Ballarat Health Services

DRUG GUIDELINE

ADRENALINE (epinephrine) - Intravenous, intramuscular, intraosseous and endotracheal)

SCOPE (Area): **FOR USE IN:** Intensive Care Unit, Coronary Care Unit, ED, CVS and Theatre
EXCLUSIONS: Paediatrics (seek Paediatrician advice) and General Wards
SCOPE (Staff): Medical, Nursing and Pharmacy

Note: Adrenaline (epinephrine) is the Therapeutic Goods Administration's official drug name. For simplicity in this guideline it will be referred to as adrenaline.

BRAND NAMES
No brand names.

PHARMACOLOGY AND PHARMACOKINETICS
Adrenaline is a naturally occurring sympathomimetic agent acting as a nonselective agonist at adrenergic receptor sites. Adrenaline is a positive inotrope and chronotrope ($beta_1$ receptors); vasodilator at low doses ($beta_2$ receptors); vasoconstrictor at high doses (alpha receptors); bronchial smooth muscle relaxant ($beta_2$ receptors) and stabilises mast cells. Adrenaline also mobilises liver glycogen resulting in hyperglycaemia and possibly glycosuria. It has a rapid onset of action (1-2 minutes), a short duration of action (2-10 minutes) and fast elimination when the infusion is ceased due to the short half-life of 5 minutes. Adrenaline is predominantly metabolised by monoamine oxidase (MAO) and catechol-o-methyl transferase (COMT) in the liver and tissues. Sodium metabisulfite or sodium bisulfite is present as a preservative.

INDICATIONS
- Anaphylaxis.
- Cardiac arrest including ventricular fibrillation, pulseless ventricular tachycardia, asystole and electromechanical dissociation.
- Hypotension – as an inotrope.
- Bradycardias - as a chronotrope.
- Bronchospasm and laryngeal spasm causing respiratory distress.
- Life threatening angioneurotic oedema.
- Inotropic support in acute heart failure and cardiogenic shock, acute exacerbation of chronic heart failure, septic shock.
- **Other indications of adrenaline are not covered by this guideline.**

CONTRAINDICATIONS

Absolute:

- **Phaeochromocytoma.**

Relative:

- **Cardiac dilation.**
- **Known hypersensitivity to sympathomimetics.**

PRECAUTIONS

- **Hypotension due to hypovolaemia** - correct before using adrenaline.
- **Extravasation** – can cause tissue necrosis and sloughing.
- **Local ischaemic necrosis –** can occur with repeated injections to the same site.
- **Patients with high lactate -** adrenaline predictably increases lactate levels, as such increasing lactate may not indicate worsening perfusion.
- **Tachyarrhythmias or tachycardia.**
- **Pulmonary hypertension** – may be worsened by adrenaline-induced pulmonary vasoconstriction.
- **Hyperthyroidism, diabetes, hypertension or the elderly** - increased risk of adverse effects with adrenaline.
- **Occlusive or cerebrovascular disease** – increased risk of peripheral ischaemia and stroke**.**
- **Acidosis, hypercapnia or hypoxia** – can decrease adrenaline's effectiveness and/or increase its adverse reactions. Correct before commencing adrenaline where possible.
- **Ischaemic heart disease, heart failure or arrhythmias -** increased risk of arrhythmias, angina and myocardial ischaemia with adrenaline use.
- **Aortic stenosis and hypertrophic cardiomyopathy**- adrenaline may increase outflow obstruction.
- **Risk of systolic anterior motion of the mitral valve and/or dynamic left ventricular outflow tract obstruction.**
- **Closed angle glaucoma –** adrenaline increases intraocular pressure due to pupillary dilation.
- **Parkinson's Disease –** adrenaline may increase rigidity and tremor.
- **Allergy –** adrenaline ampoules and minijets contain sodium metabisulfite or sodium bisulfite, which can cause severe allergy in susceptible patients (asthmatics are of greatest risk).

PREGNANCY AND BREASTFEEDING

Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS

Do not withhold use of adrenaline due to concerns surrounding drug interactions.

- **Beta blockers (anaphylaxis)** – $beta_2$ blockade of receptors in the lungs can prevent adrenaline-induced bronchodilation. Anaphylaxis in patients taking beta-blockers may be refractory to treatment with usual doses of adrenaline; increase dose of adrenaline (being alert for possible hypertension) and give glucagon.
- **Drugs with arrhythmogenic, hypertensive or vasoconstrictive effects** – adrenaline increases the risk of these effects when co-administered with these drugs. Use combinations cautiously, monitoring ECG, blood pressure and haemodynamic parameters.
- **Cocaine -** risk of fatal arrhythmias with adrenaline when cocaine misused in the previous 24 hours. Avoid where possible. Topical use may also potentiate adrenaline's actions.
- **Beta blockers (general)** - may allow the alpha receptor-mediated effects of adrenaline (vasoconstriction) to predominate, leading to marked hypertension followed by bradycardia.

Reduce adrenaline dose if using a nonselective beta-blocker (oxprenolol, pindolol, propranolol). Monitor heart rate and blood pressure closely when adrenaline is used with any beta blocker.

- **Tricyclic antidepressants -** dysrhythmias and hypertension may result when used with adrenaline, and the vasopressor effect may be enhanced. Avoid combination if possible, otherwise reduce adrenaline dosage and monitor for dysrhythmias and hypertension.
- **Clozapine –** adrenaline may not have same pressor effects, vasopressin may be preferred.
- **SNRIs, atomoxetine –** may increase tachycardia and pressor effects of adrenaline. Avoid if possible.
- **Entacapone** – may inhibit the metabolism of adrenaline, increasing heart rate and potential for arrhythmias. Reduce adrenaline dosage and monitor carefully.
- **Monoamine oxidase inhibitors (phenelzine, tranylcypromine, moclobemide), selegiline and linezolid** – may inhibit the metabolism of adrenaline resulting in hypertension. Use with caution.
- **Alpha$_1$-blockers (eg prazosin, phenoxybenzamine, phentolamine) and lurasidone in overdose –** may lead to hypotension rather than an increase in blood pressure due to unopposed beta effect.
- **Ergot derivatives** – co-administration with adrenaline may increase vasoconstriction and increase risk of severe hypertension. Avoid if possible.
- **Spironolactone** – may decrease the vasoconstricting effect of adrenaline by an unknown mechanism. Monitor.

DOSAGE AND ADMINISTRATION

Requires continuous ECG monitoring.
For administration only

- **in Intensive Care Unit, Coronary Care Unit, ED, CVS and Theatre**
- **by MET or Code Blue**

Administer via CVC only – see Precautions re extravasation. A large peripheral vein (antecubital or proximal to this) or midline may be used in an emergency where central access is planned, or short term to avoid insertion of a CVC. If administering peripherally use a dedicated line and monitor the site for extravasation (a second peripheral line is required for other infusions/access). Do not administer on lines where other infusions may be bolused or flushed.

Adrenaline 1 mg/10 mL (1:10,000) minijets may be substituted below for Adrenaline 1 mg/10 mL (1:10,000) ampoules if they are available.

Anaphylaxis dosing:

Intramuscular injection (preferred)
Use adrenaline 1 mg/1 mL (1:1,000) ampoules.
Adrenaline 10 microgram/kg (**maximum** of 500 microgram = 0.5 mg = 0.5 mL from 1 mg/mL ampoule) IM (thigh preferred).
May be repeated every 3-5 minutes if required.

If not responding to IM administration, consider intravenous infusion (see below).

Intravenous injection – **NOT FOR USE IN CORONARY CARE UNIT**
IV injection has an increased risk of arrhythmias, and is only to be considered if IV infusion is not immediately available. Anaphylaxis dose is 1/10th or less of resuscitation dose.
Use adrenaline 1 mg/10 mL (1:10,000) ampoules.
Mild reaction: Adrenaline 10 microgram (0.1 mL from 1 mg/10 mL ampoule) by slow IV injection.
Repeat dose or escalate dose titrating to response.
Moderate reaction: Adrenaline 1-2 microgram/kg (e.g. 50 microgram = 0.5 mL from 1 mg/10 mL ampoule) by slow IV injection over 2-5 minutes.
Repeat dose or escalate dose titrating to response.

IV (or intraosseous) injection resuscitation dose (via CVC where possible):
Use adrenaline 1 mg/10 mL (1:10,000) ampoules **OR** 1 mg/1 mL (1:1,000) ampoules.
Adrenaline 1 mg/10 mL (1 ampoule) **OR** 1 mg/1 mL (1 ampoule) by slow IV injection.
Repeat dose every 4 minutes (every second cycle CPR) if needed.

Endotracheal resuscitation dose (rarely used):
****not for use in Coronary Care Unit****
Use adrenaline 1 mg/10 mL (1:10,000) minijets.
Adrenaline 1-2 mg (10-20 mL from ONE to TWO minijets) undiluted. Wait until end of exhalation and then administer via endotracheal tube.

IV infusion (via CVC):
Use adrenaline 1 mg/1 mL (1:1,000) ampoules to prepare infusion.
Withdraw 6 mL from a 100 mL glucose 5% minibag.
Adrenaline 6 mg (6 mL from SIX ampoules) added to remaining 94 mL glucose 5% in the minibag.
Total Volume: 100 mL.
Final concentration: 60 microgram/mL.
Starting rate: 1-3 microgram/min (1-3 mL/hr).
Rate increase: Can increase rate every 3-5 minutes. Use blood pressure, heart rate and cardiac output to titrate dose.
Coronary Care Unit dose range: 1-5 microgram/min (1-5 mL/hr).
Coronary Care Unit maximum rate: 5 microgram/min (5 mL/hr).
ICU, ED, CVS and Theatre usual rate range: 1-20 microgram/min (1-20 mL/hr). Higher rates may be required.
ICU, ED, CVS and Theatre maximum rate: 120 microgram/min (120 mL/hr) in extreme cases.
Ceasing infusion: Wean slowly with clinical assessment to avoid hypotension.

Syringe Unit/Pump IV infusion (via CVC):

Use adrenaline 1 mg/1 mL (1:1,000) ampoules to prepare infusion.

Adrenaline 3 mg (3 mL from THREE ampoules) diluted to 50 mL with glucose 5% in a luer lock syringe.

Total Volume: 50 mL.

Final concentration: 60 microgram/mL.

Rate: as for IV infusion above.

Process for changing syringes to minimise disruption to infusions given the short drug half-life:

- Prepare the replacement syringe and prime a new syringe line
- Attach a second syringe pump module to the controller (AKA 'the brain') and program as per the currently running infusion
- Commence new infusion on the pump and then changeover the connected line with the replacement line
- Stop completed infusion pump

General Administration Information

- **Infusion preparation:**
  Mix infusion thoroughly after adding adrenaline to avoid inadvertently giving a more concentrated dose.
  Discoloured solutions (pink or brown) or solutions containing precipitates should not be used.
  Glucose 5% can be substituted for different compatible IV fluid as requested by the Medical Officer.
  Infusion stable for 24 hours.
- **Infusion pump:** Alaris LVP or syringe unit with Guardrails® or ED syringe pump.
- **Routes of administration:**
  IV injection: Yes
  IV intermittent infusion (15-60 minutes): No
  IV continuous infusion: Yes
  IM injection: Yes, into thigh (not buttocks). Avoid repeated injection to the same site.
  Subcut injection: Yes (but not in anaphylaxis). Avoid repeated injection to the same site.
- **Compatible/incompatible IV drugs/fluids:**
  Consult the Australian Injectable Drugs Handbook ('Yellow book') in your ward area. **Assume all unlisted drugs and IV fluids are incompatible – contact Pharmacy for further advice.**

MONITORING (INCLUDING BLOOD TESTS)

- Assess for organ ischaemia due to vasoconstriction including kidneys, gastrointestinal tract and peripheral extremities – see adverse effects.
- Monitor electrolytes (especially potassium and magnesium) at baseline and at least daily.
- Lactate is often used as a marker of tissue perfusion - monitor lactate at baseline and as clinically indicated – see Precautions.
- Dose range and clinical goals should be documented by the Medical Officer.
- A diminished therapeutic effect may occur with prolonged adrenaline infusions due to down-regulation of receptors.

NURSING PRACTICE POINTS

- Continuous ECG monitoring during infusion, look for arrhythmias and ECG changes.
- Baseline 12 lead ECG, and then daily and with rhythm changes or chest pain.

- When patient is unstable or infusion rate requires adjustment, monitor blood pressure every 2-5 minutes, or continuously via arterial line. Doses above 5 microg/min ideally require continuous monitoring via arterial line.
- When blood pressure stable, monitor blood pressure every 15-30 minutes, or continuously via arterial line. Doses above 5 microg/min ideally require continuous monitoring via arterial line.
- Record ALL vital signs at least hourly.
- Monitor and record neurovascular observations every 30-60 minutes, look for peripheral ischaemia.
- If adrenaline is being administered peripherally, monitor IV site for blanching and extravasation – see Precautions. Monitor limb distal to IV site for signs of ischaemia.
- Consider 2 hourly glucose monitoring.
- Monitor fluid balance.
- All injections and infusions are to be labelled as per CPP0022 Labelling of Injectable Medicines and Lines.

ADVERSE EFFECTS

- **Common** - anxiety, headache, fear, palpitations, tachycardia, restlessness, tremor, dizziness, dyspnoea, weakness, sweating, pupil dilation, pallor, hypokalaemia and hyperglycaemia.
- **Infrequent** - excessive increase in blood pressure, ventricular arrhythmias, pulmonary oedema, angina, urinary retention, hallucinations, psychosis, metabolic acidosis, peripheral ischaemia and necrosis.
- **Rare** - allergic reaction (sodium metabisulfite and sodium bisulfite in products).
- **Overdose or rapid IV administration** - arrhythmias (ventricular and supraventricular), severe hypertension, cerebral haemorrhage and pulmonary oedema.

DRUG PRESENTATIONS AND STORAGE

Adrenaline 1 mg/1 mL ampoules (1:1,000).
Adrenaline 1 mg/10 mL ampoules (1:10,000). Minijets unavailable.
Store below 25°C. Do not refrigerate or freeze. Protect from light.
