MIL

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This Medicines Information Leaflet is produced locally to encourage prescribing which is cost effective to the NHS. Information will be given on quality improvement issues and the costs to hospital and community.

Guidelines for Prescribing & Administration of Amiodarone in Adults

Amiodarone is an effective but complex anti-arrhythmic drug.[1] In addition to Class III effects (prolongation of the action potential across cardiac tissue) amiodarone has weak activity affecting calcium channels and alpha and beta adrenoceptors.[1,2] Amiodarone should be initiated only under hospital or specialist supervision,[3] which may include initiation by GPs under direction of a Cardiologist and a Shared Care Protocol.

Indications for use

Amiodarone is indicated for use in the treatment of severe cardiac rhythm disorders **not responding to other therapies or when other treatments cannot be used**.[4] Specific licensed indications for both oral and intravenous amiodarone include:[4]

- Ventricular tachycardia
- Refractory atrial fibrillation (and certain forms of pre-excited atrial fibrillation)
- Severe cardiac rhythm disorders when other drugs cannot be used (on advice of Cardiology only)

In addition, the intravenous injection of amiodarone may be used in cardiopulmonary resuscitation for defibrillation-resistant ventricular fibrillation (see overleaf).

When to use IV or ORAL therapy

Amiodarone should be administered **orally**, using the loading regime below, unless the patient is acutely unwell. Intravenous amiodarone can be used acutely when a rapid response is required until the patient's cardiac rhythm is stabilised and oral therapy can be initiated.[2,4] Oral therapy should be initiated concomitantly at the usual **loading** dose (see Dose & Administration table) and IV therapy phased out gradually allowing an overlap period of at least 24 hours. Absorption of oral amiodarone is slow and elimination relatively fast initially so the overlap is to avoid a significant fall in levels.[6]

If patients are unable to take medicines orally, the IV maintenance dose is about 50% of the oral maintenance dose.[6] If the patient is only partially loaded orally it is necessary to give the full IV loading dose.[6]

Contraindications & cautions

- Avoid in sinus bradycardia or AV block;
- Avoid in severe arterial hypotension;
- Avoid in severe conduction disturbances or sinus node disease **unless** a pacemaker has been fitted;
- Avoid in thyroid dysfunction;
- Avoid in iodine sensitivity (56mg iodine per ampoule);
- Use with caution in combination with any other drugs which may prolong the QT interval (eg.tricyclic antidepressants)

None of the above apply to the use of amiodarone for cardiopulmonary resuscitation of shock resistant ventricular fibrillation. Before surgery, the anaesthetist should be informed that the patient is taking amiodarone.

Dose & Administration

ORAL	
➢ Loading	The recommended oral loading regime for amiodarone is:[3,4] 200mg TDS for 7 days Then 200mg BD for 7 days
➢ Maintenance	200mg daily Consider reducing the dose to 100mg daily once the patient is stabilised, if sufficient to control the arrhythmia
➢ Accelerated loading	For ventricular arrhythmias only: 400mg TDS for 7 days then maintenance dosing as above
INTRAVENOUS	
➢ Route	IV amiodarone is irritant and needs to be given via the **central** IV route except in an emergency***** (see below)
➢ Loading	Initial dose of 5mg/kg in 250ml glucose 5% infused over 20 minutes to 2 hours[1,3,4,8]
➢ Maintenance	If necessary (according to response) this may be followed by repeat infusions up to a total dose of 1200mg over 24 hours[1,3,4,8] Thereafter administer every 24 hours
➢ Compatible fluids	Amiodarone **must only** be diluted in **glucose 5%**; do not use sodium chloride 0.9%.[3,4,8] Flush with glucose 5%
➢ Concentration	Do not dilute to less than 0.6mg per ml (at least 150mg in 250ml) as stronger solutions are more stable[9]
➢ Fluid restriction	If the patient is fluid restricted and has a central line, concentrations of up to 15-18mg per ml have been used in critical care areas.[8,9]
➢ Giving set	Must be given via rate-controlled pump
➢ Monitoring	ECG and blood pressure monitoring is required during IV administration; hypotension & bradycardia risk[1,3,4,8]

***PERIPHERAL IV ADMINISTRATION**

Intravenous amiodarone should be administered centrally. Amiodarone given peripherally may result in serious tissue damage.[4] In exceptional situations where placement of a central line is not possible, is high risk or will delay vital treatment, a

peripheral vein with good blood flow (such as the antecubital fossa) may be used via a large bore cannula or long line. Under no circumstances administer more than 2mg per ml by the peripheral IV route. Peripheral administration **must not** be continued beyond 24 hours.

Recommended monitoring

Prior to starting treatment with amiodarone the following baseline monitoring should be carried out:[3,4]

- Liver function (LFTs)
- Thyroid function (tri-iodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH) should all be measured)
- Chest X-ray
- Serum potassium
- Blood pressure and heart rate and rhythm

The baseline results must be communicated to the GP on discharge for comparison with future results. Liver and thyroid function (preferably free T4, free T3 and TSH) should then be monitored every 6 months. A chest X-ray should be performed if the patient complains of persistent cough or breathlessness and specialist referral undertaken if there is a suspicion of amiodarone-induced lung disease.

Interactions with other medicines

Amiodarone has the potential to interact with many medicines, either by competing for metabolism via the same liver enzymes or due to additive side effects (see below). It is **always** recommended to check for interactions when prescribing amiodarone. Following chronic therapy the elimination half-life of oral amiodarone is approximately 60 days[5] therefore interactions may persist for up to 16 weeks after the amiodarone has been stopped.[7]

Adverse effects

Amiodarone is a potentially toxic but very effective drug.[2] It is highly protein bound (more than 95%), is extensively distributed into body tissues and accumulates in muscle and fat.[1] Adverse effects are common but many are dose-related so the lowest effective dose should be used to minimise the risk.[1,2]
Side effects of amiodarone include:[3,4]

- Nausea, vomiting and taste disturbances;
- Photosensitivity is common and patients should be advised to avoid direct exposure to the sun, wear hat, shirt and shorts as minimal attire in the sun and use a high sun-protection factor on exposed areas particularly the scalp, face and arms; phototoxicity can also occur. With prolonged use, persistent slate-grey skin discoloration can occur;
- Jaundice and altered LFTs (particularly raised transaminases which may require dose reduction or withdrawal if accompanied by acute liver disorders); *very rarely* chronic liver disease including cirrhosis;
- Bradycardia; *less commonly* onset or worsening of arrhythmia & conduction disturbances;
- Hypotension (usually moderate or transient). Cases of hypotension or collapse have been reported following overdosage or too rapid injection;
- Pulmonary toxicity (eg. interstitial pneumonitis and fibrosis);
- Tremor & sleep disorders; *less commonly* peripheral neuropathy and myopathy (usually reversible on withdrawal); be aware of possible ophthalmic neuropathy;
- Hypothyroidism or hyperthyroidism; thyrotoxicosis can occur up to 6 months after amiodarone has been stopped;
- Reversible corneal microdeposits (sometimes night glare);
- Injection site reactions such as pain, erythema, oedema, necrosis, extravasation, infiltration, inflammation, induration, thrombophlebitis, phlebitis, cellutitis, infection, pigmentation changes (often following **peripheral** IV administration).

References:

1. Sweetman SC (Ed). Martindale: The Complete Drug Reference. 36th Ed. Accessed via www.medicinescomplete.com October 2011.
2. McEvoy GK (Ed). American Hospital Formulary Service (AHFS) Drug Information. Accessed via www.medicinescomplete.com October 2011.
3. British National Formulary (BNF) 61. British Medical Association & the Royal Pharmaceutical Society of Great Britain. March 2011.
4. Cordarone X (Amiodarone) Intravenous (Sanofi-Aventis). Summary of Product Characteristics (SPC). Accessed via www.medicines.org.uk October 2011.
5. Dollery C (Ed). Therapeutic Drugs. 2nd Ed. UK 1999.
6. Personal communication. Lisa Thorpe. Sanofi-Aventis Medical Information Department. September 2011. *In confidence.*
7. Stockley IH. Drug Interactions. 9th Ed. Uk 2010.
8. University College London Hospitals. Injectable Drug Administration Guide 3rd Ed 2010.
9. UKCPA Critical Care Group: Minimum Infusion Volumes for Fluid Restricted Critically Ill Patients, 3rd Ed 2006.

Emergency Use in Cardiopulmonary resuscitation only**:**

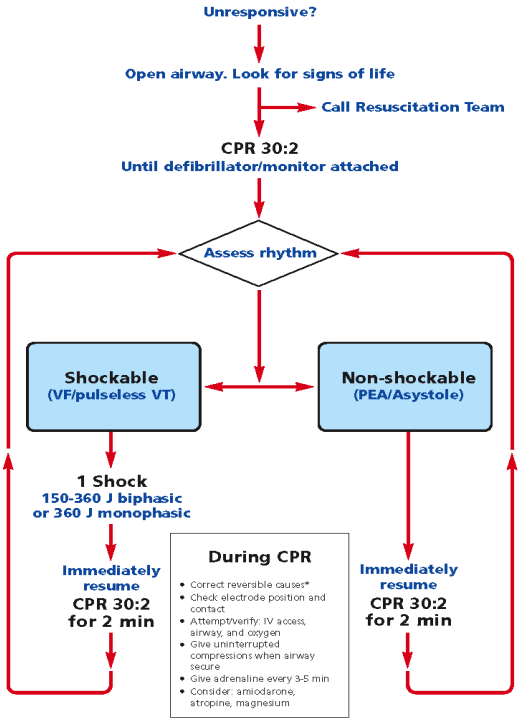
To treat ventricular fibrillation or pulseless ventricular tachycardia in cardiac arrest **refractory to defibrillation**, after adrenaline consider:[3]

- 150-300 mg intravenous injection of **amiodarone** (from a prefilled syringe *or* diluted to 10-20ml in glucose intravenous infusion 5%)[1,3,4,8]
- Inject rapidly over **at least** 3 minutes[1,3,4,8]
- An additional 150 mg (or 2.5 mg/kg body-weight) IV dose may be considered after 15 minutes if ventricular fibrillation persists[1,4,8]
- This may be followed by an infusion of 1 mg/minute for 6 hours and then 500 micrograms/minute, up to a total maximum daily dose of 2 g[1]

See below for Adult Advanced Life Support Algorithm

Note: IV Amiodarone is not effective at terminating sustained monomorphic ventricular tachycardia. IV Lidocaine or DC cardioversion are the treatments of choice.

ADULT ADVANCED LIFE SUPPORT ALGORITHM



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