Accept shared care agreement and prescribe ongoing treatment as detailed in the request, taking into any account potential drug
- Adjust the dose of amiodarone prescribed as advised by the specialist.
- Conduct the required monitoring
- Communicate any abnormal results to the specialist.
- Manage adverse effects as detailed and discuss with specialist team when required.
- Stop amiodarone and make an urgent referral to the specialist if hyperthyroidism, thyrotoxicosis, new or worsening arrhythmia or heart block, ophthalmological effects, hepatotoxicity, pulmonary toxicity or bullous skin reactions are suspected.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.

- Stop treatment as advised by the specialist.

Pregnancy, Paternal Exposure and Breastfeeding

It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

Pregnancy:

Due to the risk of neonatal goitre, amiodarone should only be prescribed in pregnancy if there is no alternative. Under these circumstances prescribing and monitoring will be the responsibility of the initiating specialist.

Breastfeeding:

Amiodarone is excreted into the breast milk in significant quantities; breast feeding is considered contraindicated due to the potential risk of iodine-associated adverse effects in the infant.

Information for healthcare professionals: https://www.sps.nhs.uk/medicines/amiodarone/

Indications for Referral to Specialist

- Stop amiodarone and make an urgent referral to the specialist if hyperthyroidism, thyrotoxicosis, new or worsening arrhythmia or heart block, ophthalmological effects, hepatotoxicity, pulmonary toxicity or bullous skin reactions are suspected.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.
- Stop treatment as advised by the specialist.

Further information and supporting documents

- British Heart Foundation – anti-arrhythmics: https://www.bhf.org.uk/informationsupport/heart-matters-magazine/medical/drug-cabinet/anti-arrhythmics
- eBNF accessed via BNF (British National Formulary) | NICE on 15/01/2021
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