

## AMIODARONE (Adults) – Prescribing Support (June 2015 updated March 2016)

- Treatment should be initiated only under hospital or specialist supervision.
- Monitor for signs of pulmonary toxicity:
  - Dyspnoea, non-productive cough and deterioration in general health.
  - Refer urgently to specialist if pulmonary toxicity suspected
- Check for drug interactions even after amiodarone is stopped (average half life = 50 days)
- 6 monthly monitoring : U&Es, LFTs, TFTs, adverse effects

### Licensed Indication

Oral amiodarone is indicated for the treatment of severe cardiac rhythm disorders when other drugs are ineffective or contra-indicated including:

- 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.
- Tachyarrhythmias associated with Wolff-Parkinson-White syndrome.

Treatment should be initiated only under hospital or specialist supervision. Clear information must be provided by the hospital specialist to the GP including:

### Dosage

**Loading dose:** 200 mg THREE times daily for 1 week reduced to 200 mg TWICE daily for a further week.

**Maintenance dose:** Usually 200 mg ONCE daily thereafter or the minimum effective dose required to control the arrhythmia (100mg daily may be sufficient in elderly patients). In rare cases a maintenance dose of above 200mg may be required.

### Contraindications

- Sinus bradycardia and sino-atrial heart block. In patients with severe conduction disturbances or sinus node disease, amiodarone should be used only in conjunction with a pacemaker.
- Evidence of history of thyroid dysfunction or known hypersensitivity to iodine or to amiodarone.
- Combination with drugs which may induce Torsades de Pointes.
- Pregnancy - except in exceptional circumstances.
- Breastfeeding.

### Drug interactions

Consult the latest edition of the British National Formulary: <https://www.medicinescomplete.com/mc/bnf/current/> or Summary of Product Characteristics (SmPC) for full details: <https://www.medicines.org.uk/emc/medicine/25742>

Amiodarone has a long half-life (average half life of 50 days). There is potential for drug interactions to occur several weeks or months after stopping treatment. Amiodarone is metabolised by the cytochrome P450 system and therefore has the potential to cause many drug interactions. Specialist advice may be required when changing prescribing of interacting drugs:

Drug/Therapeutic group	Interaction
<b>Statins</b>	Increased risk of myopathy, restrict simvastatin dose to 20mg daily
<b>Anticoagulants</b>	Enhanced anticoagulant effect of warfarin, phenindione and dabigatran. Consider warfarin dose reduction and monitor patient closely
<b>Digoxin</b>	The dose of digoxin should be reduced by between 30% to 50% when co-prescribed with amiodarone and further dose adjustments depending on digoxin levels
<b>Grapefruit</b>	May increase the plasma concentration of amiodarone
<b>Diltiazem, verapamil, beta-blockers, antivirals: simeprevir and sofosbuvir, daclatasvir and fixed dose combination sofosbuvir + ledipasvir.</b>	Increased risk of bradycardia, AV block and myocardial depression
<b>Antiepileptic</b>	Metabolism of phenytoin is inhibited which can increase plasma concentrations. Consider reducing phenytoin dose and and monitor patient closely.

<b>Drugs that prolong the QT interval</b>	Amiodarone prolongs the QT interval and concurrent treatment with other drugs known to prolong the QT interval is contraindicated due to the increased risk of Torsades de Pointes Anti-arrhythmics, anti-psychotics, antihistamines, anti-malarials. Lithium, tricyclic anti-depressants. IV erythromycin, moxifloxacin co-trimoxazole or pentamidine
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### Adverse effects

Amiodarone can cause serious adverse effects affecting the lung, liver, thyroid gland, heart, eyes, skin or peripheral nervous system. Most adverse effects are seen with long term use and may therefore present first to GPs. Symptoms suggestive of pulmonary toxicity or hyperthyroidism require urgent specialist referral.

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### Adverse effects (Continued)

System	Adverse effect
<b>Gastrointestinal</b>	Nausea and vomiting and taste disturbance
<b>Eye disorders</b>	Corneal micro deposits are common and are associated with coloured halos in dazzling light or blurred vision which may affect driving at night. Discontinuation of amiodarone is not required. Refer for a specialist opinion if visual disturbances.
<b>Skin</b>	Photosensitivity is common and may persist after amiodarone is stopped due to its long half life. Advise patients to avoid exposure to direct sunlight and to use protective measures e.g. total sun block or protective clothing. Amiodarone may cause blue grey skin discolouration which slowly reverses after treatment is stopped
<b>Respiratory</b>	Onset of dyspnoea or non-productive cough may be related to pulmonary toxicity. Presenting features can include non-productive cough and deterioration in general health (fatigue, weight loss and fever). Refer urgently if no clear cause for cough or SOB or if pulmonary toxicity is suspected.
<b>Liver</b>	Amiodarone may be associated with cirrhosis, hepatitis, jaundice and hepatic failure. Monitor liver function tests routinely (see monitoring section).
<b>Endocrine</b>	Both hyperthyroidism and hypothyroidism can occur during or soon after treatment is started because of the iodine content in amiodarone. <b>Hypothyroidism:</b> Amiodarone may need to be withdrawn or the dose reduced and/or levothyroxine treatment started. <b>Hyperthyroidism:</b> May occur during amiodarone treatment or, up to several months after discontinuation.
<b>Cardiovascular</b>	Too high a dosage may lead to severe bradycardia and to conduction disturbances with the appearance of an idioventricular rhythm, particularly in elderly patients or during digitalis therapy. In these circumstances, amiodarone treatment should be withdrawn.

### Monitoring

**Results outside the local laboratories 'normal' range** should trigger a consultation with a specialist or referral back to secondary care, for patient review and where necessary a change of therapy or dose.

The following should be checked at baseline by the initiating specialist or hospital and then every 6 months in primary care by the patient's GP:

- **History and Examination (H&E)** – baseline and annually.
- **H&E relating to adverse effects-** Ask about breathlessness and non-productive cough, relating to possible pulmonary toxicity at each review visit.
- **Thyroid Function Test:**
  - If TFTs are borderline repeat test in 6 weeks.
  - Thyroid stimulating hormone (TSH) monitor at baseline, every 6 months thereafter, if thyroid dysfunction is suspected and for up to 12 months after discontinuation. If TSH is abnormal measure Free T4 and T3.
  - *Hyperthyroidism* diagnosed if high free T4 associated with high or high/normal free T3 and undetectable TSH – prompt withdrawal of amiodarone and specialist referral.
  - *Hypothyroidism* supported by increase in TSH and an exaggerated TSH response to TRH; also T3 and T4 levels may be low.
- **U&Es (serum K)**

- **LFTs (ALT)** – discontinue treatment if severe liver function abnormalities or clinical signs of liver disease develop.
- **Chest X-ray** at baseline (also see below).
- **Heart rate & ECG** at baseline then annually.
  - Amiodarone induces ECG changes: QT interval lengthening corresponding to prolonged repolarisation with the possible development of U-waves and deformed T-waves; these changes are evidence of its pharmacological action and do not reflect toxicity.
  - Treatment should be discontinued in case of onset of 2nd or 3rd degree A-V block, sino-atrial block or bifascicular block.

The following are also recommended as and when necessary based on other medications or presenting symptoms.

- **Digoxin level** (if on digoxin) - assess serum digoxin level if dose increased or toxicity is suspected.
- **INR** (if on warfarin) - monitor INR levels, adjust warfarin dose accordingly.
- **Refer urgently to specialist - if pulmonary toxicity suspected**
- **Eye examination** - assess if new or worsening visual symptoms occur e.g. blurred or decreased vision  
Appearance of optic neuropathy and/or optic neuritis requires amiodarone withdrawal due to the potential progression to blindness

### References

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