

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Anapen 300 micrograms in 0.3 ml solution for injection in a pre-filled syringe.

2. Qualitative and Quantitative Composition

Each millilitre contains 1 mg of adrenaline (epinephrine).

One dose of 0.3 ml contains 300 micrograms of adrenaline (epinephrine).

Excipients: sodium metabisulphite (E223), sodium chloride for full list of excipients, see section 6.1.

3. Pharmaceutical Form

Solution for injection.

Clear colourless solution practically free from particles.

4. Clinical particulars

4.1. Therapeutic Indications

Emergency treatment for acute allergic reactions (anaphylaxis) caused by peanuts or other foods, drugs, insect bites or stings, and other allergens as well as exercise-induced or idiopathic anaphylaxis.

4.2. Posology and Method of Administration

Use only by the intramuscular route.

Anapen consists of a pre-filled syringe of adrenaline (epinephrine) contained in an auto-injection device. The whole is referred to as an auto-injector.

One Anapen injection should be administered intramuscularly immediately on the appearance of the signs and symptoms of anaphylactic shock. These may occur within minutes of exposure to the allergen and are most commonly manifested by urticaria, flushing or angioedema; more severe reactions involve the circulatory and respiratory systems. Inject Anapen only into the anterolateral aspect of the thigh, not the buttock. The injected area may be lightly massaged for 10 seconds following injection.

The effective dose is typically in the range 0.005 - 0.01 mg/kg but higher doses may be necessary in some cases.

Use in adults: The usual dose is 300 micrograms. Larger adults may require more than one injection to reverse the effect of an allergic reaction. In some circumstances a single dose of adrenaline (epinephrine) may not completely reverse the effects of an acute allergic reaction and for such patients a repeat injection may be given after 10 - 15 minutes.

Use in children: The appropriate dose may be 150 micrograms (Anapen Junior 150 micrograms) or 300 micrograms (Anapen 300 micrograms) of adrenaline (epinephrine), depending on the body weight of the child and the discretion of the doctor. The auto-injector of Anapen Junior 150 micrograms is designed to deliver a single dose of 150

micrograms adrenaline(epinephrine), A dosage below 150 micrograms cannot be administered in sufficient accuracy in children weighing less than 15 kg and use is therefore not recommended unless in a life-threatening situation and under medical advice.

A double syringe pack is available in certain markets.

Anapen auto-injector is intended for immediate self administration by a person with a history of anaphylaxis and is designed to deliver a single dose of 300 micrograms (0.3 ml) adrenaline (epinephrine). For stability reasons 0.75 ml is left in the syringe after use but the unit cannot be used again and should be safely discarded.

4.3. Contra-indications

Hypersensitivity to adrenaline (epinephrine) or to any of the excipients (see section 4.4. for further Information on sulphites).

4.4. Special Warnings and Precautions for Use

Anapen contains sodium metabisulphite which can cause allergic-type reactions including anaphylactic symptoms and bronchospasm in susceptible people, especially those with a history of asthma. Patients with these conditions must be carefully instructed in regard to the circumstances under which Anapen should be used.

All patients who are prescribed Anapen should be thoroughly instructed to understand the indications for use and the correct method of administration. Anapen is indicated as emergency supportive therapy only and patients should be advised to seek immediate medical attention following administration.

Use with caution in patients with heart disease e.g. coronary heart and cardiac muscle diseases (angina may be induced), cor pulmonale, cardiac arrhythmias or tachycardia. There is a risk of adverse reactions following adrenaline (epinephrine) administration in patients with hyperthyroidism, cardiovascular disease (severe angina pectoris, obstructive cardiomyopathy and ventricular arrhythmia and hypertension), phaeochromocytoma, high intraocular pressure, severe renal impairment, prostatic adenoma leading to residual urine, hypercalcemia, hypokalemia, diabetes, or in elderly or pregnant patients. Repeated local injection can result in necrosis at sites of injection from vascular constriction. Accidental intravascular injection may result in cerebral haemorrhage due to a sudden rise in blood pressure. Accidental injection into hands or feet may cause loss of blood flow to adjacent areas due to vasoconstriction.

4.5. Interactions with other Medicinal products and other Forms of Interaction

The effects of adrenaline (epinephrine) may be potentiated by tricyclic antidepressants mixed noradrenargic-serotoninerpic antidepressants like venlafaxine, sibutramine or milnacipran and monoamine oxidase inhibitors (sudden blood pressure increase and possible cardiac arrhythmia), COMT blocking agent, thyroid hormones, theophylline, oxytocin, parasympatholytics, certain antihistamines (diphenhydramine, chlorpheniramine), levodopa and alcohol.

Severe hypertension and bradycardia may occur when adrenaline (epinephrine) is administered with non-selective beta-blocking medicinal products.

Concurrent therapy with sympathomimetics may potentiate the effects of adrenaline (epinephrine).

Use Anapen with caution in patients receiving medicinal products which may sensitise the heart to arrhythmias, e.g. digitalis, quinidine, halogenated anaesthetics.

The pressor effects of adrenaline (epinephrine) may be counteracted by administration of rapidly acting vasodilators or alpha adrenergic blocking medicinal products. Anti-anaphylactic effects can be antagonised by beta-blocking agents, especially non-selective beta blockers.

Adrenaline (epinephrine) inhibits insulin secretion and diabetic patients may require upward adjustment of their insulin or other hypoglycaemic therapy.

4.6. Pregnancy and Lactation

There are no adequate or well controlled studies of adrenaline (epinephrine) in pregnant women. Adrenaline (epinephrine) should only be used in pregnancy if the potential benefit justifies the potential risk to the foetus. Adrenaline (epinephrine) may dramatically reduce placental blood flow, although anaphylactic shock will do this too. Adrenaline (epinephrine) is not orally bioavailable; any adrenaline (epinephrine) excreted in breast milk would not be expected to have any effect on the nursing infant.

4.7. Effects on Ability to Drive and Use Machines

It is not recommended that patients should drive or use machines following administration of adrenaline (epinephrine), since patients will be affected by symptoms of the anaphylactic shock.

4.8. Undesirable Effects

The occurrence of undesirable effects depends on the sensitivity of the individual patient and the dose applied.

Common adverse reactions even at low doses due to adrenaline (epinephrine) include palpitations, tachycardia, sweating, nausea, vomiting, respiratory difficulty, pallor, dizziness, weakness, tremor, headache, apprehension, nervousness anxiety, coldness of extremities.

Less frequently reported effects include hallucinations, syncopes, hyperglycaemia, hypokalaemia, metabolic acidosis, mydriasis, difficulty in micturition with urinary retention, muscle tremor.

Adverse reactions which occur at higher doses or in susceptible individuals are cardiac arrhythmias (ventricular fibrillation/cardiac arrest), sudden rise of blood pressure (sometimes leading to cerebral haemorrhage) as well as vasoconstriction (e.g. in the skin, mucous tissues and kidneys).

Anapen contains a sulfite that may cause allergic-type reactions including anaphylactic reactions or life-threatening or less severe asthmatic episodes in certain susceptible patients.

4.9. Overdose

Overdose or accidental intravascular injection of adrenaline (epinephrine) may cause cerebral haemorrhage from a sudden rise of blood pressure. Death may result from acute pulmonary oedema arising from peripheral vascular constriction and cardiac stimulation.

The pressor effects of adrenaline (epinephrine) may be counteracted by rapidly acting vasodilators or alpha adrenergic blocking medicinal products. Should prolonged hypotension follow such measures, it may be necessary to administer another pressor medicinal product, such as noradrenaline.

Acute pulmonary oedema with respiratory embarrassment following adrenaline (epinephrine) overdose should be managed by administration of a rapidly acting alpha adrenergic blocking medicinal product such as phentolamine and/or with intermittent positive pressure respiration.

Adrenaline (epinephrine) overdose may also result in transient bradycardia followed by tachycardia; these can be followed by potentially fatal cardiac arrhythmias which may be treated by beta adrenergic blocking medicinal products. These must be preceded or accompanied by an alpha-adrenergic blocker to control the alpha-mediated effects on the peripheral circulation.

5. Pharmacological properties

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: adrenergic and dopaminergic agents, adrenaline (epinephrine).

ATC code: C01 CA 24

Adrenaline (epinephrine) is a naturally occurring catecholamine secreted by the adrenal medulla in response to exertion or stress. It is a sympathomimetic amine which is a potent stimulant of both alpha and beta adrenergic receptors and its effects on target organs are therefore, complex. It is the medicinal product of choice to provide rapid relief of hypersensitivity reactions to allergies or to idiopathic or exercise induced anaphylaxis.

Adrenaline (epinephrine) has a strong vasoconstrictor action through alpha adrenergic stimulation. This activity counteracts the vasodilatation and increased vascular permeability leading to loss of intravascular fluid and subsequent hypotension, which are the major pharmacotoxicological features in anaphylactic shock. Through its stimulation of bronchial beta adrenergic receptors, adrenaline (epinephrine) has a powerful bronchodilator action which alleviates wheezing and dyspnoea. Adrenalin (epinephrine) also alleviates pruritus, urticaria and angioedema associated with anaphylaxis.

5.2. Pharmacokinetic Properties

Adrenaline (epinephrine) is rapidly inactivated in the body, mostly in the liver by the enzymes COMT and MAO. Much of a dose of adrenaline (epinephrine) is excreted as

metabolites in urine. The plasma half life is about 2 - 3 minutes. However, when given by subcutaneous or intramuscular injection, local vasoconstriction may delay absorption so that the effects may last longer than the half life suggests.

5.3. Preclinical Safety Data

Adrenaline (epinephrine) has been widely used in the clinical management of allergic emergencies for many years. There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. Pharmaceutical particulars

6.1. List of Excipients

Sodium chloride,
sodium metabisulphite (E223),
hydrochloric acid,
water for injections.

6.2. Incompatibilities

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

6.3. Shelf Life

2 years.

6.4. Special Precautions for Storage

Do not store above 25 °C. To protect from light, store in the original package.

6.5. Nature and Contents of Container

Anapen consists of a pre-filled syringe contained in a single use auto-injection device. The syringe contains adrenaline (epinephrine) solution. The auto-injection device delivers 0.3 ml of this solution. The immediate container is a glass syringe sealed by a rubber plunger at one end, and at the other end by a rubber needle shield.

Syringe BD (Becton Dickinson) borosilicate glass type 1, 27G 1/2".

Plunger BD (Becton Dickinson) black chlorobutyl rubber PH 701/50.

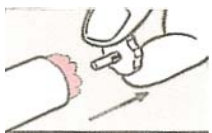
In pack sizes of 1 or 2.

Not all pack sizes may be marketed.

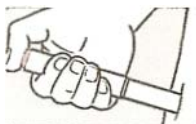
6.6 Instruction for Use and Handling



Remove the black needle cap, which pulls the rubber protective shield off the needle.



Remove the black safety cap from the red firing button.



Hold the needle end of the device against the outer thigh and press the firing button. The injection may be made, if necessary, through light clothing.



Hold in position for 10 seconds, then remove. Replace the black needle cap after use.

For single use only. Discard safely immediately after use. Full graphics are shown on label and in patient leaflet.

A needle-free trainer auto injector device is available

7. Marketing Authorisation Holder

Lincoln Medical Ltd
13 Boathouse Meadow Business Park
Cherry Orchard Lane
Salisbury SP2 7LD
United Kingdom

8. Marketing Authorisation Number

PL 18813/0001

9. Date of First Authorisation/Renewal of Authorisation

11th July 2001/4th August 2006

10. Date of (Partial) Revision of the Text

4th August 2006