

# Anapen<sup>®</sup> adrenaline (epinephrine)

Right dose, first time

Anapen 500 micrograms in 0.3 ml solution for injection in a pre-filled syringe.  
Anapen 300 micrograms in 0.3 ml solution for injection in a pre-filled syringe.  
Anapen Junior 150 micrograms in 0.3 ml solution for injection in a pre-filled syringe.

**QUALITATIVE AND QUANTITATIVE COMPOSITION:** Anapen 500 micrograms in 0.3ml solution for injection: Each millilitre contains 1.66mg of adrenaline (epinephrine). One dose of 0.3ml contains 500 micrograms of adrenaline (epinephrine); 1:600 Anapen 300 micrograms in 0.3ml solution for injection: Each millilitre contains 1mg of adrenaline (epinephrine). One dose of 0.3ml contains 300 micrograms of adrenaline (epinephrine); 1:1000 Anapen Junior 150 micrograms in 0.3ml solution for injection: Each millilitre contains 0.5mg of adrenaline (epinephrine). One dose of 0.3ml contains 150 micrograms of adrenaline (epinephrine); 1:2000. **EXCIPIENTS:** sodiumchloride, sodium, metabisulphite (E223), hydrochloric acid, water for injections. **PHARMACEUTICAL FORM:** Solution for injection. Clear colourless solution practically free from particles. **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. **POSLOGY AND METHOD OF ADMINISTRATION:** Use only by the intra muscular route. Anapen and Anapen Junior consist 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 a goeodema; more severe reactions involve the circulatory and respiratory systems. Inject Anapen or Anapen Junior 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 0.005-0.01mg/kg but higher doses may be necessary in some cases. Use in adults: The usual dose is 300 micrograms. For adults with a mean weight of 60kg or more or adults at high risk of severe anaphylaxis the 300 micrograms dose may not be sufficient and these patients should use Anapen 500 micrograms in the auto-injector. 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: Anapen 500 micrograms is not recommended for 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. Larger children 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 (with a second syringe) may be given after 10-15 minutes. 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 15kg 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 500 micrograms (0.3ml), 300 micrograms (0.3ml) or 150 micrograms (0.3ml) (Anapen Junior) adrenaline (epinephrine). For stability reasons 0.75ml is left in the syringe after use but the unit cannot be used again and should be safely discarded. **CONTRAINDICATIONS:** Hyper sensitivity to adrenaline (epinephrine) or to any of the excipients (see section below for further information on sulphites) **SPECIAL WARNINGS AND PRECAUTIONS FOR USE:** Anapen or Anapen Junior 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 or Anapen Junior should be used. All patients who are prescribed Anapen or Anapen Junior should be thoroughly instructed to understand the indications for use and the correct method of administration. Anapen or Anapen Junior 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, cardio vascular disease (severe angina pectoris, obstructive cardiomyopathy and ventricular arrhythmia and hypertension), phaeochromocytoma, high intraocular pressure, severe renal impairment, prostatic adenoma leading to residual urine, hypercalcaemia, hypokalaemia, diabetes, or in elderly or pregnant patients. Repeated local injection can result in necrosis at sites of injection from vascular constriction. Accidental intra vascular 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. **INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:** The effects of adrenaline (epinephrine) may be potentiated by tricyclic antidepressants, mixed noradrenergic-serotonergic anti depressants like even lalfaxine, sibutramine or milnacipran and monoamine oxidase inhibitors (sudden blood pressure increase and possible cardiac arrhythmia), COMT blocking agent, thyroid hormones, the ophylline, 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 or Anapen Junior with caution in patients receiving medicinal products which may sensitise the heart to arrhythmias, e.g. digitalis, quinidine, halogenated anaesthetics. The press or 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. **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 bio available; any adrenaline (epinephrine) excreted in breast milk would not be expected to have any effect on the nursing infant. **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. **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 and coldness of extremities. Less frequently reported effects include hallucinations, syncope, hyperglycaemia, hypokalaemia, metabolic acidosis, mydriasis, difficulty 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 or Anapen Junior contains a sulphite that may cause allergic-type reactions including anaphylactic reactions or life-threatening or less severe asthmatic episodes in certain susceptible patients. **OVER DOSE:** 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 edema arising from peripheral vascular constriction and cardiac stimulation. The press or 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 press or medicinal product, such as noradrenaline. Acute pulmonary edema with respiratory embarrassment following adrenaline (epinephrine) overdose should be managed by

administration of a rapidly acting alphaadrenergic 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 alphamediated effects on the peripheral circulation. **PHARMACODYNAMIC PROPERTIES:** Pharmacotherapeutic group: adrenergic and dopaminergic agents, adrenaline (epinephrine) ATC code: C01CA24. Adrenaline (epinephrine) is a naturally occurring catecholamine secreted by the adrenal medullain 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 hyper sensitivity reactions to allergies or to idiopathic or exercise induced anaphylaxis. Adrenaline (epinephrine) has a strong vasoconstrictor or action through alpha adrenergic stimulation. This activity counteracts the vasodilatation and increased vascular permeability leading to loss of intra vascular 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. Adrenaline (epinephrine) also alleviates pruritus, urticaria and angioedema associated with anaphylaxis. **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. **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. **INCOMPATIBILITIES:** In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. **SHELF LIFE:** Anapen 500 micrograms in 0.3ml solution for injection: 24months; Anapen 300 micrograms in 0.3ml solution for injection: 24 months; Anapen Junior 150 micrograms in 0.3ml solution for injection: 21months. **SPECIAL PRECAUTIONS FOR STORAGE:** Do not store above 25°C. To protect from light, store in the original package. **NATURE AND CONTENTS OF CONTAINER:** Anapen or Anapen Junior 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 0.3ml 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, 27G1/2". Plunger BD (Becton Dickinson) black chlorobutyl rubber PH701/50. In pack sizes of 1 or 2. Not all pack sizes may be marketed. **LEGAL CATEGORY:** POM. **MARKETING AUTHORISATION HOLDER:** Lincoln Medical Ltd, Unit 8 Wilton Business Centre Wilton, Salisbury SP2 0AH, United Kingdom. **MARKETING AUTHORISATION NUMBER:** PL18813/0003 Anapen 500 micrograms in 0.3ml solution for injection; PL18813/0001 Anapen 300 micrograms in 0.3ml solution for injection; PL18813/0002 Anapen Junior 150 micrograms in 0.3ml solution for injection. **DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION:** PL18813/0003 1 June 2009; PL18813/0001 11 July 2001/4 August 2006; PL18813/0002 11 July 2001/4 August 2006. **DATE OF (PARTIAL) REVISION OF THE TEXT:** 1 June 2009.

Please see full SPC text before prescribing these products. This is available on [www.anapen.co.uk](http://www.anapen.co.uk)

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