MONOGRAPH

AmiODAROne

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	Intravenous – PCC, Theatre, Emergency Department Oral – All clinical areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

Dosage/Dosage Adjustments/ Administration	Preparation	Compatibility	Monitoring

DRUG CLASS

Amiodarone is a class III anti-arrhythmic drug [1].

Amiodarone is a High Risk Medicine.

amiODAROne may be confused with amLODIPine. Double check medication.

INDICATIONS AND RESTRICTIONS

For use under the direction of a cardiologist in emergency medicine and critical care areas.

Treatment or prophylaxis of severe tachyarrhythmias refractory to other treatment (e.g. supraventricular nodal, ventricular, junctional ectopic or paroxysmal supraventricular tachycardia, atrial flutter and fibrillation)[1-3]

CONTRAINDICATIONS[1, 3, 4]

- Hypersensitivity to amiodarone or any component of the formulation.
- Known iodine hypersensitivity (may not be applicable to patients with shellfish or contrast media allergy, as these allergies are generally not due to iodine)
- Cardiogenic shock

- Second- or third-degree heart block (without pacemaker)
- Symptomatic bradycardia (without pacemaker)
- Sick sinus syndrome (without pacemaker)

PRECAUTIONS[1, 4]

- Thyroid dysfunction including goitre or nodules – increases risk of hypo- or hyperthyroidism
- Electrolyte disturbances (e.g., hypokalaemia, hyperkalaemia, hypomagnesaemia) – increased risk of arrythmias; correct before starting treatment where possible
- Wolff Parkinson White Syndrome (WPW) with pre exited atrial fibrillation/flutter
- Pre-existing pulmonary disease – less reserve to cope with pulmonary adverse effects
- Concomitant administration with drugs that prolong the QT interval – increased risk of arrhythmia
- Check QT interval is <500 milliseconds before use – may increase risk of arrhythmia by prolonging the QT interval
- Formulations containing benzyl alcohol may be associated with “gasping syndrome” in neonates (>99 mg/kg/day of benzyl alcohol), use with caution in this patient subgroup
- Significant drug interactions exist which may require dose adjustments. Refer to Interactions

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

IV

- Amiodarone 150 mg/3 mL Ampoule (Benzyl alcohol content 60.6 mg per ampoule[5])

Oral

- Amiodarone 100 mg tablet
- Amiodarone 5 mg/mL suspension (Extemporaneous preparation – Restricted to patients where tablet is not suitable or contraindicated; to be supplied at clinical pharmacists’ discretion).

Imprest location: Formulary One

DOSAGE, DOSAGE ADJUSTMENTS

IV Amiodarone must only be administered in a critical care setting e.g. NICU, PCC, Theatre, Emergency Department.

Neonates: Refer to Neonatal Medication Protocols

Dosing in Overweight and Obese Children: Dose based on measured body weight

Treatment of shock resistant ventricular arrythmias during cardiopulmonary resuscitation (shockable rhythms)

Intravenous (IV) or Intraosseous (IO)

- Children ≥4 weeks – 18 years: 5 mg/kg (maximum 300 mg) as a rapid bolus after the 3rd shock[3, 4, 6, 7].
  - Dose may be repeated after the 5th shock. In acute treatment, dose can be repeated if required up to a cumulative maximum of 15 mg/kg/DAY or 900 mg/DAY whichever is less.
  - Cumulative maximum of 15 mg/kg/DAY or 900 mg/DAY whichever is less.

Serious tachyarrhythmias (e.g. supraventricular tachycardia, junctional ectopic tachycardia, paroxysmal supraventricular tachycardia)

IV infusion children ≥4 weeks – 18 years

- ***Loading dose***: 5 mg/kg (Maximum 300 mg) [3, 4, 6, 10].
  - Additional loading dose of 1 – 5 mg/kg may be repeated if required.
  - Maximum cumulative loading dose in acute treatment is 15 mg/kg/DAY or 900 mg/DAY whichever is less[3, 4].
  - *Following loading dose, a continuous intravenous infusion may be initiated.*

- **Continuous infusion:** dosing is in microg/kg/**minute**, initiate only if required.
  - Initial 5 microg/kg/**minute** increase as needed up to a maximum of 15 microg/kg/minute[3, 4, 6, 10].
  - Maximum of 1200 mg/**DAY**[6, 10, 11].
  - Wean IV infusion as soon as clinically appropriate and switch to oral therapy if required[4].

Oral

An oral loading dose is required unless duration of IV therapy is more than 2 weeks. Oral and IV therapy can be given concurrently if required for a few days[8].

- ***Children ≥4 weeks – 12 years:*** Initially 5 mg/kg (maximum 200 mg) TWICE daily for 7 – 10 days, then 5 mg/kg (maximum 200 mg) ONCE daily thereafter[4, 6]. Aim to titrate to the lowest effective dose once symptoms are controlled.

- ***Children > 12 years:*** Initially 200 mg THREE times a day for 7 days, then 200 mg TWICE a day for 7 days, then reduce to 200 mg ONCE daily thereafter[4, 6].
  Aim to titrate to the lowest effective dose once symptoms are controlled.

Renal impairment:

- No dose adjustment required[4]

Hepatic impairment:

- Amiodarone and its active metabolite are primarily eliminated by hepatic metabolism[1, 3, 4]
- If hepatic enzymes exceed 3 times upper limit of normal during maintenance therapy or double in a patient with elevated baseline, consider dose reduction or discontinuing. Seek specialist advice[1, 4, 12]

PREPARATION AND ADMINISTRATION

Oral Administration:

- Food increases the rate and extent of absorption of amiodarone. It should be taken consistently in relation to food (always with OR without food)[4]
- Avoid grapefruit or grapefruit juice during treatment with amiodarone[1]
- Tablets may be crushed and dispersed in water.
  - Do NOT give the solution for injection orally as it is an irritant[10].
  - Extemporaneous oral suspension 5 mg/mL can be made by Pharmacy Compounding Services (PCS) when tablets not suitable / contraindicated. Contact clinical pharmacist.

Intravenous Administration:

- Prepare amiodarone solution in non-PVC bags/syringes [8, 9].
  - BD Plastipak® syringes do not contain the plasticiser diethylhexyl phthalate (DEHP) and may be used to administer amiodarone[13].
  - PVC-containing giving sets (tubing) may be used if non-DEHP containing giving sets are unavailable.

Emergency Situations ONLY (Pulseless Ventricular Arrythmia)

- Patients ≤ 30 kg:
  - Dilute 150 mg in glucose 5% to a final volume of 30 mL to make a 5 mg/mL solution[4, 8,]
  - Give only the required dose by rapid IV injection [4, 8, 9].
- Patients >30 kg requiring a dose of greater than 150 mg:
  - Dilute dose in 10 - 20 mL of glucose 5% and give only the required dose by rapid IV injection.
- IV amiodarone injection should be followed with a fluid bolus of sodium chloride 0.9% or glucose 5%[8].
- Slower administration is required for patients with a pulse (perfusing tachycardia)[4].

Non-emergency situations - IV loading dose/ continuous infusion:

Use the following standardised concentrations:

	Concentration (in Glucose 5%)
Peripheral Administration	100 mg in 50 mL (2 mg/mL)
CVAD	300 mg in 50 mL (6 mg/mL)

Administer the loading dose (using a standard concentration syringe) over 20 – 120 minutes via syringe driver followed by a continuous infusion. Adjust rate based on patient response.[8, 9]

- Central venous access device (CVAD) administration (preferred):
  - Administer the required dose at the prescribed rate via syringe driver[8, 9].
  - Continuous maintenance infusions can be given over 24 hours via syringe driver[8].
- Peripheral administration:
  - Administer the required dose at the prescribed rate via syringe driver[8, 9].
  - Amiodarone is an irritant, a 0.22-micron filter is recommended to reduce phlebitis[4, 9]
  - If repeated doses are required, administration via CVAD is recommended[2 8]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids[8]:

Glucose 5% ONLY

Compatible at Y-site[3, 8]:

Note – different compatibilities exist for different concentrations of amiODAROne[8]

2 mg/mL solution: Isavuconazole, metoprolol

6 mg/mL solution: atropine, calcium chloride, ciprofloxacin, fentanyl, fluconazole, gentamicin, insulin (Novorapid), labetalol, midazolam, morphine sulphate, tobramycin, vancomycin.

INCOMPATIBLE drugs[3, 8, 9]:

Incompatible fluids: Plasma-Lyte 148, sodium chloride solutions (sodium chloride 0.9% can only be used to flush the line after IV injection), Total Parenteral Nutrition (TPN), Intralipid.

Incompatible drugs: Aciclovir, aminophylline, amoxicillin-clavulanic acid, azithromycin, cefotaxime, ceftazidime, dexamethasone, digoxin, flucloxacillin, foscarnet, fosfomycin, ganciclovir, heparin sodium, hydrocortisone sodium succinate, meropenem, micafungin, phenobarbital, piperacillin-tazobactam, potassium phosphates, sodium bicarbonate, sodium phosphates, sugammadex, thiopental sodium, verapamil.

Only commonly used drugs are listed above. This is not a complete list of incompatible drugs. Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

Emergency IV administration (including emergency loading doses)

- Continuous blood pressure and cardiac monitoring during resuscitation / IV loading dose. Severe circulatory collapse and hypotension can occur with concentrated or rapid infusions[1, 14].
- For peripheral infusions, monitor injection site for signs of pain and inflammation[4].

Oral / IV infusion

- Vital signs including blood pressure, heart rate and respiratory rate as per Paediatric Acute Recognition and Response Observation Tool (PARROT)[14]
- Continuous cardiac monitoring should be considered for all IV amiodarone infusions[10, 15]
- Baseline measurements as soon as feasible[1, 10, 15]
    - Serum electrolytes (potassium and magnesium) – repeat every 6 months

- Thyroid and liver function tests – repeat every 3 to 6 months. Continue to monitor for a year post cessation of treatment
- Lung function including chest x-ray – repeat annually
- 12 lead electrocardiograms (ECG) to ensure QT interval < 500 milliseconds – repeat annually
- Eye examination including fundoscopy and slit lamp examination: repeat within the first 4 months to detect early onset optic neuritis or neuropathy

Serum amiodarone concentration monitoring is not routinely recommended. Toxicity may still occur when concentration is within therapeutic range[1]

ADVERSE EFFECTS

Intravenous (acute treatment)

Benzyl alcohol (excipient in amiodarone injection) may cause "gasping syndrome" (respiratory distress, gasping, metabolic acidosis) in neonates.

Common: Hypotension, bradycardia, injection site reaction, arrhythmia[10].

Rare: Hot flush, atrioventricular block, sinoatrial arrest, transaminitis (due to polysorbate 80 in formulation), hyperhidrosis, agranulocytosis, neutropenia[10, 16].

Oral (long term therapy)

Common: Hypothyroidism, corneal deposits, visual disturbances, photosensitivity, pulmonary toxicity, altered taste or smell, nausea/vomiting, abdominal pain, headache, ataxia, tremor, constipation, anorexia, elevated liver enzymes, fatigue[1, 3, 4, 10].

Infrequent: Arrhythmias, dry mouth, myopathy, peripheral neuropathy[1, 3, 4, 10].

Rare: Alopecia, aplastic or haemolytic anaemia, thrombocytopenia, vertigo, epididymo-orchitis, optic neuritis, hepatotoxicity[1, 3, 4, 10].

STORAGE

IV ampoules [17]

Solution should be clear to slight yellow in colour stored in colourless glass ampoules

Store below 25°C, protect from light

Oral

Tablets[18]: Store below 30°C

PCS extemporaneous 5 mg/mL suspension: Store between 2 - 8°C. Refrigerate, do not freeze.

INTERACTIONS

AmiODAROne is associated with an extensive range of drug-drug interactions.

Consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

***Please note: The information contained in this guideline is to assist with the preparation and administration of **Amiodarone**. Any variations to the doses recommended should be clarified with the prescriber prior to administration**

Related CAHS internal policies, procedures and guidelines
Emergency guideline: Supraventricular tachycardia
High Risk Medicine
Intraosseous Access
Junctional Ectopic Tachycardia
Medication Preparation, Checking and Administration
Medication Safety

Related external legislation, policies and guidelines
Amiodarone Neonatal

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