Amiodarone

Traffic light classification- Amber 1
Information sheet for Primary Care Prescribers
RMOC have produced documentation for standardising the shared care of amiodarone but the final version is yet to be published. Once this is available we will adapt our protocol to the format recommended by RMOC.

Licensed Indications
Atrial flutter and fibrillation and tachyarrhythmias of paroxysmal nature including, supraventricular, nodal and ventricular tachycardias; ventricular fibrillation when other medicines cannot be used.
Tachyarrhythmias associated with Wolff-Parkinson-White syndrome.

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 testing.

Medicines Initiation
Amiodarone is suitable for prescribing in primary care following specialist recommendation or initiation.

Products available
Amiodarone is available generically, as 100mg and 200mg tablets.

Dosages and route of administration
When given orally amiodarone is given as 200mg three times a day for 1 week, then 200mg twice a day for 1 week, then 200mg daily or the minimum required to control the arrhythmia.

Duration of treatment
Treatment is potentially lifelong.

Monitoring Requirements and Responsibilities for primary care

Pre-treatment testing is the responsibility of the initiating specialist and should include TFTs (T4, T3 and TSH), LFTs, U&E, ECG and potassium level and Chest X-ray.

Ongoing monitoring in primary care:

Frequency	Required tests					
	TFTs*	LFT	U&E	Chest X ray	ECG	Opthalm-ological
6 monthly	✓	✓	✓			
12 monthly				✓	✓	✓**

Also ask about breathlessness and non-productive cough, relating to possible pulmonary toxicity, at each review visit

*TFTs should be measured for up to 12 months following discontinuation **(amiodarone has a half-life of 20 to 100 days).** Serum TSH should be measured when thyroid dysfunction is suspected.
** And any time that new or worsening visual symptoms occur (a common side effect is a "blue halo" effect when looking into bright lights at nightime). Encourage patient to attend optometrist annually.

In warfarinised patients, more frequent monitoring of INR is required during initiation or dose change of amiodarone until INR is stable and for at least 6 weeks after stopping amiodarone treatment; initially weekly for the first 7 weeks of treatment or until INR stable. The dose of warfarin required may be around one-third less than without amiodarone treatment.

Explicit criteria for review and discontinuation of the medicine

Due to the long half-life of amiodarone, clinical problems (e.g. hyperthyroidism, photosensitivity) may occur/ persist for up to a year after stopping the medication. In case of amiodarone toxicity refer to the appropriate specialists for further assessment and get back to the initiating cardiologist for antiarrhythmic review.

Adverse effect	Frequency of adverse effect (%)	Investigation & Diagnosis	Treatment
Pulmonary toxicity (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.
Hyperthyroidism	2	Free T4, T3, TSH	If TFTs are borderline repeat test in 6 weeks. Amiodarone-associated hyperthyroidism should be diagnosed only if high circulating free T4 is associated with high or high/normal free T3 and undetectable TSH; refer immediately to initiating specialist/ endocrinologist.
Hypothyroidism	6	Free T4, T3, TSH	Diagnosis of hypothyroidism following development of symptoms is supported by increase in TSH and an exaggerated TSH response to Thyrotropin-releasing hormone (TRH); also T3 and T4 levels may be low. If deranged, refer to initiating specialist/

			endocrinologist.
Liver toxicity	1	LFTs	If deranged, stop and refer immediately to initiating specialist/gastroenterology.
Optic neuropathy	0.13	Ophthalmologic examination	If optic neuropathy/neuritis is suspected, refer urgently to ophthalmology and discuss the possibility of stopping amiodarone & alternative antiarrhythmic therapy with patient's cardiologist
Pro-arrhythmia	<1	ECG	Stop amiodarone, refer to initiating cardiologist
Tremor	<10	History and clinical examination	Reduce dosage or withdraw if possible
Peripheral Neuropathy Myopathy	<1	History and clinical examination	Usually reversible on withdrawal of the medicine
Bradycardia	2-4	Examination, ECG	If severe, discuss with cardiologist whether to stop amiodarone or insert pacemaker
Nausea, anorexia	30	History + examination	Reduce dosage
Corneal micro-deposits	>90	Slit-lamp examination	None. Most patients on amiodarone develop corneal microdeposits (reversible on withdrawal of treatment) which rarely interfere with vision but drivers may be dazzled by headlights at night.
Photosensitivity	4-9	History, examination	Shield skin from light during treatment and for several months after discontinuing amiodarone and to use a wide-spectrum sunscreen to protect against both long UV and visible light
Blue discolouration of skin	<9	Examination	Reduce dosage if possible

Contraindications

- Pregnancy and lactation.
- Sinus bradycardia and sino-atrial heart block: In patients with severe conduction disturbances (high grade AV block, bifascicular or trifascicular block) or sinus node disease, amiodarone should be used only in conjunction with a pacemaker.
- Evidence of history of thyroid dysfunction: Thyroid function tests should be performed prior to therapy in all patients.
- Known hypersensitivity to iodine or to amiodarone, or any of the excipients.

- Patients with the rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take amiodarone

Relevant Precautions

- **Heart failure** -caution should be exercised as heart failure may be worsened.
- **ECG changes** –Treatment should be discontinued in cases of onset of second or third-degree AV block, sino-atrial block, or bifascicular block.
- **Elderly patients** may be more susceptible to bradycardia and conduction defects if too high a dose is employed
- **Cardiac disorders** – Amiodarone may increase the defibrillation threshold and/or pacing threshold in patients with an implantable cardioverter defibrillator or pacemaker, which may adversely affect the efficacy of the device. Regular tests are recommended to ensure the proper function of the device after initiation of treatment or change in posology.

Clinically relevant medicine interactions and their management
Due to the long half-life of amiodarone, the onset of drug interactions may be slow after initiating amiodarone, and interactions may be observed for several months after discontinuation of amiodarone.

- **Grapefruit juice** inhibits cytochrome P450 3A4 and may increase the plasma concentration of amiodarone, so should be avoided during treatment with amiodarone.
- **Warfarin** – dose should be reduced and INR more frequently monitored required (see monitoring requirements)
- **Phenytoin** – Dose should be reduced if signs of overdose appear, plasma levels may be measured.
- **Digoxin** –Amiodarone may increase plasma digoxin levels. Clinical, ECG and biological monitoring is required and digoxin dosage should be halved.
- Combined therapy with drugs known to **prolong the QT interval** is contra-indicated due to the increased risk of torsades de pointes, such as:
    - Class 1a anti-arrhythmics e.g. quinidne, procainamide, disopyramide
    - Class III anti-arrhythmics e.g. sotalol, bretylium
    - Intravenous erythromycin, co-trimoxazole or pentamidine injection
    - Some anti-psychotics e.g. chlorpromazine, thioridazine, fluphenazine, pimozide, haloperidol, amisulpride and sertindole
    - Lithium and tricyclic anti-depressants
    - Certain antihistamines e.g. terfenadine, astemizole, mizolastine
    - Anti-malarials e.g.quinine, mefloquine, chloroquine, halofantrine
    - Moxifloxacin
- Combination with the following drugs is not recommended;
    - **Beta blockers, verapamil and diltiazem**- potentiation of negative chronotropic properties
    - **Stimulant laxatives** –risk of hypokalaemia
    - **Fluouroquinolones**- risk of QTc prolongation
- Co-administration of amiodarone with other drugs known to prolong the QT interval (e.g clarithromycin) must be based on a careful assessment of risks vs benefits- monitor for QT prolongation.

- Caution should be exercised in **drugs which may cause hypokalaemia and/or hypomagnesaemia** (increasing the risk of Torsades de Pointe).
- **Flecainide** – Amiodarone increases plasma levels - flecainide dose may be reduced by 50%.
- **Antivirals**- co-administration of amiodarone with sofosbuvir in combination with another HCV direct acting antiviral (such as daclatasvir, simeprevir, or ledipasvir) is not recommended as it may lead to serious symptomatic bradycardia.
- Drugs metabolised by **cytochrome P450 3A4** e.g. ciclosporin, tacrolimus, sildenafil and statins may reach higher concentrations if co-administered with amiodarone, which may lead to possible toxicity. Maximum recommended dose of **simvastatin** is 20mg od when used with amiodarone**.**

For further information on contraindications, precautions, adverse effects and interactions refer to the BNF or Summary of Product Characteristics for amiodarone, available at https://www.medicines.org.uk/emc.

Information given to patient

- Patient information leaflet available at https://www.medicines.org.uk/emc
- Patients should be informed that they will require 6 monthly blood tests while taking the medication.
- Patients should be informed of possible side effects.
- Patients should be advised to promptly report any unexplained dry cough and/or shortness of breath or any new or worsening visual symptoms.
- Patients should be advised to keep out of direct sunlight and to use a high factor, wide-spectrum sunscreen while taking amiodarone and for a few months after finishing taking it.
- Patients should be advised to avoid consuming grapefruit juice whilst taking amiodarone.

References

1. Cordarone 100mg tablets- Zentiva. Summary of Product Characteristics [14/10/2020] on Electronic Medicines Compendium: (accessed on 05.08.2021) via www.medicines.org.uk/
2. Atrial fibrillation: diagnosis and management. NICE clinical guideline 196 (30 June 2021). Available: Overview | Atrial fibrillation: diagnosis and management | Guidance | NICE
3. NHS England Items which should not routinely be prescribed in primary care: guidance for CCGs, June 2019. Available: items-which-should-not-routinely-be-prescribed-in-primary-care-v2.1.pdf (england.nhs.uk)
4. BNF Online, Available A to Z of Drugs | BNF content published by NICE, accessed [05.08.21]

Version Control- **Guideline title**			
Version	Author(s)	Date	Changes
1.1	Irina Varlan	05.08.2021	The Amiodarone information sheet was adapted into a SCP. No changes in monitoring. Awaiting final RMOC SCP for amiodarone to align local protocol.