Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre contains 0.5 mg of adrenaline (epinephrine)
One dose of 0.3ml contains 150 micrograms of adrenaline (epinephrine)
Excipients with known effect: sodium metabisulfite (E223)
Each 0.3 ml (150 micrograms) dose contains 0.51 mg of sodium metabisulfite (E223).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection in a pre-filled syringe
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 allergensas well as exercise-induced or idiopathic anaphylaxis.

4.2 Posology and method of administration

The patient should always carry 2 units of auto injectors in case the first administration fails or if one dose is not sufficient.

Posology
The effective dose is typically in the range 5-10 micrograms per kilogram of bodyweight but higher doses may be necessary in some cases.

Paediatric population
Use in children:
The appropriate dose may be 150 micrograms (Anapen Junior) or 300 micrograms (Anapen) of adrenaline (epinephrine), depending on the body weight of the child and the discretion of the doctor. Children and adolescents over 30 kg in weight should be prescribed Anapen 300 micrograms. Larger children may require more than one injection to reverse the effect of an allergic reaction. In the absence of clinical improvement or if deterioration occurs, a second injection with an additional Anapen Junior may be administered 5–15 minutes after the first injection. It is recommended that patients are prescribed two Anapen Junior which they should carry at all times. The auto-injector of Anapen Junior 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.

Method of administration
For intramuscular injection.
Anapen Junior 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 Junior 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 Junior only into the anterolateral aspect of the thigh, not the buttock.
The injected area may be lightly massaged for 10 seconds following injection to accelerate absorption. The auto-injector is designed to inject through clothing or directly through the skin.

Anapen Junior 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 150 micrograms (0.3 ml) adrenaline (epinephrine). For stability reasons 0.77 ml is left in the syringe after use but the unit cannot be used again and should be safely discarded.

The patient/carer should be informed that following each use of Anapen:

- They should call for immediate medical assistance, ask for an ambulance and state 'anaphylaxis' **even if symptoms appear to be improving (see section 4.4).**
- Conscious patients should preferably lie flat with legs elevated but sit up if they have breathing difficulties. Unconscious patients should be placed on their side in the recovery position.
- The patient should if possible remain with another person until medical assistance arrives.

4.3 Contraindications

Hypersensitivity to adrenaline (epinephrine) or to any of the excipients listed in section 6.1 (see section 4.4 for further information on sodium metabisulfite). There are no absolute contraindications for use in allergic emergency situations.

4.4 Special warnings and precautions for use

All patients who are prescribed Anapen Junior should be thoroughly instructed to understand the indications for the use and the correct method of administration (see section 6.6). It is strongly advised also to educate the patient's immediate associates (e.g. parents, caregivers, teachers) for the correct usage of Anapen Junior in case support is needed in the emergency situation.

Anapen Junior is indicated as emergency supportive therapy only and patients should be advised to seek immediate medical attention following administration, in order to have close monitoring of the anaphylactic episode and further treatment as required.

The patient/carer should be informed about the possibility of biphasic anaphylaxis which is characterised by initial resolution followed by recurrence of symptoms some hours later.

Patients with concomitant asthma may be at increased risk of a severe anaphylactic reaction.Use with caution in patients with heart disease e.g coronary heart and cardiac muscle diseases (angina may be induced), cor pulmonale, cardiac arrythmias 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.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially sodium free.

Patients should be warned regarding related allergens and should be investigated whenever possible so that their specific allergens can be characterised.

Anapen Junior contains sodium metabisulfite 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 Junior should be used.

4.5 Interaction with other medicinal products and other forms of interaction

The effects of adrenaline (epinephrine) may be potentiated by tricyclic antidepressants mixed noradrenargic-serotoninergic 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 Junior 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 Fertility, pregnancy and lactation

Pregnancy
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.

Breastfeeding
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

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, and 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 Junior contains sodium metabisulfite which may cause allergic-type reactions including anaphylactic reactions, life-threatening or less severe asthmatic episodes in certain susceptible patients.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

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: cardiac stimulants excl. cardiac glycosides, adrenergic and dopaminergic agents, adrenaline (epinephrine)

ATC code: C01CA24

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. Adrenaline (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.

To investigate the pharmacokinetics, pharmacodynamics, and the depth of adrenaline injection with Anapen, one PK/PD randomized, open-label, cross-over study was conducted. The impact of adrenaline administration at two sites in the thigh of 18 normal weight male volunteers, using either Anapen or a prefilled syringe was investigated. In addition, it was also studied the treatment of 12 overweight women with Anapen. The depot depth was measured by ultrasonography, plasma adrenaline was evaluated by UPLC-mass spectrometry, and heart rates (HR) were measured using a Holter monitor.
The adrenaline pharmacokinetics and cardiovascular responses in both sets of data were well correlated both in the time-course and relative amplitude. Adrenaline plasma levels showed a double peak, with parallel changes in HR. The first peak, of potential vital importance in anaphylaxis treatment, occurred at approximately 10 min post-injection, with Cmax and AUC significantly higher with Anapen than with pre- filled syringes with longer needles. The magnitude of the second peak, which lasted up to 2 h, did not differ among the various conditions. Unexpectedly, in overweight women treated with Anapen administered at inferior anterior third of the thigh, despite the injection being subcutaneous the magnitude of the first peak was similar to that observed in men, and the overall bioavailability was enhanced.

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 metabisulfite (E223)

Hydrochloric acid (foradjustment of pH)
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

18 months.

6.4 Special precautions for storage

Do not store above 25°C. Keep the auto-injector in the outer carton in order to protect from light

6.5 Nature and contents of container

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 0.3 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"
Exposed needle length: 10 mm ± 1.5 mm.
Plunger
BD (Becton Dickinson) black chlorobutyl rubber PH 701/50

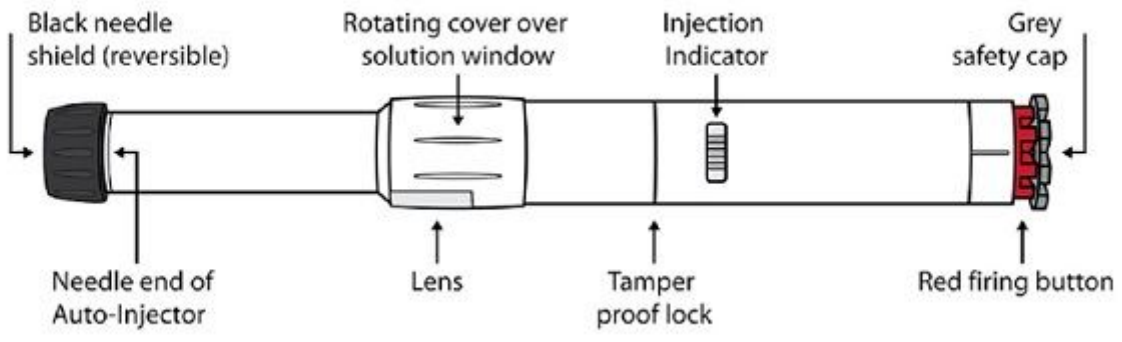
In pack sizes of 1 or 2 with a thermoformed tray protection into the cardbox. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

See Section 4.2 for instructions to be conveyed to the patient/carer regarding actions to be taken following each use of Anapen.

Instructions for use

A Parts of the Anapen Autoinjector:
Before using the Anapen Auto-Injector, the patient needs to know about the parts of the Auto-Injector. These are shown in the picture.



· **Rotating cover over solution window:**
Thepatient rotates the cover over the solution window to line up the lenses with the solution window on the auto-injector body.

• **Solution window:** Thepatient looks through the lens into this window before the injection to check that the solution is clear and ready to use.

• **Injection indicator:** Before the injection, the patient can see a white plastic plunger through the window. This means that the Anapen Auto-Injector has not been fired by mistake or tampered with. After the injection, the injection indicator turns red. This indicates that the Anapen Auto-Injector has been fired correctly.

• **Black needle shield (reversible):** This protects the needle when the patient is not using the Anapen Auto-Injector. The patient pulls the needle shield off before the injection. After the injection, the patient turns the black needle shield around and puts it back onto the same end of Anapen Auto-Injector, to cover the needle.

• **Grey safety cap:** This covers the red firing button. It stops the button from being pushed by mistake.

The patient must not remove the black needle shield or the grey safety cap until they need to use the Anapen Auto-Injector.

B. Checking the Anapen Auto-Injector

Before using the Anapen Auto-Injector, the patient must check it as follows:

1. Rotate the cover over the solution window fully anti-clockwise as shown by the arrow to line up the lenses with the solution window on the auto-injector body.

2. Look through the lens into the **solution window**. Check that the solution is clear and colourless.

If it is cloudy, coloured or contains particles, discard the Anapen Auto-Injector.

3. Make sure that the **injection indicator** is not red. If it is red, this means that the Anapen Auto-Injector has already been fired and you must discard it.

4. Rotate the cover over the solution window fully back clockwise as shown by the arrow, to ensure that the solution window is covered. Put the Anapen Auto-Injector back in the carton until you need to use it.

C. Using the Anapen Auto-Injector

If the black needle shield has been removed, the patient must **not put their thumb, fingers or hand over the open end (needle end) of the Anapen Auto-Injector.**

To use the Anapen Auto-Injector, the patient must follow the steps below:

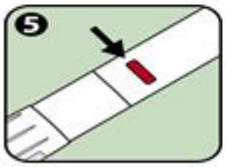
1. Remove the black needle shield by pulling hard in the direction of the arrow.

This also removes a grey protective needle shield.

2. Remove the grey safety cap from the red firing button by pulling as indicated by the arrow.

3. Hold the open end (needle end) of Anapen against the outer part of the thigh. If necessary, Anapen can be used through light clothing, such as denim, cotton or polyester.

4. Press the red firing button so that it clicks. Keep holding the Anapen Auto-Injector against the outer thigh for 10 seconds. Slowly remove Anapen from the thigh. Then gently massage the injection area.



5. **The injection indicator will have turned red.** This shows that the injection is complete. If the injection indicator is not red, injection must be repeated with a new Anapen.

6. After the injection, the needle sticks out. To cover it, click the wide end of the black needle shield back on the open end (needle end) of Anapen Auto-Injector (as indicated by the arrow).

Immediately after using Anapen the patient should call the emergency services, ask for an ambulance and say anaphylaxis. The patient should explain to the paramedic that he/she has received an injection of adrenaline into his/her thigh muscle and show them them box and these instructions.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Bioprojet Pharma
9 Rue Rameau
75002 Paris
France

8 MARKETING AUTHORISATION NUMBER

PA22580/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

February 2026