

<p style="text-align: center;">Adrenaline (epinephrine) 1:1000 Injection BP Summary of Product Characteristics</p>
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1. NAME OF THE MEDICINAL PRODUCT

Adrenaline (epinephrine) 1:1000 Injection BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Adrenaline (epinephrine) 1:1000 Injection BP may be used as follows:

- to provide rapid relief in the treatment of severe hypersensitivity reactions to drugs and other allergens
- in the emergency treatment of anaphylactic shock.

4.2 Posology and method of administration

Adrenaline (epinephrine) 1:1000 Injection BP may be administered undiluted by subcutaneous or intramuscular 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

IM Injection:

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

Half doses of adrenaline (epinephrine) may be safer for patients who are taking amitriptyline, imipramine or a beta blocker.

Children: The following doses of Adrenaline (epinephrine) 1:1000 Injection BP 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

Hypersensitivity to adrenaline (epinephrine) or to any of the excipients.

Use during labour

Use with local anaesthesia of peripheral structures including digits and ear lobes.

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.

Use if the solution is discoloured.

4.4 Special warnings and special precautions for use

Adrenaline (epinephrine) should only be administered with great caution in the elderly, or those with cardiovascular disease, including hypertension and ischaemic heart disease, or hyperthyroidism, or in patients with long standing asthma or emphysema who have reached an age at which degenerative heart disease is prevalent, (increased susceptibility to the pressor and arrhythmogenic effects of adrenaline (epinephrine) in these patient groups), patients with diabetes mellitus (risk of hyperglycaemia with use of adrenaline (epinephrine)), or in patients with closed-angle glaucoma (increased intra-ocular pressure due to mydriatic effect of adrenaline (epinephrine)).

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

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

Adrenaline (epinephrine) 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.

The solution should not be mixed 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 (epinephrine), resulting in exaggerated pressor and/or arrhythmogenic effects. Beta-blockers, especially non-selective ones, increase the pressor effect, resulting in hypertension, and decrease the bronchodilatory effect of adrenaline (epinephrine). (See section 4.2 *Posology and method of administration*).

Adrenaline (epinephrine) 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. (See section 4.4 *Special warnings and special precautions for use*).

4.6 Pregnancy and lactation

Adrenaline (epinephrine) 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

The most commonly reported adverse reaction is headache. Adverse reactions may occur at therapeutic doses, and include the following:

Endocrine disorders: Glucose tolerance impaired.

Metabolism and nutrition disorders: Decreased appetite.

Psychiatric disorders: Anxiety, fear, irritability, psychotic disorder.

Nervous system disorders: Headache, tremor, restlessness, insomnia, confusional state

Cardiac disorders: Palpitation, arrhythmia.

Vascular disorders: Hypertension, peripheral coldness.

Respiratory, thoracic and mediastinal disorders: Dyspnoea.

Gastrointestinal disorders: Dry mouth, salivary hyper-secretion, vomiting.

Skin and subcutaneous tissue disorders: Hyperhidrosis.

Renal and urinary disorders: Dysuria, urinary retention.

General disorders and administration site conditions: Asthenia.

Hypertension and cardiac arrhythmias, including ventricular fibrillation, may result from interaction between adrenaline (epinephrine) and certain other medicines (see section 4.5 *Interactions*).

4.9 Overdose

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 (epinephrine). A rapidly-acting vasodilator such as glyceryl trinitrate has also been used.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: R03AK01 Group: Epinephrine and other drugs for obstructive airway disease

Adrenaline (epinephrine) 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 (epinephrine) 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 (epinephrine) 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 (epinephrine) 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. The enzymes responsible for the chemical inactivation of exogenous or hormonal adrenaline are catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO). In general, adrenaline (epinephrine) 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 (epinephrine) and similar catecholamines (in particular, noradrenaline/norepinephrine). 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/norepinephrine) is, however, enzymatically regulated by monoamine oxidase. Adrenaline (epinephrine) 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Metabisulphite
Sodium Chloride
Water for Injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C.

Keep the container in the outer carton in order to protect from light.

6.5 Nature and contents of container

Ph.Eur. Type 1 colourless glass ampoules, 1 ml.

Pack size: 10 x 1 ml ampoules.

6.6 Special precautions for disposal and handling.

If only part of an ampoule is used, discard the remaining solution.

7. NAME AND ADDRESS OF MARKETING AUTHORISATION HOLDER

Taro Pharmaceuticals Ireland Ltd.,
Lourdes Road,
Roscrea,
County Tipperary,
Ireland

8. MARKETING AUTORISATION NUMBER

PL 20910/0002

9. DATE OF FIRST AUTHORISATIO/RENEWAL OF AUTHORISATION

23/10/2007

10 DATE OF REVISION OF THE TEXT

23/10/2007

11. DOSIMETRY (IF APPLICABLE)

**12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS
(IF APPLICABLE)**

Legal Status

POM