Prescribing guidance - Amiodarone

Drug	Amiodarone
Specialty	Cardiology/Cardiac Surgery
Indication	Used in the prevention of life threatening arrhythmias or to maintain sinus rhythm in patients with atrial fibrillation (AF), particularly when other drugs are ineffective or contraindicated. In secondary care, amiodarone may be: ▪ administered intravenously for life threatening tachyarrhythmias ▪ given orally as treatment for or prophylaxis against AF following cardiac surgery It should only be initiated in hospital or under specialist supervision in an out-patient setting.
Background	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.
Contra-indications to amiodarone administration	Sinus bradycardia 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
Before initiation	Baseline assessments to be carried out by Consultant <u>before</u> initiation: ECG LFTs Serum Potassium Serum Magnesium TSH Chest X Ray taken within previous 3-6 months
Dose	200mg three times a day for one week, then 200mg twice a day for one week then 200mg once a day or the minimum required to control arrhythmia thereafter. In hospital, higher loading dose regimens may be used for patients with VT. Amiodarone is available as 100mg and 200mg scored tablets.
Clinically important interactions	Amiodarone is metabolised via the CYP3A4 isoenzyme and is a strong P-glycoprotein inhibitor meaning it has numerous drug interactions often requiring dose reductions. Please note this is not a complete list – please refer to the current BNF or SPC for further information. ▪ **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 Interaction reaches its peak effect after about six weeks and may persist for a month or more after amiodarone withdrawn.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 <u>weekly</u> 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. ▪ **NOACs** (Apixaban, Dabigatran, Edoxaban, Rivaroxaban) – may cause moderate increase in levels of NOACs. Use with caution and consider dose reduction of NOAC. ▪ **Ciclosporin, tacrolimus, theophylline** – amiodarone increases plasma levels. ▪ **Grapefruit/grapefruit juice** – increases amiodarone plasma levels. Avoid.
Patient education	It is essential that patients are aware of the possible adverse effects of amiodarone as well as the benefits. Consider giving them the “Information for patients and carers” leaflet.

Monitoring

	Rationale	Baseline	After loading	At 6 months	Annually	Every 6 months
ECG (SR/AF/other)	Assess response to treatment. Depending on indication efficacy ranges from 50 to 80%.	✓	✓		✓	
Heart rate	Bradycardia is usually dose related (1-10%).	✓	✓		✓	
Blood pressure	May cause hypotension, usually during loading dose period.	✓	✓		✓	
U&Es (K/Mg)	Deficiencies may precipitate arrhythmias.	✓	✓		✓	
Thyroid function (TSH/T4/T3)	May cause hypothyroidism or hyperthyroidism which can be fatal (1-10%).	✓	✓	✓	✓	✓
Liver function (ALT or AST)	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%). Acute liver disorders with high serum transaminases [over 3 times normal range] and/or jaundice, including hepatic failure,which can be fatal (1-10%).	✓		✓	✓	✓
Chest X ray	Pulmonary toxicity including hypersensitivity pneumonitis, alveolar/interstitial pneumonitis or fibrosis may occur (1-10%)	✓	Repeated if clinically indicated			
Eye examination	Corneal microdeposits usually limited to the area under the pupil, Usually only discernable by slit-lamp examinations (>10%).If vision affected undertake a complete eye exam.	Complete full eye examination 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	✓	Repeat if new agents added to patients usual prescription			

Adverse events

Adverse Event	Incidence	Diagnosis	Action required
Bradycardia	1-10%	Exam & ECG	If severe stop amiodarone or insert pacemaker.
Pro-arrhythmia	<1%	ECG	Stop amiodarone.
Hypothyroidism	1-10%	Free T_4, TSH	Refer to local protocols. Consider levothyroxine.
Hyperthyroidism	2%	Free T_4, TSH	Refer to local protocols. Consider initiating anti-thyroid drug therapy and consider stopping amiodarone.
Liver disorders	1%	LFTs > 3 x ULN	Consider stopping amiodarone.
Pulmonary toxicity	2-17%	CXR & PFTs	Stop amiodarone, Consider corticosteroid therapy.
Corneal micro-deposits	>90%	Slit-lamp examination	Usually harmless. Refer to ophthalmologist if visual disturbance develops. Advise patient not to drive.
Optic neuropathy	Unknown	Ophthalmological examination	Consider stopping amiodarone.
Gastrointestinal symptoms, nausea	30%	History & examination	Reduce dosage.
Photosensitivity	4-9%	History & exam	Use sunblock (SPF>15).
Rashes, blue discolouration of skin	<9%	Examination	Reduce dosage.
Peripheral neuropathy	Unknown	History & exam	Consider stopping amiodarone.
Disturbed sleep, insomnia, nightmares	Unknown	History	Reduce dosage.
Vertigo	Unknown	History	Reduce dosage. Advise patient not to drive.

Further Information

Connolly SJ. Evidence-Based. Analysis of Amiodarone Efficacy and Safety (1999) *Circulation* **100**:2025-2034.