Adrenaline Hydrochloride Injection

PRODUCT INFORMATION

DESCRIPTION
Adrenaline is (R)-1-(3,4-dihydroxyphenyl)-2-methylaminoethanol; C₉H₁₃NO₃. It is a white odourless crystalline powder, soluble in solutions of mineral acids and alkalis. CAS 51-43-4. Its chemical structure is:

![Chemical Structure of Adrenaline](image)

Adrenaline 1:10,000 is a sterile solution of adrenaline hydrochloride in water containing adrenaline hydrochloride 0.1 mg/mL and not more than 0.2% sulfur dioxide from an equivalent amount of sodium bisulfite as an antioxidant. The solution also contains sodium chloride, sodium citrate, citric acid monohydrate and hydrochloric acid. The solution contains no antimicrobial preservatives.

PHARMACOLOGY
Adrenaline is a direct-acting sympathomimetic agent exerting its effect on alpha and beta adrenoreceptors. Major effects are increased systolic blood pressure, reduced diastolic pressure, tachycardia, hyperglycaemia and hypokalaemia. It is a powerful cardiac stimulant. It has vasopressor properties, an antihistaminic action and is a bronchodilator. Its action is rapid in onset and of short duration.

Adrenaline is rapidly distributed to the heart, spleen, several glandular tissues and adrenergic nerves. It crosses the placenta and is excreted in breast milk. It is approximately 50% bound to plasma proteins. The onset of action is rapid and after intravenous infusion the half life is approximately 5-10 minutes.

Adrenaline is rapidly metabolised in the liver and tissues. Up to 90% of the IV dose is excreted as metabolites in the urine.

INDICATIONS
Adjunctive use in the management of cardiac arrest.

CONTRAINDICATIONS
Contraindications are relative as this product is intended for use in life-threatening emergencies.

The following contraindications should be considered: hyperthyroidism, hypertension, ischaemic heart disease, diabetes mellitus, narrow angle glaucoma and known sensitivity to sympathomimetic amines.

Adrenaline should not be used in the presence of cardiac dilation.
Adrenaline should not be used in most patients with arrhythmias and cerebral arteriosclerosis, where vasopressor drugs may be contraindicated eg. in thyrotoxicosis, in obstetrics when maternal blood pressure is in excess of 130/80.

Adrenaline is also contraindicated in shock (other than anaphylactic shock), in patients with organic brain damage, during general anaesthesia with halogenated hydrocarbons or cyclopropane.

Adrenaline should not be injected into fingers, toes, ears, nose or genitalia.

**PRECAUTIONS**

Use with caution in patients with ventricular fibrillation, prefibrillatory rhythm, tachycardia, myocardial infarction, phenothiazine induced circulatory collapse, urination difficulty and prostatic hypertrophy.

Adrenaline injection MIN-I-JET should be used with caution in patients suffering from autonomic dysreflexia (hyperreflexia), particularly in spinal cord injury (e.g. tetraplegics).

Administer slowly with caution to elderly patients and to patients with hypertension, diabetes mellitus, hyperthyroidism and psychoneurosis. Use with extreme caution in patients with long-standing bronchial asthma and emphysema who have developed degenerative heart disease. Anginal pain may be induced when coronary insufficiency is present. Use with caution in patients with narrow angle glaucoma.

Adrenaline may delay the second stage of labour by inhibiting contractions of the uterus.

Syncope has occurred following administration to asthmatic children.

In patients with Parkinsonian syndrome the drug increases rigidity and tremor.

Intra-arterial administration should be avoided since marked vasoconstriction may result in gangrene.

Intramuscular injection into the buttocks should be avoided as gas gangrene is a possibility.

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

Adrenaline Injection MIN-I-JET contains a sulfite which may cause allergic type reactions in certain susceptible individuals.

Endotracheal administration of adrenaline can contaminate the colorimeter carbon dioxide detector and lead to its false-positive colour change (fixed yellow discolouration).

The adrenaline is in a single use MIN-I-JET prefilled syringe. Once the unit is assembled and used, any remaining portion of the solution must be discarded with the entire unit.
Use in pregnancy (Category A)
Adrenaline has been given 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 foetus having been observed.

Adrenaline may delay the second stage of labour by inhibiting contractions of the uterus.

Use in lactation
Adrenaline is excreted in breast milk.

Interactions with other drugs
Adrenaline should not be administered with other sympathomimetic agents because of the danger of additive effects and increased toxicity such as an increased risk of serious cardiac arrhythmias.

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

The effects of adrenaline may be potentiated by tricyclic antidepressants, some antihistamines and thyroid hormones.

Halothane and other anaesthetics such as cyclopropane and trichlorethylene increase the risk of adrenaline-induced ventricular arrhythmias and acute pulmonary oedema if hypoxia is present.

Severe hypertension and bradycardia may occur with non-selective beta-blocking drugs. Propranolol inhibits the bronchodilator effect of adrenaline. The risk of cardiac arrhythmias is higher when adrenaline is given to patients receiving digoxin or quinidine.

There is an increased the risk of hypotension and tachycardia with alpha blockers.

Drugs which cause potassium loss (corticosteroids, potassium-depleting diuretics, aminophylline, theophylline) may increase the risk of hypokalaemia.

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

Patients on monoamine oxidase inhibitors should not receive sympathomimetic treatment. There is an increased risk of adverse events with concurrent use, or use within 2 weeks, of monoamine oxidase inhibitors and sympathomimetic treatment.

Entacapone may potentiate the chronotropic and arrhythmogenic effects of adrenaline. Use of adrenaline and levodopa may increase the risk of cardiac adverse effects of levodopa.
Adrenaline is physically incompatible with alkalis, metals, oxidising agents, sodium warfarin, hyaluronidase and many other drugs; it forms polymers with sodium bicarbonate.

**ADVERSE REACTIONS**

Common symptomatic adverse events include anxiety, restlessness, tachycardia, tremor, weakness, dizziness, headache, dyspnoea, cold extremities, pallor, sweating, nausea, vomiting, sleeplessness, hallucinations and flushing or redness of face and skin. Psychomotor agitation, disorientation, impaired memory and psychosis may occur.

The following adverse events are also possible: stress cardiomyopathy; bowel necrosis (in patients whose intestinal blood flow is already compromised); local vasoconstriction and hypoxia of mucosa, which may lead to compensatory rebound congestion of the mucosa (in case of endotracheal administration); pallor and thrombocytosis.

The potentially severe adverse effects of adrenaline arise from its effect upon blood pressure and cardiac rhythm. Ventricular fibrillation may occur and severe hypertension may lead to cerebral haemorrhage and pulmonary oedema.

**DOSAGE AND ADMINISTRATION**

Do not use if the injection is brown or contains a precipitate.

Adults: In cardiopulmonary resuscitation the initial dose is 1 mg (10 mL of 1:10,000) delivered intravenously, preferably through a central line, and repeated every 3 to 5 minutes during CPR. Further bolus doses or continuous infusion may be required to maintain an adequate blood pressure after the patient generated pulse has returned.

Elderly patients: The adult dose is used but should be given very slowly with caution as these patients may be more sensitive to adrenaline.

Children: In children the dose is 0.1 mL/kg bodyweight (0.01 mg/kg) repeated every five minutes if necessary.

**OVERDOSAGE**

**Effects**

Cardiac arrhythmias leading to ventricular fibrillation and death.

Severe hypertension leading to pulmonary oedema and cerebral haemorrhage.

Overdosage of adrenaline can result in severe metabolic acidosis because of elevated blood concentration
of lactic acid.

**Treatment**
Combined alpha and beta adrenergic blocking agents such as labetalol may counteract the effects of adrenaline, or a beta blocking agent may be used to treat supraventricular arrhythmias and phentolamine to control the alpha mediated effects on the peripheral circulation. Rapidly acting vasodilators such as nitrates and sodium nitroprusside may also be helpful.

**PRESENTATION**
Adrenaline Injection is available in a single use prefilled MIN-I-JET syringe containing 1 mg adrenaline hydrochloride in 10 mL (1:10 000).

Do not use if the injection is brown or contains a precipitate.

**STORAGE**
Store below 25EC. Protect from light.

Manufactured by: International Medication Systems Ltd
1886 Santa Anita Avenue, South El Monte 91733, California USA

Distributed by: CSL Limited, A.C.N. 051 588 348
45 Poplar Road, Parkville 3052, Victoria Australia

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