NHS England Guidance: Medicines of Low Value

AMIODARONE POSITION STATEMENT

Summary

Routine initiation of amiodarone is not recommended by NHS WEL CCGs. This is in line with NHS England's (NHSE) national guidance on items which should not routinely be prescribed (1).

Amiodarone is **Amber (Specialist initiated – Primary Care to continue)** for those patients who meet criteria.

- **New Patients:** Primary Care Prescribers should not initiate amiodarone for any new patient unless there is a clear need for amiodarone to be prescribed and is undertaken in a cooperation arrangement with a multidisciplinary team including specialist cardiology input.
- **Existing patients:** All patients established on amiodarone should be reviewed for suitability of therapy. Ensure there is a clear indication for amiodarone therapy and this is documented in the patient record. Note: NICE have issued the following "Do not do" recommendation - **Do not offer amiodarone for long term rate control (in atrial fibrillation)**." If patients are taking amiodarone and in atrial fibrillation, in agreement with a Specialist, switch to an appropriate treatment option unless they meet exceptions below.
- **Exceptions:** must be initiated by a Specialist and only continued* for patients where other treatments cannot be used, have failed or is in line with NICE Guidance CG196. Treatment may also be suitable in patients prior and post cardioversion, or in specific patients who also have heart failure or left ventricular impairment. Amiodarone can be used for treating a number of arrhythmias particularly when other drugs are ineffective or contra-indicated, including paroxysmal supraventricular, nodal and ventricular tachycardias, atrial fibrillation and flutter, ventricular fibrillation, and tachyarrhythmias associated with Wolff-Parkinson-White syndrome (initiated in hospital or under specialist supervision).

NHS England category: Products of low clinical effectiveness, where there is a lack of robust evidence of clinical effectiveness or there are significant safety concerns (1).

***Disclaimer**: NHSE recommend that amiodarone should only be continued under a under a shared care arrangement. Historically in WEL CCGs, amiodarone has held amber status on the formulary (Specialist Initiated – Primary Care to continue). In consultation with Cardiology colleagues at Barts Health NHS Trust, it has been agreed at the Waltham Forest & East London Medicines Optimisation and Commissioning Committee to maintain this formulary status locally in WEL CCGs, with the development of Primary Care prescriber information to support safe prescribing and management in Primary Care (see Appendix I).

Amiodarone has an important place in the treatment of severe cardiac rhythm disorders where other treatments either cannot be used or have failed. It has potential major toxicity and its use requires monitoring both clinically and via laboratory testing (1).

Careful monitoring of amiodarone is essential; Primary Care prescriber information (see Appendix I) help clarify the responsibilities of primary care. In general, a 6 monthly review of patients is advocated (or sooner, if required). Due to the long half-life of this drug, monitoring may continue for 12 months after treatment discontinuation (2).

Amiodarone interacts with many drugs, including some commonly prescribed treatments. There is an opportunity when reviewing patients to check for use of potentially interacting drugs, and to confirm that treatment with amiodarone is still indicated (2).

Advice for Primary Care

1. Ensure there is a clear indication for amiodarone therapy and this is documented in the patient record.
2. Review all patients on amiodarone with an indication for atrial fibrillation - assess suitability of switching to an alternative if patients are taking amiodarone for rate control.
3. In agreement with Specialists in Secondary Care, de-prescribe amiodarone if not indicated. Switch all suitable patients to an appropriate treatment option.
4. If on-going treatment with amiodarone is indicated:
    - Prescribe in-line with the national recommendations
    - Monitor the patient six-monthly (or sooner, if required).
    - Check for adverse effects and signs of toxicity
    - Check the amiodarone dosage
    - Check for drug interactions

    Refer also to Primary Care Prescriber information (see Appendix I).

Resources

PrescQIPP on behalf of NHS England have developed a Patient Information Leaflet (available here).

References

1. **NHS England and NHS Clinical Commissioners.** *Items which should not routinely be prescribed in primary care: Guidance for CCGs:* NHS England, [Online] June 2019 https://www.england.nhs.uk/medicines/items-which-should-not-be-routinely-prescribed/
2. **Optum in partnership with The Centre for Medicines Optimisation at Keele University**. *ScriptSwitch Rapid Update:* New Products added to NHS England's List of 'low priority' treatments. 1 July 2019

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Appendix 1: Primary Care Prescriber Information - Amiodarone

Amiodarone is a class III antiarrhythmic drug that reduces the incidence of arrhythmias by increasing the duration and refractory period of the cardiac action potential and prolonging the QT interval. Regular monitoring is essential because it does have potentially serious side effects that can be minimised with appropriate identification and prompt withdrawal. Amiodarone has a very long half-life (mean $t_{1/2}$ 58 days [range 15-142 days]). Its effects may continue for some time (possibly months) after stopping therapy.

The routine prescribing of amiodarone is not recommended by NHS WEL CCGs. This is in line with NHS England's (NHSE) national guidance on items which should not routinely be prescribed (1). Amiodarone is Amber (Specialist initiated – Primary Care to continue) for those patients who meet the exceptionality criteria as outlined in the indication box below.

NHSE recommend that amiodarone should only be continued under a under a shared care arrangement. Historically in WEL CCGs, amiodarone has held amber status on the formulary (Specialist Initiated – Primary Care to continue). In consultation with Cardiology colleagues at Barts Health NHS Trust, it has been agreed at the Waltham Forest & East London Medicines Optimisation and Commissioning Committee to maintain this formulary status locally in WEL CCGs. This Primary Care prescriber information has been developed to support the safe prescribing and management of amiodarone in Primary Care.

For further information on the properties of amiodarone, please refer to the current Summary of Product Characteristics (www.medicines.org.uk) and BNF monograph

Indication	Route & Dose	Contraindications to amiodarone administration	Actions and Monitoring undertaken by specialist before initiation	Duration of treatment	Stopping criteria	Follow up and on-going monitoring by the GP
For the treatment of arrhythmias. Must be initiated by a Specialist and only continued for patients where other treatments cannot be used, have failed or is in line with NICE Guidance NG196. Treatment may also be suitable in patients prior and post cardioversion or in specific patients who also have heart failure or left ventricular impairment. Amiodarone should only be initiated in hospital or under specialist supervision in an out-patient setting.	Oral: 200 mg 3 times a day for 1 week, then reduced to 200 mg twice daily for a further week, followed by maintenance dose, usually 200 mg daily or the minimum dose required to control arrhythmia.	• Bradycardia <50 beats per min • Second or third degree atrioventricular block • Severe conduction disturbances or sinus node disease only use with a pacemaker • Evidence or history of thyroid dysfunction (caution) • Known hypersensitivity to iodine or amiodarone • Lactation (amiodarone is secreted in significant quantities in breast milk) • Pregnancy	• ECG • LFTs • Serum Potassium • Serum Magnesium • TSH *See table below*	Dependant on indication, can be long term	Pulmonary toxicity Alanine aminotrasferase levels ≥ 3 x upper limit of normal	See table below.

Key Safety Notices (for instance: notification if prescribing must be brand specific or BNF cautionary and advisory warnings):
MHRA/CHM advice: Sofosbuvir with daclatasvir; sofosbuvir and ledipasvir (May 2015); simeprevir with sofosbuvir (August 2015): risk of severe bradycardia and heart block when taken with amiodarone. Avoid concomitant use unless other antiarrhythmics cannot be given**.**

Amiodarone Monitoring Requirements

Summary of amiodarone monitoring					
What to monitor:		**Rationale (% risk per annum)**	**Baseline**	**Every 6 months**	**Annually**
ECG (SR / AF / other)		Assess response to treatment. Depending on indication, efficiency ranges from 50-80% long term[1]. Bradycardia is usually dose related (1-10%)[2].	✓		✓
Blood Pressure		May cause hypotension, usually during loading dose period.	✓		✓
U&Es	K^+	Deficiencies in electrolytes may precipitate arrhythmias.	✓		✓
	Mg^+		✓		✓
Thyroid function	TSH	May cause hypothyroidism or hyperthyroidism which can be fatal (1-10%)**Error! Bookmark not defined.**.	✓	✓	✓
	T_4		✓	✓	✓
	T_3		✓	✓	✓
Liver function	AST or ALT	Isolated increase in serum transaminases, usually 1.5 to 3 times normal range occurring at beginning of therapy. May return to normal with dose reduction or even spontaneously (>10%)**Error! Bookmark not defined.**. Acute liver disorders with high serum transaminases [over 3 times normal range] and/or jaundice, including hepatic failure, which can be fatal (1-10%)**Error! Bookmark not defined.**.	✓	✓	✓
Chest x-ray		Pulmonary toxicity including hypersensitivity pneumonitis, alveolar/interstitial pneumonitis or fibrosis, pleuritis, bronchiolitis obliterans organising pneumonia (BOOP)], sometimes fatal, may occur (1-10%)**Error! Bookmark not defined.**.	Undertake if clinically indicated		
Eye exam		Corneal microdeposits usually limited to the area under the pupil, usually only discernable by slit-lamp examinations (>10%)**Error! Bookmark not defined.**. If vision affected undertake an eye exam.	Undertake if clinically indicated		
Check for drug interactions		Amiodarone is metabolised via the CYP 3A4 isoenzyme and is a strong P-glycoprotein inhibitor meaning it has numerous drug interactions often requiring dose reductions**Error! Bookmark not defined.**. **Clinically important interactions (please note this is not a complete list – please refer to the current BNF or SPC for further information):** • **Drugs inducing Torsade de Pointes** or **Prolonging the QT Interval** – see SPC for further detail. • **Warfarin** - amiodarone potentiates effect. Interaction reaches its peak effect after about six weeks and may persist for a month or more after amiodarone withdrawn. Reduce warfarin dose by 30-50%. Check INR weekly during first 6 weeks of treatment. • **Digoxin** – amiodarone increases plasma levels. Dose reductions of up to 50% usually required. • **Verapamil** – amiodarone increases levels. Reduce verapamil dose. • **Simvastatin & Atorvastatin** – increased incidence of myopathy. Simvastatin - restrict daily dose to 20mg. Atorvastatin - restrict daily dose to 40mg. • **DOACs (Apixaban, Dabigatran, Edoxaban, Rivaroxaban)** – may cause moderate increase in levels of DOACs. Use with caution and consider dose reduction of DOAC. • **Ciclosporin, tacrolimus, theophylline** – amiodarone increases plasma levels. • **Grapefruit/grapefruit juice –** increases amiodarone plasma levels. Avoid large quantities.			

[1] Connolly SJ. Evidence-Based. Analysis of Amiodarone Efficacy and Safety (1999) *Circulation* **100**:2025-2034
[2] Summary of Product Characteristics, Amiodarone 100mg tablets, Accord Healthcare ltd https://www.medicines.org.uk/emc/product/6019/smpc# last updated 17/05/2017, accessed 19/05/2021

Key: SR - sinus rhythm, AF - atrial fibrillation, U&Es - urea and electrolytes, K^+ - potassium, Mg^+ - magnesium, TSH - thyroid stimulating hormone, T_4 - levothyroxine, T_3 - triiodothyronine, AST - aspartate transaminase, ALT - alanine transaminase

Document Management

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