Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Jext 150 micrograms solution for injection in pre-filled pen

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Jext 150 micrograms: One pre-filled pen delivers one dose of 0.15ml solution for injection containing 150 micrograms of adrenaline (as tartrate).
1 ml solution contains 1mg adrenaline (as tartrate).
Excipients with known effect: Sodium metabisulphite (E223) and sodium chloride.
Jext contains less than 1 mmol sodium (23 mg) per dose.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection in pre-filled pen.
Clear and colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Jext is indicated in the emergency treatment of severe acute allergic reactions (anaphylaxis) to insect stings or bites, foods, drugs and other allergens as well as idiopathic or exercise induced anaphylaxis.

4.2 Posology and method of administration

Posology
Paediatric population
Patients between 15 kg and 30 kg in weight:
The usual dose is 150 micrograms.
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 life-threatening situation and under medical advice. Children and adolescents over 30 kg in weight should be prescribed a Jext 300 micrograms.

An initial dose should be administered as soon as symptoms of anaphylaxis are recognised.

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

In the absence of clinical improvement or if deterioration occurs, a second injection with an additional Jext may be administered 5–15 minutes after the first injection. It is recommended that patients are prescribed two Jext pens which they should carry at all times.

Method of administration
For intramuscular use.
For single use.
Jext is for intramuscular administration into the anterolateral thigh.
It is designed to inject through clothing or directly through the skin.

Massage around the injection area is advised to accelerate absorption.

Please refer to section 6.6 for detailed instructions for use.

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

- 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 feet 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

There are no absolute contraindications to the use of Jext during an allergic emergency.

4.4 Special warnings and precautions for use

Do not remove yellow cap until ready for use.

Jext should be administered into the anterolateral thigh. The injection is delivered immediately after the black needle shield of the auto-injector is pressed firmly against the skin or other surface. Patients should be advised not to inject Jext into the gluteus maximus due to the risk of accidental injection into a vein.
The patient should be instructed to dial 999, ask for ambulance, state anaphylaxis toseek emergency medical assistance immediately after administering the first dose 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.

Jext contains sodium metabisulphite which may rarely cause severe hypersensitivity 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 Jext should be used.

Due to an increased risk of adverse reactions following administration of adrenaline special caution should be taken in patients with cardiovascular diseases including angina pectoris, obstructive cardiomyopathy, cardiac arrhythmia, cor pulmonale, atherosclerosis and hypertension.

Special caution should also be taken in patients with hyperthyroidism, phaeochromocytoma, narrow angle glaucoma, severe renal impairment, prostatic adenoma leading to residual urine, hypercalcaemia, hypokalaemia and diabetes.

Caution should also be taken in elderly and pregnant patients.

In case of injection performed by a caregiver, the patient should be instructed not to move and immobilisation of the patient's leg should be ensured during injection to reduce the risk of laceration. The product is for single use only and cannot be reused.

In patients with thick sub-cutaneous fat layer, there is a risk of adrenaline being administered in the sub-cutaneous tissue which may result in a slower adrenaline absorption (see section 5.2) and a suboptimal effect. This may increase the need for a second Jext injection (see section 4.2).

Peripheral ischaemia following accidental injection into hands or feet may cause decreased blood flow to adjacent areas due to vasoconstriction.

All patients who are prescribed Jext 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 the Jext in case support is needed in the emergency situation.

There is often a prolonged period between supply of Jext and an allergic reaction requiring adrenaline. Patients should be advised to regularly check Jext and ensure it is replaced within the expiry period.

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.

4.5 Interaction with other medicinal products and other forms of interactions

Caution is indicated in patients receiving drugs that may sensitise the heart to arrhythmias, including digitalis and quinidine. The effects of adrenaline may be potentiated by tricyclic antidepressants, monoamine oxidase inhibitors (MAO-inhibitors) and catechol-O-methyl transferase inhibitors (COMT inhibitors), thyroid hormones, theophylline, oxytocin, parasympatholytics, certain antihistamines (diphenhydramine, chlorpheniramine), levodopa and alcohol. Adrenaline inhibits the secretion of insulin, thus increasing the blood glucose level. It may be necessary for diabetic patients receiving adrenaline to increase their dosage of insulin or oral hypoglycaemic drugs. The alpha- and beta-stimulating effect of adrenaline can be inhibited by concomitant use of alpha- and beta-blocking drugs as well as parasympathomimetic drugs.

4.6 Fertility, pregnancy and lactation

Pregnancy
Clinical experience in the treatment of anaphylaxis during pregnancy is limited. Adrenaline should only be used during pregnancy if the potential benefit justifies the potential risk for the foetus.

Breastfeeding
Adrenaline is not orally bioavailable; any adrenaline excreted in breast milk would not be expected to have any effect on the nursing infant.

Fertility
There is no clinical data with respect to fertility for the use of Jext.

4.7 Effects on ability to drive and use machines

Jext has no or negligible influence on the ability to drive and use machines, however,patients are not recommended to drive or use machines following administration of adrenaline, since they will be affected by the anaphylactic reaction.

4.8 Undesirable effects

Summary of the safety profile
Side effects associated with adrenaline's alpha and beta receptor activity may include cardiovascular effects as well as undesirable effects on the central nervous system.

Tabulated list of adverse reactions
The following table is based upon post marketing experience with the use of adrenaline. The frequency cannot be estimated from the available data.

System Organ Class	Adverse Drug Reaction
Metabolism and nutrition disorders	Hyperglycaemia, hypokalaemia, metabolic acidosis
Nervous system disorders	Tremor, dizziness, headache, paraesthesia, hypoaesthesia
Cardiac disorders	Palpitations, tachycardia, angina pectoris, arrhythmia, stress cardiomyopathy, syncope
Vascular disorders	Peripheral ischaemia*, increased blood pressure**
Gastrointestinal disorders	Nausea, vomiting
Musculoskeletal and connective tissue disorders	Muscle rigidity
General disorders and administration site conditions	Injection site reaction*, asthenia, hyperhidrosis, chest discomfort

*Accidental injection into digits and hands may result in localised symptoms of peripheral ischaemia, including injection site coldness, pallor, paraesthesia and hypoaesthesia as well as local reactions such as injection site bruising, pain, bleeding and swelling.
**Isolated cases of hypertension and hypertensive crisis have been reported.

Adrenaline has been shown to elicit several effects upon the body through adrenergic receptor activation, including hyperglycaemia, hypokalaemia, and metabolic acidosis. These effects have not been reported from the use of adrenaline auto-injectors.

Description of selected adverse reactions
Jext contains sodium metabisulphite which may rarely cause severe hypersensitivity reactions including anaphylactic symptoms and bronchospasm (see section 4.4. Special warning and precautions for use).

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;
Website: www.hpra.ie

4.9 Overdose

Overdose or inadvertent intravascular injection of adrenaline may cause cerebral haemorrhage and ventricular arrhythmiasresulting from a sharp rise in blood pressure. Myocardial ischaemias and necroses as well as renal impairment may occur. Fatalities may also result from pulmonary oedema because of peripheral vascular constriction together with cardiac stimulation.
Pulmonary oedema may be treated with alpha-blocking agents such as phentolamine. In case of arrhythmias these may be treated with beta-blocking agents.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cardiac stimulants excl. cardiac glycosides,adrenergic and dopaminergic agents.
ATC code: C01CA24.

Adrenaline is a catecholamine which stimulates the sympathetic nervous system (both alpha and beta receptors) by which cardiac rate, cardiac output and coronary circulation is raised. Adrenaline through its action on beta receptors on bronchial smooth muscles causes bronchial smooth muscle relaxation which alleviates wheezing and dyspnoea.

5.2 Pharmacokinetic properties

Adrenaline is a naturally occurring substance produced by the adrenal medulla and secreted in response to exertion or stress. It is rapidly inactivated in the body mostly by the enzymes COMT and MAO. The liver is rich in these enzymes and is an important, although not essential, tissue in the degradation process. Much of the dose of adrenaline is accounted for by excretion of metabolites in the urine.
The plasma half-life of adrenaline is about 2.5 min. However local vasoconstriction may retard absorption, so that the effects can last longer than the half-life would predict. Massage around the injection area is advised to accelerate absorption.

In an exploratory PK/PD study the mean plasma concentration-time curves were biphasic with a first peak within approx. 8-10 min followed by a slower increase until a second peak (plateau) was reached after approx. 30-40 min following injection of Jext. There was however a large variability in shape of the individual plasma concentration-time profiles. The results suggest that the adrenaline absorption in patients with a thick sub-cutaneous fat layer (i.e. STMD, skin to muscle depth >20mm) is slower than in subjects with a thinner sub-cutaneous fat layer.
Whereas plasma exposure was apparently comparable between Jext and IM injection in the first 16 minutes for the overall population, when data were evaluated by STMD cohort, the plasma exposure up to 30 minutes was generally lower in Jext compared to manual IM injection in the STMD > 20 mm cohort. The point estimates of the Jext to manual IM injection ratio were 0.39 (90% CI 0.20-0.75) for $AUC_{0\text{-}8\ mins,}$0.56 (90% CI 0.31-0.99) for $AUC_{0\text{-}16\ mins}$ and 0.66 (90% CI 0.39-1.12) for $AUC_{0\text{-}30\ mins}$ suggesting consistently lower exposure in the first 30 minutes following administration with Jext compared to manual IM injection in the STMD > 20 mm cohort.

5.3 Preclinical safety data

Adrenaline has been utilised in the treatment of allergic emergencies for many years. There is no preclinical data of relevance available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Sodium Metabisulphite (E223)
Hydrochloric Acid (for pH adjustment)
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

22 months

6.4 Special precautions for storage

Store below 25°C.
Do not freeze.

Jext is provided in a plastic carry case in order to protect Jext while being carried by the patient/carer or during storage. Jext should be removed from the carry case before use and should be removed during inspection of the product. It is recommended to return Jext to the carry case after inspection.

6.5 Nature and contents of container

Pre-filled pen (single dose pen) comprisingan auto-injector with a cartridge. The cartridge is made of glass (type 1), sealed with a latex free grey rubber plunger and a latex free bromobutyl rubber seal within an anodised aluminium cap. The auto-injector and carry case is made of plastic.

Exposed needle length:
Jext 150 micrograms: 13 mm
Jext 300 micrograms: 15 mm

Pack-size: Single pack with 1 pre-filled pen. Multipack with 2 pre-filled pens.
Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

Jext is a single-use pre-filled pen designed for easy use.

The pre-filled pen is operated by simply pressing the black injector tip against the outer thigh. This will activate a plunger, which pushes a concealed needle through the membrane on the black injector tip into the muscle and injects a dose of adrenaline. This can be done through clothing.

Jext 150 micrograms contains 1.4 ml of adrenaline injection 1 mg/ml which is designed to deliver a single dose (0.15 ml) of 150 micrograms adrenaline when activated. After activation of the auto-injector 1.25 ml remains in the pre-filled pen. Discard any unused solution.

A small air bubble may occur in Jext. It has no influence on either the use or the efficacy of the product.

Educational materials regarding the correct use, storage and care of Jext are available to prescribers, patients and caregivers including a Jext Trainer pen without needle or adrenaline for practising or instructing others in the correct use of Jext.

Note: the yellow cap prevents the device from activating, and should not be removed before injection is required. The black injector tip should be kept away from the hand.

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

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

Check the solution periodically through the viewing window of the unit to make sure the solution is clear and colourless. Replace and discard the pre-filled pen if the solution is discoloured or contains a precipitate, or at the latest before the expiry date.
The expiry date is indicated on the label and Jext should not be used after this date.

7 MARKETING AUTHORISATION HOLDER

ALK-Abello A/S
Boge Alle 6-8
DK-2970 Horsholm
Denmark

8 MARKETING AUTHORISATION NUMBER

PA1255/006/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th February 2011Date of last renewal: 12th October 2015

10 DATE OF REVISION OF THE TEXT

March 2021