MONOGRAPH

ADRENALINE (EPINEPHRINE)

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	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 <u>DISCLAIMER</u>



QUICKLINKS					
<u>Dosage/Dosage</u> <u>Adjustments</u>	Administration	Compatibility	Monitoring		

DRUG CLASS

Adrenaline is a direct acting sympathomimetic agent which exerts its effect on alpha and beta-adrenoreceptors.^{1,2}

The major effects of adrenaline are increased systolic blood pressure, reduced diastolic blood pressure, tachycardia, hyperglycaemia, hypokalaemia and bronchodilation.¹

Adrenaline has a rapid onset of action with a short duration of action.¹

Adrenaline is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

- Anaphylactic and allergic reactions²
- Severe bronchospasm and mucosal oedema in croup, asthma, bronchiolitis, and post extubation:

Nebulised adrenaline relaxes bronchial smooth muscle and constricts mucosal and bronchial muscle vessels, relieving congestion and oedema.³

Cardiac arrest:

Adrenaline improves coronary perfusion, cardiac contractility and stimulates spontaneous contractions.¹

Inotropic support:

Adrenaline is a vasopressor and has direct action on beta-1 receptors increasing cardiac contractility (positive inotrope).¹

Severe Hypotension

CONTRAINDICATIONS

- There are no absolute contraindications to giving adrenaline in anaphylactic reactions;
 adrenaline is often lifesaving.²
- Hypersensitivity to adrenaline or any component of the formulation.
- Phaeochromocytoma¹

PRECAUTIONS

- All adrenaline products contain a sulphite which may cause allergic reactions in susceptible people. The possibility of an allergic reaction to sodium metabisulphite should be considered in asthmatic patients who show paradoxical worsening of their condition following the use of this drug.¹
- Use with caution in severe renal impairment. 5
- Use with caution in patients with hyperthyroidism, hypertension, ischaemic heart disease, obstructive cardiomyopathy, hypertrophic cardiomyopathy, aortic stenosis, diabetes mellitus, narrow angle glaucoma and known allergy to sympathomimetic amines due to the direct catecholamine effect of adrenaline. 1,2,5
- Adrenaline should not be injected into fingers, toes, ears, nose, or genitalia.¹
- Patients receiving cardiac glycosides, quinidine, some antihistamines, thyroid hormones, or tricyclic antidepressants may have increased effects of adrenaline or risk of arrhythmias.¹

FORMULATIONS1

Listed below are products available at Perth Children's Hospital (PCH), other formulations may be available, check with pharmacy if required:

- Ampoule: 1 in 10,000 (1 mg/10 mL)
- Ampoule: 1 in 1000 (1 mg/mL)
- Auto-Injector (EpiPen® Jr.) *: 150 microgram / 0.3 mL
- Auto-Injector (EpiPen®) *: 300 microgram / 0.3 mL
- Auto-Injector (Anapen-500®) *: 500 microgram / 0.3 mL
- Adrenaline Acid Tartrate (Auspman®) vial: 10 mg/10 mL
- Pre-filled syringes (Baxter®): 500 micrograms in 30 mL, 3 mg in 50 mL.
- * EpiPen[®] Jr, EpiPen[®], and Anapen[®] are to be used only in the outpatient and ambulatory care setting.

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Refer to Neonatal Medication Protocols

The doses below are within the standard reference range for each indication; however, depending on the indication, the dosage of adrenaline (epinephrine) may need to be adjusted depending on the patient's clinical needs and response.

Anaphylactic reactions

IM Injection (Age > 4 weeks):

- < 10 kg: 10 micrograms/kg/dose (0.01 mL/kg/dose of adrenaline 1 in 1000 (1 mg/mL) ampoule).²
- ≥ 10 kg: Refer to dose banding table below: 6

Age	Estimated weight (kg)	Dose 10 microg/kg/dose (Maximum 500 microg/dose)	Volume of adrenaline 1 in 1000 (1 mg/mL)
1 - 2 years	10 kg	100 micrograms	0.1 mL
2 - 3 years	15 kg	150 micrograms	0.15 mL
4 – 6 years	20 kg	200 micrograms	0.2 mL
7 – 10 years	30 kg	300 micrograms	0.3 mL
10 – 12 years	40 kg	400 micrograms	0.4 mL
≥ 12 years	≥50 kg	500 micrograms	0.5 mL

IM injection into mid-anterolateral (outer mid) aspect of the thigh is preferred. Repeat dose every 5 minutes as required.⁷

EpiPen® Jr, EpiPen®, and Anapen® are to be used only in the outpatient and ambulatory care setting.

- EpiPen® Jr. 150 microg is used in children weighing 7.5 kg 20 kg.
- EpiPen[®] 300 microg is for children > 20 kg.
- Anapen[®] 500 microg is used for > 50 kg^{6,7}

Use IV administration only if response to repeated IM doses and volume expansion is inadequate. Continuous monitoring of electrocardiogram (ECG), pulse oximetry and blood pressure (BP) is essential. IV infusion is safer than bolus injection, which is only used for imminent cardiac arrest.⁷

IV infusion:

Age >4 weeks: Initially 0.1 microgram/kg/minute then titrate according to response.^{2,7} See the <u>Administration - Low strength infusion</u> section for detailed preparation and administration advice for use in anaphylaxis.

IV injection:

Age >4 weeks: Initially 1 microgram/kg/dose over 1 minute (0.01 mL/kg/dose of adrenaline 1 in 10,000 (1 mg/10 mL) ampoule) up to a maximum of 50 micrograms (0.5 mL). Titrate dose according to response.¹⁰

Severe bronchospasm in croup, asthma, bronchiolitis and post extubation

Nebulised:

Age > 4 weeks: Adrenaline 1 in 1000 (1 mg/mL) ampoule: 0.5 mg/kg/dose (0.5 mL/kg/dose) up to a maximum of 5 mg (5 mL) undiluted.^{3,7}

The dose can be made up to a total volume of 5 mL with sodium chloride 0.9% if required to dilute small volumes. Run oxygen flow rate at 8 L/minute via nebuliser. Repeat adrenaline dose after 15 minutes if required.

Cardiac arrest

IV or Intraosseous injection:

Birth to 18 years: initially 10 micrograms/kg/dose (0.1 mL/kg/dose of adrenaline **1 in 10,000** (**1 mg/10 mL**) ampoule) up to a maximum of 1 mg as a single dose.^{5,7,9} Refer to Advanced Paediatric Life Support algorithm.⁸

Shockable algorithm: give after 2nd shock and then every 4 minutes (every 2nd loop).⁸

Non Shockable algorithm: give immediately and then every 4 minutes (every 2nd loop).8

If no circulatory access achieved, give via Endotracheal Tube (ETT)

100 micrograms/kg/dose (0.1 mL/kg/dose of adrenaline **1 in 1000 (1 mg/mL)** ampoule) up to a maximum of 2.5 mg as a single dose. ^{7,10}

Refer to <u>Advanced Paediatric Life Support</u> algorithm. Timing of administration should adhere to the Shockable and Non-Shockable algorithms.⁸

Inotrope infusion for support in acute heart failure, cardiogenic shock and septic shock (low cardiac output, hypotension)

Adrenaline prescribed for inotropic support is restricted for use in critical care areas ONLY.

IV infusion:

Birth to 18 years: initially 0.05–0.1 microgram/kg/minute, then titrate according to response.^{7,9}

Severe Hypotension

Restricted for use under the direction of a Cardiologist, Intensivist, Anaesthetist or Emergency Department Physician in an emergency.

IV injection:

Birth to 18 years: 1 microgram/kg/dose (maximum 50 micrograms); titrate to haemodynamic effect.^{9,10}

Renal impairment: No dosage adjustment required¹⁰

Hepatic impairment: No dosage adjustment required 10

RECONSTITUTION & ADMINISTRATION

Intravenous Infusion - CVAD

- Adrenaline administered via syringe pump must only be given in critical care and emergency medicine areas where continuous monitoring occurs.
- Standard concentration listed below also applies to neonates outside of NICU.

Patient's Weight	Concentration (In Sodium Chloride 0.9%)	Notes	
10 kg or less	500 micrograms in 30 mL (17 microg/mL)	In a 3 kg patient, 0.1 microg/kg/min = 1 mL/hr	
Above 10 kg	3 mg in 50 mL (60 microg/mL)	In a 20 kg patient, 0.1 microg/kg/min = 2 mL/hr	

<u>Intravenous Infusion – Low Strength</u>

Adrenaline low strength infusions must be administered using Infusomat[®] Space Line Safe Set "UV-protect" (giving set without additional in-line additive port).

<u>Low strength</u> standard concentration infusion (<u>6 mg in 1000 mL</u>) may be used for:

- Administration via Peripheral Intravenous Catheter (PIVC) in an emergency situation (e.g., anaphylaxis) in all clinical areas
- Older/overweight children, patients requiring very low dose at consultant's discretion or patients with unstable blood pressure.
- Add 6 mg (6 x adrenaline 1 in 1000 (1 mg/ mL) ampoules) to a 1000 mL bag of a compatible fluid:
- 1 mL/kg/hour of this dilution = 0.1 micrograms/kg/minute.

Intravenous Injection

- Adrenaline 1 in 10,000 (1 mg/10 mL) ampoule can be given neat as an intravenous push.⁴
- Administration via a CVAD is preferred. If given via a PIVC each dose should be followed with a sodium chloride 0.9% flush.⁴
- Severe Hypotension:
 - Dilute 10 microgram/kg (0.1 mL/kg) of adrenaline 1 in 10,000 (1 mg/10 mL) to a final volume of 10 mL with sodium chloride 0.9%
 - Maximum: 500 micrograms in 10 mL
 - 1 mL of this dilution = 1 microgram/kg/dose (in patients up to 50kg)

Intramuscular Injection

 EpiPen® Jr., EpiPen® and Anapen® and are used only in outpatient and ambulatory care settings – Neat adrenaline 1 in 1000 (1 mg/mL) ampoules are to be used in ED and inpatient areas.

- EpiPen[®] Jr., EpiPen[®] and Anapen[®] should only be injected into the mid-anterolateral (outer mid) aspect of the thigh.⁷
- Limit risk of injury by holding the leg of an infant or child firmly in place while administering adrenaline using an autoinjector. 10
- Do not allow the patient to stand or walk until they are haemodynamically stable, which is usually a minimum of 1 hour after 1 dose of adrenaline and 4 hours if more than 1 dose of adrenaline has been administered.⁶
- If a repeat dose of IM adrenaline is required, avoid injecting into the same site.⁴

Endotracheal Tube (ETT)

Instil quickly down the ETT then flush with 1–2 mL of sodium chloride 0.9%⁷

Nebulised

 A medical officer must supervise the administration of nebulised adrenaline in patients on general ward areas for croup. (See <u>Monitoring</u> below)

COMPATIBILITY

Compatible fluids:

<u>Adrenaline acid tartrate</u>: solutions of adrenaline acid tartrate are commonly used in practice despite the lack of compatibility and stability information. Always inspect solutions closely for signs of incompatibility after preparation and during infusion.⁴

<u>Adrenaline hydrochloride</u>: Sodium chloride 0.9%, glucose 5%, glucose 10%, glucose in sodium chloride solutions, Hartmann's.⁴

Compatible at Y-site:

Although the following drugs are compatible via Y-site, their co-administration may affect the infusion rate of adrenaline. Therefore, it is recommended that adrenaline be administered separately via a dedicated intravenous line.

Adrenaline hydrochloride:

Amikacin, amiodarone, amphotericin B liposomal (AmBisome), anidulafungin, ascorbic acid injection, atracurium, atropine sulfate, azithromycin, aztreonam, benzatropine, benzylpenicillin, calcium chloride, calcium gluconate, caspofungin, cefazolin, cefotaxime, cefoxitin, ceftazidime, chlorpromazine, clindamycin, clonidine, colistimethate sodium, ceftriaxone, cefuroxime, ciclosporin, daptomycin, dexamethasone, dexmedetomidine, digoxin, dobutamine, dopamine, ephedrine sulfate, ertapenem, erythromycin, esmolol, fentanyl, fluconazole, furosemide glycopyrronium (glycopyrrolate), glyceryl trinitrate, (frusemide), gentamicin, hydrocortisone, hydromorphone, imipenem-cilastatin, ketamine, labetalol, levetiracetam, lidocaine (lignocaine), linezolid, magnesium sulfate, metaraminol, methylprednisolone sodium succinate, metoclopramide, metoprolol, metronidazole, midazolam, milrinone, morphine sulfate, moxifloxacin, naloxone, noradrenaline (norepinephrine), octreotide, ondansetron, phenylephrine, piperacillintazobactam, potassium chloride, rocuronium, sodium nitroprusside, tigecycline, thiopental sodium, tobramycin, vancomycin, vecuronium, verapamil, voriconazole, zoledronic acid¹⁰

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

INCOMPATIBLE drugs:

Aciclovir, aminophylline, azathioprine, diazepam, dantrolene, ganciclovir, hyaluronidase, indometacin, micafungin, phenobarbital (phenobarbitone), phenytoin sodium, sodium bicarbonate, sulfamethoxazole-trimethoprim, thiopental sodium.^{4, 10}

MONITORING

Cardiac arrest, inotropic support, severe hypotension, anaphylaxis:

Electrocardiogram (ECG), continuous pulse oximetry, Blood Pressure (BP) and urine output.⁷ Other monitoring parameters may be required in special circumstances, consult your clinical pharmacist or prescribing clinician if required.

Severe bronchospasm in croup, asthma and bronchiolitis:

Emergency Department: ECG monitoring and continuous medical supervision is recommended. All children requiring nebulised adrenaline in the Emergency Department should be observed for at least 3 hours. PCC review is required if > 3 doses of nebulised adrenaline is administered.

General Wards: Nebulised adrenaline may be given to a child with moderately severe croup on a general ward. It may be ordered by a Resident, but the Registrar must always be notified of the decision. The medical officer is required to supervise the administration of the adrenaline and observe the child for 15 minutes afterwards. Be aware that upper airway narrowing may recur after about 60 minutes. PCC review is required if > 3 doses of nebulised adrenaline is administered.

Post extubation in the Post Anaesthetic Care Unit (PACU):

- Nebulised adrenaline must be administered under direct supervision of a PACU nurse via 1:1 nursing.
- Ensure continuous cardiorespiratory monitoring including respiratory rate, oxygen saturation, heart rate and blood pressure during and after administration.
- ECG monitoring may be required if indicated, and / or as directed by the Anaesthetist.

Liaise with the prescribing Anaesthetist / Duty Anaesthetist pre and post administration to ensure adequate communication and allow for medical review as required.

ADVERSE EFFECTS

Common: anxiety, headache, fear, palpitations, tachycardia, restlessness, tremor, dizziness, dyspnoea, weakness, sweating, pallor, hyperglycaemia.²

Infrequent / Rare: excessive increase in blood pressure, ventricular arrhythmias, pulmonary oedema, angina, hyperthyroidism, peripheral ischaemia and necrosis, allergic reaction (sodium metabisulphite in products).²

Frequency not known: dry mouth.5

STORAGE

- Ampoules: Store below 25°C, protect from light.¹
- EpiPen®Jr., EpiPen® and Anapen®: Store below 25°C, protect from light. Do NOT refrigerate.¹

The solution in EpiPen®Jr., EpiPen® and Anapen® should be examined regularly through the inspection window. Discard and replace if the solution is cloudy, coloured or contains particles.

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Related CAHS internal policies, procedures and guidelines

Adrenaline (Epinephrine) Autoinjector – Use of Patient's Own Device

Allergic Reactions and Anaphylaxis Management in Planned Allergy Challenges (Immunology)

Allergy and Adverse Drug Reaction Management

Anaphylaxis - ED Guideline

Croup - ED Guideline

Croup Health Facts Sheet

Emergency Drug Calculator - PCH ED

High Risk Medicines

Inhaled Medication Administration Guideline

Intramuscular (IM) Injections

Medication Administration

Medication Management and Anaphylaxis Protocol – Hospital in the Home (HiTH)

Resuscitation Equipment and Trolley Checking

References

- MIMS Australia Pty Ltd. MIMS [Internet]. St Leonards, NSW: CMP Medica Australia Pty Ltd; 2024 [cited March 2024].
- 2. Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists., Pharmaceutical Society of Australia., The Royal Australian College of General Practitioners. Australian medicines handbook. Adelaide SA: Australian Medicines Handbook; 2024 [cited March 2024].
- 3. UpToDate: Lexicomp 2024 Management of Croup. Available from Management of croup UpToDate (health.wa.gov.au) Accessed March 2024
- 4. Burridge N, Collard N, Symons K, Society of Hospital Pharmacists of Australia. Australian injectable drugs handbook [Internet]. Collingwood, Vic.: The Society of Hospital Pharmacist of Australia; 2024 [cited March 2024].

^{**}Please note: The information contained in this guideline is to assist with the preparation and administration of adrenaline (epinephrine). Any variations to the doses recommended should be clarified with the prescriber prior to administration**

- 5. British Medical Association and The Royal Pharmaceutical Society of Great Britain. British National Formulary for Children. United Kingdom: Pharmaceutical Press; 2024 [Cited March 2024].
- 6. Australian Society of Clinical Immunology and Allergy. ASCIA Guideline Acute Management of Anaphylaxis 2023. Available from: ASCIA Guidelines Acute management of anaphylaxis -Australasian Society of Clinical Immunology and Allergy (ASCIA)
- 7. Australian Medicines Handbook, Pharmaceutical Society of Australia, Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists, Royal Australian College of General Practioners. AMH children's dosing companion 2024 [cited March 2024].
- 8. Advanced Paediatric Life Support Australia. Paediatric Advanced Life Support algorithm 2017. Available from: https://www.apls.org.au/algorithm-paediatric-advanced-life-support.
- 9. Epinephrine (Adrenaline). In:NeoFax® [Internet]. Greenwood Village (CO): IBM Corporation; 2024 [cited March 2024]
- 10. Bennett PN, Brown MJ, Sharma P, Elsevier. Clinical pharmacology [Internet]. Edinburgh: Churchill Livingstone/Elsevier; 2024 [cited March 2024].

Useful resources (including related forms)

ASCIA Guidelines – Acute management of Anaphylaxis

This document can be made available in alternative formats on request for a person with a disability.

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Adrenaline (Epinephrine)