IRISH MEDICINES BOARD ACT 1995, as amended

Medicinal Products (Control of Placing on the Market) Regulations, 2007, as amended

PA1255/002/001
Case No: 2079103

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

ALK-Abello A/S

Boge Alle 6-8, **DK-2970 Horsholm**, **Denmark**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

EpiPen Junior 0.15 mg, solution for injection

the particulars of which are set out in the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **06/07/2010** until **24/10/2011**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

EpiPen Junior 0.15 mg, solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 0.5 mg adrenaline (Epinephrine). A single dose (0.3 ml) contains 0.15 mg (150 microgram) adrenaline (Epinephrine).

Excipient: Sodium Metabisulphite.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear and colourless solution in a pre-filled pen (Auto-injector).

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

The Auto-Injectors are indicated in the emergency treatment of a severe anaphylactic shock or allergic reaction to allergens e.g. insect stings or bites, foods or drugs.

4.2 Posology and method of administration

Usual paediatric dose for allergic emergencies is 0.15 mg adrenaline for intramuscular use depending upon the body weight of the patient (0.01 mg/kg body weight). However, the prescribing physician has the option of prescribing more or less than these amounts based on careful assessment of each individual patient and recognising the life-threatening nature of reactions for which this is being prescribed. The physician should consider using other forms of injectable adrenaline if lower doses are felt to be necessary for small children.

In the absence of clinical improvement or if deterioration occurs after the initial treatment, a second injection with an additional EpiPen Junior Auto-Injector may be necessary. The repeated injection may be administered after about 5 – 15 minutes.

The patient must consult a physician after injection in order to have relevant actions taken for further evaluation and/or treatment.

4.3 Contraindications

There are no known absolute contraindications to the use of EpiPen Junior during an allergic emergency.

4.4 Special warnings and precautions for use

Adrenaline is ordinarily administered with extreme caution to patients who have a heart disease. Adrenaline should only be prescribed to those patients, but also those suffering from diabetes, hyperthyroidism, hypertension and elderly individuals if the potential benefit justifies the potential risk.

Accidental injection into hands or feet resulting in peripheral ischaemia has been reported. Patients may need treatment following the accidental injection.

EpiPen Junior 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 care-fully instructed in regard to the circumstances under which Epipen Junior should be used.

The Auto-Injectors should be injected into the anterolateral aspect of the thigh. Patients should be advised not to inject into the buttock.

4.5 Interaction with other medicinal products and other forms of interaction

Caution is indicated in patients receiving drugs that may sensitise the heart to arrhythmias, including digitalis, mercurial diuretics or quinidine. The effects of adrenaline may be potentiated by tricyclic antidepressants and monoamine oxidase inhibitors (MAO-inhibitors).

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.

Observe. The β-stimulating effect can be inhibited by simultaneous treatment with β-blocking drugs.

4.6 Pregnancy and lactation

Clinical experience in the treatment of pregnant women is limited. As adrenaline is a substance that naturally occurs in the body, it is unlikely that this drug would have any detrimental effects on fertility.

Adrenaline should be used during pregnancy only if the potential benefits justify the potential risk for the foetus.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Side effects associated with adrenaline's alpha and beta receptor activity may include symptoms such as tachycardia and hypertension as well as undesirable effects on the central nervous system. Usual side effects are hyperhidrosis, nausea, vomiting, headache, dizziness, asthenia, tremor and anxiety. Cardiac arrhythmia may follow administration of adrenaline. Peripheral ischaemia following accidental injection of the pens in hands or foot have been reported (see 4.4 Warnings and precautions).
In rare cases stress cardiomyopathy has been seen in patients treated with adrenaline.

4.9 Overdose

Overdose or inadvertent intravascular injection of adrenaline may cause cerebral haemorrhage resulting from a sharp rise in blood pressure. Fatalities may also result from pulmonary oedema because of peripheral vascular constriction together with cardiac stimulation.
Pulmonary oedema may be treated with α-blocking agents such as phentolamine. In case of arrhythmias these may be treated with β-blocking agents.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cardiac stimulants excl. cardiac glycosides.
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. Adrenaline is rapidly inactivated and much of the dose of adrenaline is accounted for by excretion of metabolites in the urine.

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(Catechol-O-Methyltransferase) and MAO (Mono Amine Oxidase). 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.

According to Remington's Pharmaceutical Sciences, the plasma half-life of adrenaline is about 2.5 min. However, by subcutaneous or intramuscular routes, local vasoconstriction retards absorption, so that the effects occur insidious and last much longer than the half-life would predict. Massage around the injection area is advised.

5.3 Preclinical safety data

Adrenaline has been utilised in the treatment of allergic emergencies for many years. No preclinical studies have been performed in connection with this application.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride
Sodium Metabisulfite
Hydrochloric Acid (for pH adjustment)
Water for Injections

6.2 Incompatibilities

Adrenaline and its salts are rapidly destroyed in solution with oxidising agents. Oxidation can be inhibited by addition of anti-oxidants. The solution darkens in colour upon exposure to air or light.

6.3 Shelf Life

18 months

6.4 Special precautions for storage

Keep container in the outer carton in order to protect from light. Do not store above 25°C. Do not refrigerate or freeze.

Check the solution periodically through the viewing window of the unit to make sure the solution is clear and colourless. Discard and replace the Auto-Injector if the solution is discoloured or contains a precipitate, or at the latest

by expiration date. The expiry date is indicated on the label and the Auto-Injector should not be used after this date.

6.5 Nature and contents of container

The immediate container/closure system consists of a glass cartridge sealed by a rubber plunger at one end and by rubber diaphragm which has been inserted into an aluminium hub with attached stainless steel needle at the other end. The glass cartridge contains the product.

The Auto-Injector administration device:

Glass cartridge container:
Type I, Borosilicate Glass

Diaphragm - Stopper:
PH 701/50/Black (butyl rubber plunger)

Needle - Hub - Sheath:
Needle: Siliconised Type 304 stainless steel
Hub: Anodised 3003 aluminium alloy
Sheath: Synthetic polyisoprene

Pack size: Auto-injector single dose containing 2 ml.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

For single use only. The Auto-Injectors must be discarded immediately after use.

During instruction of the patient in correct use of the EpiPen the prescribing doctor may use an “EpiPen TRAINER”.

The EpiPen Auto-Injector contains 2 ml of adrenaline injection 0.5 mg/ml which is designed to deliver a single dose (0.3 ml) of 0.15 mg adrenaline when activated. After activation of the Auto-Injector 1.7 ml remains in the Auto-Injector.

Do not remove grey safety cap until ready for use.

Under no circumstances place the black end of the EpiPen Auto-Injector on or near your thumbs, fingers or hands. Accidental injection into hands or fingers resulting in peripheral ischaemia has been reported. See section 4.4, special warnings and precuation for use. The EpiPen Auto-Injector should be used on the outer thigh. The injection is activated immediately the black end of the EpiPen Auto-Injector comes into contact with any skin or other surface.

The EpiPen Auto-Injectors are designed for easy use by the lay person and has to be considered as a first aid. The Auto-Injector should simply be jabbed firmly against the outer portion of the thigh from a distance of approximately 10 cm. There is no need for more precise placement in the outer portion of the thigh. When EpiPen Auto-Injector is jabbed against the thigh, it releases a spring activated plunger, pushing concealed needle into the thigh muscle and expelling a dose of adrenaline:

1. Grasp EpiPen Auto-Injector in dominant hand, with thumb closest to grey safety cap.
2. With the other hand pull off grey safety cap.
3. Hold the EpiPen Auto-Injector in a distance of approximately 10 cm away from the outer thigh. The black tip should point towards the outer thigh.
4. Jab firmly into the outer thigh, so that the EpiPen Auto-Injector is at a right angle to (at a 90 degree angle) the outer thigh.
5. Hold in place for 10 seconds. The EpiPen Auto-Injector should be removed and safely discarded.
6. Massage the injection area for 10 seconds.

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

Instruction for use is enclosed in the package.

7 MARKETING AUTHORISATION HOLDER

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Bøge Allé 6-8
2970 Hørsholm
Denmark

8 MARKETING AUTHORISATION NUMBER

PA1255/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 September 2006
Date of last renewal: 25 October 2006

10 DATE OF REVISION OF THE TEXT

July 2010