

PRODUCT NAME : ADRENALINE INJECTION BP 1 IN 1000

Summary of Product Characteristics

1. TRADE NAME OF THE MEDICINAL PRODUCT

Adrenaline (Epinephrine) Injection BP 1 in 1000

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution for injection contains 1 mg of adrenaline (epinephrine) as the acid tartrate.

3. PHARMACEUTICAL FORM

Clear, colourless, sterile, aqueous solution, intended for parenteral administration to human beings.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Adrenaline is a direct-acting sympathomimetic agent.

Adrenaline may be used to provide rapid relief of severe hypersensitivity reaction to drugs and other allergens, and in the emergency treatment of anaphylactic shock.

4.2 Posology and Method of Administration

Adrenaline Injection B.P. 1/1000 (1 mg/ml) may be administered undiluted by S.C. or I.M. injection. In the shocked patient, the intramuscular route is recommended as absorption from the intramuscular site is more rapid and reliable than from the subcutaneous site.

Severe hypersensitivity reactions, anaphylactic shock

I.M. Injection:

Adults: The usual dose is 500 micrograms (0.5 ml of adrenaline 1/1000). If necessary, this dose may be repeated several times at 5-minute intervals according to blood pressure, pulse and respiratory function.

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4.2 Posology and Method of Administration cont/d.

Half doses of adrenaline may be safer for patients who are taking amityriptyline, imipramine or a beta blocker.

Children : The following doses of adrenaline 1/1,000 are recommended:

Age	Dose
Over 12 years	500 micrograms (0.5 ml) 250 micrograms (0.25 ml) if child is small or prepubertal
6 – 12 years	250 micrograms (0.25 ml)
6 months – 6 years	120 micrograms (0.12 ml)
Under 6 months	50 micrograms (0.05 ml)

If necessary, these doses may be repeated several times at 5-minute intervals according to blood pressure, pulse and respiratory function.

4.3 Contra-Indications

- 1) Use during labour
- 2) Use with local anaesthesia of peripheral structures including digits, ear lobe.
- 3) Use in the presence of ventricular fibrillation, cardiac dilatation, coronary insufficiency, organic brain disease or atherosclerosis, except in emergencies where the potential benefit clearly outweighs the risk.
- 4) Use if solution is discoloured.

4.4 Special Warnings and Special Precautions for Use

Adrenaline should only be administered with great caution in the elderly or those with cardiovascular disease (including hypertension and ischaemic heart disease), hyperthyroidism, diabetes mellitus, closed-angle glaucoma, or in patients with long standing asthma or emphysema who have reached an age at which degenerative heart disease is prevalent.

Repeat administration may produce local necrosis at the sites of injection.

Prolonged administration may produce metabolic acidosis, renal necrosis and adrenaline fastness or tachyphylaxis.

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4.4 Special Warnings and Special Precautions for Use cont/d

Adrenaline should be avoided or used with extreme caution in patients undergoing anaesthesia with halothane or other halogenated anaesthetics, in view of the risk of inducing ventricular fibrillation.

Do not mix with other agents unless compatibility is known.

4.5 Interactions with other Medicinal Products and other forms of Interaction

Concurrent use with tricyclic antidepressants, digitalis glycosides, parenterally used diuretics, guanethidine, methyl dopa, reserpine or other similar agents may potentiate the effects of adrenaline. Beta-blockers, especially non-selective ones, increase the pressor effect and decrease the bronchodilatory effect of adrenaline.

Adrenaline should be avoided or used with extreme caution in patients undergoing anaesthesia with halothane or other halogenated anaesthetics in view of the risk of inducing ventricular fibrillation.

4.6 Pregnancy and Lactation

Adrenaline should only be used during pregnancy and lactation if considered essential by the physician.

4.7 Effects on Ability to Drive and Use Machines

Not applicable as the patient would be too ill.

4.8 Undesirable Effects.

In therapeutic doses adrenaline may cause effects such as anxiety, fear, dry mouth, tremor, headache, palpitations, arrhythmias, hypertension, along with restlessness and coldness of extremities. Headache is most common. Other effects that may occur include difficulty in micturition and urinary retention, dyspnoea, altered metabolism including disturbances of glucose metabolism, sweating and hypersalivation.

Central effects of sympathomimetic agents also include insomnia, confusion, irritability, weakness and psychotic states. Appetite may be reduced and nausea and vomiting may occur.

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4. CLINICAL PARTICULARS

4.9 Overdosage

Possible signs of overdosage include restlessness, confusion, pallor, tachycardia, bradycardia, cardiac arrhythmias and cardiac arrest. Treatment is primarily symptomatic and supportive. Prompt injection of a rapid acting alpha-adrenoceptor blocking agent such as phentolamine followed by a beta-blocker such as propranolol, has been tried to counteract the pressor and arrhythmogenic effects of adrenaline. A rapidly-acting vasodilator such as glyceryl trinitrate has also been used.

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Adrenaline is a direct-acting sympathomimetic agent. It has more pronounced effects on beta- than on alpha- adrenergic receptors, although alpha effects prevail at high dose.

The effects of adrenaline include increased rate and force of cardiac contraction, cutaneous vasoconstriction and broncho-dilatation. With higher doses, stimulation of peripheral alpha-receptors results in an increase in peripheral resistance and in blood pressure.

5.2 Pharmacokinetic properties

As a result of enzymatic degradation in the gut and first-pass metabolism in the liver, adrenaline is almost totally inactive when given by mouth. It acts rapidly following subcutaneous or intramuscular injection, although absorption is slowed by local vasoconstriction (it can be hastened by massaging the injection site).

Most adrenaline that is either injected into the body or released into the circulation from the adrenal medulla, is very rapidly inactivated by processes which include uptake into the adrenergic neurones, diffusion, and enzymatic degradation in the liver and body tissues. One of the enzymes responsible for the chemical inactivation of this exogenous or hormonal adrenaline is catechol-O-methyltransferase (COMT), the other is monoamine oxidase (MAO). In general, adrenaline is methylated to metanephrine by COMT followed by oxidative deamination by MAO to 4-hydroxy-3-methoxymandelic acid (formerly termed vanillylmandelic acid: VMA), or oxidatively deaminated by MAO to 3,4-dihydroxymandelic acid which, in turn, is methylated by COMT, once again to 4-hydroxy-3-methoxymandelic acid; the metabolites are excreted in the urine mainly as their glucuronide and ethereal sulphate conjugates.

The ability of catechol-O-methyltransferase to effect introduction of a methyl group is an important step in the chemical inactivation of adrenaline and similar catecholamines (in particular, noradrenaline). It means that the termination of the pharmacological response of catecholamines is not simply dependent upon monoamine oxidase. In its role of neurotransmitter intraneuronal catecholamine (mainly noradrenaline) is, however, enzymatically regulated by monoamine oxidase. Adrenaline crosses the placenta to enter foetal circulation.

5.3 Preclinical safety data

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

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6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Metabisulphite
Sodium Chloride
Sodium Hydroxide
Hydrochloric acid
Water for Injections

6.2 Incompatibilities

Do not admix with other agents unless compatibility is known.

6.3 Shelf life

Unopened : 2 years
After reconstitution : Not applicable
After first opening : 2 years*

*If only part of an ampoule is used, the remainder should be discarded.

6.4 Special precautions for storage

Do not store above 25°C
Keep in outer carton

6.5 Nature and contents of container

1ml, clear glass ampoules, glass type 1 Ph.Eur. borosilicate glass, packed in cardboard cartons to contain 10 x 1ml ampoules.

6.6 Instructions for Use, Handling and Disposal

For SC or IM injection.
Use as directed by the physician.
Keep out of the reach and sight of children.
If only part used, discard the remaining solution.

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ADMINISTRATIVE DATA

7. MARKETING AUTHORIZATION HOLDER

Antigen International Limited,
Roscrea,
Co. Tipperary,
Ireland.

8. MARKETING AUTHORIZATION NUMBER

PL 2848/5909R.

9. DATE OF FIRST AUTHORIZATION

30th January 1991.

10. DATE OF (PARTIAL) REVISION OF THE TEXT

July 2004