

NEW ZEALAND DATA SHEET

1. Aspen Adrenaline Injection 1mg/mL and 1mg/10mL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Adrenaline acid tartrate equivalent to adrenaline 1:1,000 (1mg/mL) and adrenaline 1:10,000 (1mg/10mL)

Adrenaline is a white or creamy-white, odourless, crystalline powder or granule. It darkens in colour on exposure to air and light. The BP solubilities are: practically insoluble in water, in ethanol (96 %) and in methylene chloride. It dissolves in hydrochloric acid.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

ASPEN ADRENALINE Injection should be used only once and any residue discarded. It should not be used if it is coloured.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adrenaline 1:1,000. The drug of choice in the emergency treatment of acute severe anaphylactic reactions due to insect bites, drugs and other allergens. It may also be used for the symptomatic relief of respiratory distress due to bronchospasm.

Adrenaline 1:10,000. An adjunct in the management of cardiac arrest.

4.2 Dose and method of administration

ASPEN ADRENALINE 1:1,000 injection is preferably administered subcutaneously. It may also be administered intramuscularly but not into the buttocks. In emergency situations, adrenaline may be injected very slowly intravenously but only as the dilute solution 1:10,000.

ASPEN ADRENALINE Injection is for single use in one patient only. Discard any residue. Adrenaline injection should not be used if it is coloured.

Cardiac arrest.

Adults. The recommended dose is 1 mg intravenously, using 10 mL of the 1:10,000 solution. This may be repeated every three to five minutes. If given through a peripheral line, each dose should be followed by a flush of 20 mL of intravenous fluid to ensure delivery of the drug to the central compartment. Intracardiac administration is no longer recommended.

Children. The recommended dose is 10 microgram (0.1 mL of the 1:10,000 solution)/kg bodyweight administered intravenously. This may be repeated every three to five minutes.

Severe anaphylaxis or asthma

Adults. The usual initial dose is 100 to 500 micrograms (0.1 to 0.5 mL of the 1:1,000 solution) subcutaneously or intramuscularly. Subcutaneous doses may be repeated at 20 minute to four hour intervals depending on the response of the patient and the severity of the condition. In severe anaphylactic shock, slow and cautious

intravenous administration may be necessary to ensure absorption of the drug. A dose of 100 to 250 micrograms (1 to 2.5 mL of the 1:10,000 solution) may be administered. Alternatively 25 to 50 micrograms (0.25 to 0.5 mL of the 1:10,000 solution) may be given intravenously every five to 15 minutes following an initial dose of 500 micrograms subcutaneously or intramuscularly.

Children. 10 microgram (0.01 mL of 1:1,000 solution)/kg bodyweight subcutaneously, repeated if necessary at intervals of 20 minutes to four hours depending on the response of the patient and the severity of the condition. Single paediatric doses should not exceed 500 micrograms.

4.3 Contraindications

- Known hypersensitivity to adrenaline or sympathomimetic amines.
- Shock (other than anaphylactic shock).
- Cardiac dilatation and coronary insufficiency.
- Hypertension.
- Ischaemic heart disease.
- Arrhythmias.
- Cerebral arteriosclerosis.
- Diabetes mellitus.
- Hyperthyroidism.
- Narrow angle (congestive) glaucoma.
- Organic brain damage.
- Pheochromocytoma.
- During general anesthesia with halogenated hydrocarbons or cyclopropane.
- With local anesthesia in fingers, toes, ears, nose or genitalia: there is a danger of vasoconstriction producing sloughing of tissues in these areas.
- Labour: adrenaline may delay the second stage by inhibiting spontaneous or oxytocin induced contractions of the pregnant human uterus.
- Conditions in which vasopressor drugs may be contraindicated, e.g. thyrotoxicosis.
- In obstetrics when maternal blood pressure is in excess of 130/80 mmHg. See also section 4.5 Interaction with other medicines and other forms of interaction.

4.4 Special warnings and precautions for use

Other beta-agonist sympathomimetics. Allow sufficient time to elapse before or after administering another beta-agonist sympathomimetic agent to avoid additive effects.

Disease states. Use with extreme caution in the elderly, and in patients with cardiovascular disease, phenothiazine induced circulatory collapse, cerebrovascular insufficiency, diabetes, hypertension, chronic lung disease, angina pectoris, prostatic hypertrophy, psychoneurosis or hyperthyroidism. Use with extreme caution in patients with long standing bronchial asthma and emphysema who have developed degenerative heart disease. Angina pain may be induced when coronary insufficiency is present. Syncope has occurred following administration to asthmatic children. In patients with parkinsonian syndrome the drug increases rigidity and tremor.

General anesthesia. Concurrent use with cyclopropane, halogenated hydrocarbon or similar volatile anesthetics may produce fatal ventricular arrhythmias.

Diabetic patients. A greater increase may be produced in heart rate, blood glucose, lactate, glycerol and free fatty acids when adrenaline is administered to diabetic patients with autonomic neuropathy than in diabetic patients without neuropathy.

Circulatory support. When adrenaline is used for circulatory support, correction of hypovolaemia, metabolic acidosis, and hypoxia or hypercapnia should be carried out

beforehand or concomitantly.

Sodium metabisulfite. This product contains sodium metabisulfite, which may cause allergic reactions in susceptible individuals. The possibility of an allergic reaction to sodium metabisulfite should be considered in asthmatic patients who show paradoxical worsening of their condition following use of the drug.

Gangrene. Interarterial administration must be avoided as marked vasoconstriction may result in gangrene.

Local ischaemic necrosis can occur from repeated injections in one site.

4.5 Interaction with other medicines and other forms of interaction

Other sympathomimetic agents. Adrenaline should not be administered concomitantly with other sympathomimetic agents because of the possibility of additive effects and increased toxicity.

Rapidly acting vasodilators. These can counteract the marked pressor effects of adrenaline.

General anesthetics. Administration of adrenaline in patients receiving cyclopropane, halogenated hydrocarbon or similar volatile general anesthetics that increase cardiac irritability and seem to sensitise the myocardium to adrenaline, may result in arrhythmias including ventricular premature contractions, tachycardia or fibrillation and acute pulmonary oedema if hypoxia is present.

Cardiovascular drugs. Adrenaline should not be used in patients receiving high dosage of other drugs, e.g. quinidine, digoxin and other cardiac glycosides, that can sensitise the heart to arrhythmias.

Antihypertensive therapy. Special care is advisable in patients receiving antihypertensive therapy as severe hypertension may result.

Alpha blockers. The administration of adrenaline to patients receiving alpha-blockers may result in both hypotension and cardiac accelerating effects.

Beta-blockers. The administration of adrenaline to patients receiving nonselective beta-blockers (e.g. propranolol) may result in severe hypotension, followed by a reflex bradycardia, due to stimulation of adrenergic receptors.

Central nervous system and other drugs. Tricyclic antidepressants, some other antidepressants, some antihistamines and thyroid hormones may potentiate the effects of adrenaline, especially on heart rhythm and rate. Patients on MAOIs should not receive sympathomimetic treatment.

Drugs causing potassium loss. The hypokalaemic effect of adrenaline may be potentiated by other drugs that cause potassium loss, including corticosteroids, potassium depleting diuretics and aminophylline or theophylline; patients receiving high doses of beta 2-adrenergic agonists concomitantly should have their plasma potassium concentration monitored.

Hypoglycaemic agents. Adrenaline induced hyperglycaemia may lead to loss of blood sugar control in diabetic patients treated with hypoglycaemic agents.

Incompatibilities. Adrenaline is incompatible with oxidising agents, alkalis, copper, zinc, iron, silver and other metals.

Adrenaline has been reported to be incompatible with solutions containing the following: aminophylline, ampicillin sodium, amylobarbitone sodium, ascorbic acid, benzylpenicillin potassium, calcium chloride, calcium gluconate, cephalothin sodium, chloramphenicol sodium succinate, chlortetracycline hydrochloride, corticotrophin, diazepam, digitoxin, ergometrine maleate, erythromycin gluceptate, frusemide, hyaluronidase, hydrocortisone sodium succinate, methicillin sodium, nitrofurantoin,

noradrenaline acid tartrate, novobiocin sodium, pentobarbitone sodium, procaine, prochlorperazine edisylate, promazine hydrochloride, sodium bicarbonate, sulfadiazine sodium, suxamethonium chloride, tetracycline hydrochloride, vancomycin hydrochloride, vitamin B complex with ascorbic acid, warfarin sodium.

This list is not intended to be comprehensive. Refer to standard texts for further information.

4.6 Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy

Category A

Adrenaline has been administered to a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed. However, the use of adrenaline during labour is contraindicated because it may delay the second stage by inhibiting spontaneous or oxytocin induced contractions of the pregnant human uterus.

Lactation

Adrenaline is excreted in the breast milk. The use of adrenaline in breastfeeding women is therefore not recommended.

4.7 Effects on ability to drive and use machines

No data available.

4.8 Undesirable effects

Adrenaline may cause reactions such as fear, anxiety, tenseness, restlessness, disorientation, impaired memory, confusion, irritability, hallucinations and psychotic states. Headache, weakness, dizziness, anorexia, nausea and vomiting and difficulty in micturition with urinary retention may also occur.

Muscle tremor and hypokalaemia, psychomotor agitation, pallor, respiratory difficulty, hyperglycaemia, sweating, hypersalivation, cold extremities and insomnia have also been reported.

Palpitations, tachycardia (sometimes with anginal pain) and cardiac arrhythmias may also occur along with hypertension which in some instances may induce reflex bradycardia as can vasodilation with flushing and hypotension. Ventricular fibrillation may occur and severe hypertension may lead to cerebral hemorrhage and pulmonary oedema.

Overdosage or inadvertent intravenous injection of usual subcutaneous doses of adrenaline may cause hypertension.

Cerebrovascular or other hemorrhage and hemiplegia may result, especially in elderly patients. Inadvertent intravenous injection of adrenaline has also been reported to have caused convulsions, metabolic acidosis and renal failure with anuria.

Repeated injections of adrenaline can cause necrosis as a result of vascular constriction at the injection site. Prolonged use or overdosage of adrenaline can result in severe metabolic acidosis.

Pulmonary oedema has been associated with excessive parenteral administration of adrenaline and following topical aerosol application.

Gas gangrene, which can be fatal, has been reported following intramuscular injection of adrenaline into the buttock or thigh. This appears to have been due to *Clostridium* organisms on the skin being deposited into muscle tissue during

injection, with the vasoconstrictor properties of adrenaline enhancing the effects of the infection (see section 4.2, Dose and method of administration).

High doses may result in ventricular arrhythmias.

Rigidity and tremor may be exacerbated in patients with Parkinsonism.

Syncope episodes have been reported in children.

Psychiatric disorders may be exacerbated.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Symptoms. Overdosage with adrenaline produces a rapid rise in blood pressure resulting in cerebrovascular hemorrhage, cardiac arrhythmias leading to ventricular fibrillation and death. Pulmonary oedema may also lead to death because of the peripheral constriction and cardiac stimulation produced.

Treatment. To counteract the pressor effects of adrenaline, use rapidly acting vasodilators, e.g. nitrates or alpha-blocking agents.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Adrenaline acts on both alpha- and beta-adrenergic receptors of tissues innervated by sympathetic nerves, except the sweat glands and arteries of the face. It is the most potent alpha-receptor activator. Adrenaline stimulates the heart to increased output; raises the systolic blood pressure; lowers diastolic blood pressure; relaxes bronchial spasm and mobilises liver glycogen, resulting in hyperglycemia and possibly glycosuria.

5.2 Pharmacokinetic properties

Parenterally administered adrenaline has a rapid onset and short duration of action. The circulating drug is metabolised by the liver and other tissues. The majority is taken up and metabolised by sympathetic nerve endings.

Adrenaline is excreted in the urine, mainly in the form of metabolites.

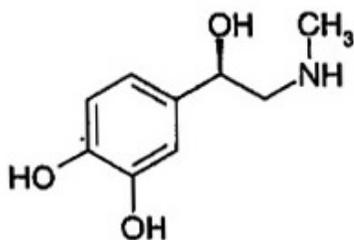
Adrenaline crosses the placenta but not the blood-brain barrier. It is also distributed into breast milk (see section 4.4, Special warnings and precautions for use and section 4.6 Fertility, pregnancy and lactation).

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

The chemical structure of adrenaline is shown below:



The chemical formula is C₉H₁₃NO₃ and the molecular weight is 183.2.
CAS: 51-43-4; Melting point: 205°C to 212°C

6.1 List of excipients

Hydrochloric acid, sodium chloride, sodium hydroxide, sodium metabisulfite, tartaric acid, water for injection.

6.2 Incompatibilities

No data available.

6.3 Shelf life

18 months from the date of manufacture.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

Ampoules, 1mg/mL (1:1,000, clear, colourless solution), 1mL: 5's, 50's*;
Ampoules, 0.1mg/mL (1:10,000, clear colourless solution), 10mL: 10's.

(*packs of 50 not currently marketed in Australia)

6.6 Special precautions for disposal (and other handling)

No data available.

7. MEDICINE SCHEDULE

1mg/mL (1:1,000): Pharmacist only medicine
0.1mg/mL (1:10,000): Pharmacist only medicine

8. SPONSOR

Pharmacy Retailing (NZ) Limited
Trading as Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland
New Zealand

9. DATE OF FIRST APPROVAL

29 April 2013

10. DATE OF REVISION OF THE TEXT

May 2019

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All sections revised	Update to the SPC-style format