

Adrenaline (Epinephrine) 1:1000 Injection BP

PL 20910/0002

UKPAR

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Adrenaline (Epinephrine) 1:1000 Injection BP**PL 20910/0002****LAY SUMMARY**

The MHRA has granted Taro Pharmaceuticals (Ireland) Limited a Marketing Authorisation (licence) for the medicinal product Adrenaline (Epinephrine) 1 in 1000 Solution for Injection BP (PL 20910/0002). This prescription-only medicine (POM) provides rapid relief in the treatment of severe hypersensitivity reactions to drugs and other allergens and may also be used in the emergency treatment of anaphylactic (allergic) shock.

Adrenaline (Epinephrine) 1 in 1000 solution for Injection BP contains the active ingredient adrenaline acid tartrate, a natural antidote to the chemicals released during an allergic reaction..

The active ingredient in this product has traditionally been named 'adrenaline' in the UK. The international name for the substance 'epinephrine'. These terms refer to the same substance. Given the history of use of the traditional name in the UK, dual labelling is to be employed in the form adrenaline (epinephrine), for the marketed product. This is in line with UK requirements.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Adrenaline (Epinephrine) 1 in 1000 Solution for Injection BP outweigh the risks, hence a Marketing Authorisation has been granted.

Adrenaline (Epinephrine) 1:1000 Injection BP

PL 20910/0002

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, a marketing authorisation for the medicinal product Adrenaline (epinephrine) 1:1000 Injection BP (PL 20910/0002) was granted on 23rd October 2007. The product is a prescription-only medicine.

This application was submitted as an abridged application according to Article 10(1) of Directive 2001/83/EC. The reference product is Adrenaline Injection BP, 1 in 1000, 1 mg in 1 ml (Antigen Pharmaceuticals Ltd), PL 02848/5909R, licensed in the UK on 30.01.1991.

Adrenaline (epinephrine) is one of a group of medicines called sympathomimetics. It is a direct-acting sympathomimetic agent. It has more pronounced effects on beta- than on alpha- adrenergic receptors, although alpha effects prevail at high dose.

Adrenaline (epinephrine) is used to provide rapid relief of severe allergic reactions. It may also be used in the treatment of shock due to an allergic reaction.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

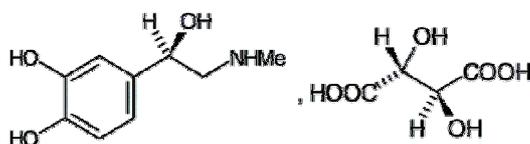
Nomenclature

rINN: Adrenaline acid tartrate (epinephrine acid tartrate)

Chemical names: (1R)-1-(3,4-dihydroxyphenyl)-2-(methylamino)ethanol hydrogen
(2R,3R)-2,3-dihydroxybutanedioate.

CAS number: 51-42-3

Structure



Molecular formula: C₉H₁₃NO₃, C₄H₆O₆

Molecular Weight: 333.3

A white to greyish-white, crystalline powder, freely soluble in water, slightly soluble in alcohol, practically insoluble in ether.

A valid Certificate of Suitability has been provided.

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

The active ingredient, adrenaline acid tartrate, is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

An acceptable justification of the proposed specifications has been provided.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data have been generated supporting a retest period of 3 years when stored in a polyethylene container.

DRUG PRODUCT**Other ingredients**

Other ingredients consist of pharmaceutical excipients, namely sodium chloride, sodium metabisulphite and water for injection. All excipients used comply with their respective European Pharmacopoeia monograph.

Satisfactory specifications and Certificates of Analysis have been provided for all excipients. No materials of animal or human origin are contained in or used in the manufacture of this product.

Impurity profiles

Satisfactory information was provided on levels of impurities in the proposed product.

Manufacture

A description and flow-chart of the manufacturing method have been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches. The results are satisfactory.

Satisfactory tests and acceptance criteria have been set for in-process testing.

Finished product specification

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System

Product is packaged in a type I clear glass ampoule with a colour break. Specifications and Certificates of Analysis for all packaging used have been provided. This is satisfactory.

Stability

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 2 years and storage conditions of "Keep in the outer container", "Protect from light" and "Do not store above 25 degrees C" have been set, which is satisfactory.

Conclusion

It is recommended that Marketing Authorisation is granted for this application.

The requirements for essential similarity of the proposed and reference products have been met with respect to qualitative and quantitative content of the active substance and pharmaceutical form. It was not necessary to demonstrate bioequivalence.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none is required for an application of this type.

CLINICAL ASSESSMENT

1 INTRODUCTION

This is a national abridged-standard, non-committee application for generic adrenaline (epinephrine) 1mg/ml solution for injection on the basis of essential similarity to innovator product Adrenaline injection BP (1in 1000, or 1mg/ml solution) from Antigen International Limited (PL 02848/5909R).

1.1 GCP ASPECTS

No clinical studies were submitted in support of this product.

1.2 THERAPEUTIC CLASS

Adrenaline (Epinephrine) is a naturally occurring catecholamine, a sympathomimetic agent.

ATC code; R03 AK01

1.3 BACKGROUND

Of the active: Adrenaline (Epinephrine) is a naturally occurring catecholamine, a potent sympathomimetic agent that is used for treatment of anaphylactic shock, relief of severe airway obstruction and in cases of intractable hypotension. The innovator / brand-leader has been authorised in the UK for a number of years and the brand leader MA was renewed recently in 2003. Epinephrine has been authorised and used worldwide for over 3 decades in different forms and situations. It is not active orally due to reasons of rapid degradation.

Application: The current application is based on essential similarity to the brand leader, PL 02848/5909R from Antigen International Limited. As both are solutions, the applicant claims exemption from the usual bioequivalence study that is a requirement for oral preparations. This is discussed further in the appropriate section II.3 of this report.

1.4 REGULATORY STATUS

The current product has no pending applications, nor had any refusals either within the EU or outside of the EEA.

1.5 INDICATIONS

Adrenaline (epinephrine) 1:1000 Injection BP may be used as follows:

- to provide rapid relief in the treatment of severe hypersensitivity reactions to drugs and other allergens
- in the emergency treatment of anaphylactic shock.

These are identical to the cited reference product and are acceptable.

1.6 DOSE AND DOSE REGIMEN

As proposed in SPC. The following are proposed;

Adrenaline (Epinephrine) 1 mg/ml Injection BP may be administered undiluted by SC or IM injection. In the shocked patient, the intramuscular route is recommended as absorption from the intramuscular site is more rapid and reliable than from the subcutaneous site.

Severe hypersensitivity reactions, anaphylactic shock

IM Injection:

Adults: The usual dose is 500 micrograms (0.5 ml of adrenaline/epinephrine 1/1000). If necessary, this dose may be repeated several times at 5-minute intervals according to blood pressure, pulse and respiratory function.

Half doses of adrenaline/epinephrine may be safer for patients who are taking amitriptyline, imipramine or a beta blocker.

Children: The following doses of Adrenaline (Epinephrine) Injection are recommended:

Age	Dose
Over 12 years	500 micrograms (0.5 ml) 250 micrograms (0.25 ml) if child is small or prepubertal
6 – 12 years	250 micrograms (0.25 ml)
6 months – 6 years	120 micrograms (0.12 ml)
Under 6 months	50 micrograms (0.05 ml)

If necessary, these doses may be repeated several times at 5-minute intervals according to blood pressure, pulse and respiratory function.

Comments: These are again identical to the cited brand leader SmPC and thus acceptable.

1.7 CONSIDERATION FOR PAEDIATRIC USE

The applicant proposes doses in children identical to the brand leader. As Epinephrine (Adrenaline) is an endogenous, naturally occurring catecholamine in both children and adults, no specific issues are expected. The doses however are tempered in children and these are appropriate.

1.8 ASSESSOR'S COMMENT

The basis of the application, the indications and posology sought and paediatric use are considered appropriate and in line with the brand leader. This is acceptable.

2 CLINICAL PHARMACOLOGY

2.1 PHARMACOKINETICS

The pharmacokinetics of Adrenaline (epinephrine) is well established. The applicant has not submitted any new data and none are expected for an application based on essential similarity.

2.2 PHARMACODYNAMICS

The pharmacodynamics of Adrenaline (epinephrine) is well established. The applicant has not submitted any new data and none are expected for an application based on essential similarity.

2.3 BIOAVAILABILITY & BIOEQUIVALENCE

The current application is for parenteral formulation as is the innovator product. The bioavailability is therefore expected to be 100%. Such formulations are exempt from bioequivalence studies by the Directive EC/83/2001 and the relevant guideline (CHMP/EWP/QWP/1401/98). The applicant has therefore not provided a biostudy and this is considered acceptable.

3 CLINICAL EFFICACY

No new Efficacy data have been submitted and none are required.

4 CLINICAL SAFETY

No new safety data have been submitted and none are required. Epinephrine, whilst naturally occurring still has its own intrinsic, risk associated with its use, which is neither inconsiderable nor negligible. However, when used in the situations adrenaline (epinephrine) is indicated, the risk: benefit ratio is considered favourable. This should be borne in mind on each occasion it is used.

5 LIST OF QUESTIONS PROPOSED

None.

6 CLINICAL EXPERT REPORT

An expert report has been provided by a suitably qualified consultant and it was acceptable.

6.1 SPC: SUMMARY OF PRODUCT CHARACTERISTICS

This is satisfactory

6.2 PIL; PATIENT INFORMATION LEAFLET

This is satisfactory

6.3 LABELS

Labels are considered medically satisfactory.

7 DISCUSSION

This application is based on a claim of essential similarity for a parenterally administered product. As the bioavailability is expected to be 100% a biostudy is not required, nor are any new efficacy and safety data. The Marketing Authorisation grant could be considered.

8 CLINICAL AND PRE-CLINICAL ASSESSORS' CONCLUSIONS

There are no preclinical issues associated with this naturally occurring, short acting, catecholamine for emergency use that has been in clinical practise for nearly 3 decades. From a clinical stand point, the risk; benefit ratio for this formulation in the indications sought is considered favourable. Marketing Authorisation grant may be considered.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Adrenaline 1:1000 Injection BP are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for application of this type.

EFFICACY

The efficacy of Adrenaline (epinephrine) 1:1000 Injection BP has been well documented in the past.

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the originator product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The benefit/risk balance is considered to be positive.

Adrenaline (Epinephrine) 1:1000 Injection BP**PL 20910/0002****STEPS TAKEN FOR ASSESMENT**

1	The MHRA received the marketing authorisation application on 18 th May 2004
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 25 th June 2004
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 18 th January 2006 and 8 th May 2006
4	The applicant responded to the MHRA's request, providing further information on the quality section on 8 th May 2006 and 3 rd December 2006
5	The application was determined on 23 rd October 2007

SUMMARY OF PRODUCT CHARACTERISTICS**1 NAME OF THE MEDICINAL PRODUCT**

Adrenaline (epinephrine) 1:1000 Injection BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution for injection contains 1 mg adrenaline (epinephrine) as the acid tartrate.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution.

4 CLINICAL PARTICULARS**4.1 THERAPEUTIC INDICATIONS**

Adrenaline (epinephrine) 1:1000 Injection BP may be used as follows:

- to provide rapid relief in the treatment of severe hypersensitivity reactions to drugs and other allergens
- in the emergency treatment of anaphylactic shock.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Adrenaline (epinephrine) 1:1000 Injection BP may be administered undiluted by subcutaneous or intramuscular injection. In the shocked patient, the intramuscular route is recommended as absorption from the intramuscular site is more rapid and reliable than from the subcutaneous site.

Severe hypersensitivity reactions, anaphylactic shock

IM Injection:

Adults: The usual dose is 500 micrograms (0.5 ml of adrenaline (epinephrine) 1/1000). If necessary, this dose may be repeated several times at 5-minute intervals according to blood pressure, pulse and respiratory function.

Half doses of adrenaline (epinephrine) may be safer for patients who are taking amitriptyline, imipramine or a beta blocker.

Children: The following doses of Adrenaline (epinephrine) 1:1000 Injection BP are recommended:

Age	Dose
Over 12 years	500 micrograms (0.5 ml) 250 micrograms (0.25 ml) if child is small or prepubertal
6 – 12 years	250 micrograms (0.25 ml)
6 months – 6 years	120 micrograms (0.12 ml)
Under 6 months	50 micrograms (0.05 ml)

If necessary, these doses may be repeated several times at 5-minute intervals according to blood pressure, pulse and respiratory function.

4.3 CONTRAINDICATIONS

Hypersensitivity to adrenaline (epinephrine) or to any of the excipients.

Use during labour

Use with local anaesthesia of peripheral structures including digits and ear lobes.

Use in the presence of ventricular fibrillation, cardiac dilatation, coronary insufficiency, organic brain disease or atherosclerosis, except in emergencies where the potential benefit clearly outweighs the risk.

Use if the solution is discoloured.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Adrenaline (epinephrine) should only be administered with great caution in the elderly, or those with cardiovascular disease, including hypertension and ischaemic heart disease, or hyperthyroidism, or in patients with long standing asthma or emphysema who have reached an age at which degenerative heart disease is prevalent, (increased susceptibility to the pressor and arrhythmogenic effects of adrenaline (epinephrine) in these patient groups), patients with diabetes mellitus (risk of hyperglycaemia with use of adrenaline (epinephrine)), or in patients with closed-angle glaucoma (increased intra-ocular pressure due to mydriatic effect of adrenaline (epinephrine)).

Repeated administration may produce local necrosis at the sites of injection.

Prolonged administration may produce metabolic acidosis, renal necrosis and adrenaline (epinephrine) fastness or tachyphylaxis.

Adrenaline (epinephrine) should be avoided or used with extreme caution in patients undergoing anaesthesia with halothane or other halogenated anaesthetics, in view of the risk of inducing ventricular fibrillation.

The solution should not be mixed with other agents unless compatibility is known.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Concurrent use with tricyclic antidepressants, digitalis glycosides, parenterally used diuretics, guanethidine, methyl dopa, reserpine or other similar agents may potentiate the effects of adrenaline (epinephrine), resulting in exaggerated pressor and/or arrhythmogenic effects. Beta-blockers, especially non-selective ones, increase the pressor effect, resulting in hypertension, and decrease the bronchodilatory effect of adrenaline (epinephrine). (See section 4.2 Posology and method of administration).

Adrenaline (epinephrine) should be avoided or used with extreme caution in patients undergoing anaesthesia with halothane or other halogenated anaesthetics in view of the risk of inducing ventricular fibrillation. (See section 4.4 Special warnings and special precautions for use).

4.6 PREGNANCY AND LACTATION

Adrenaline (epinephrine) should only be used during pregnancy and lactation if considered essential by the physician

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not applicable as the patient would be too ill.

4.8 UNDESIRABLE EFFECTS

The most commonly reported adverse reaction is headache. Adverse reactions may occur at therapeutic doses, and include the following:

Endocrine disorders: Glucose tolerance impaired.

Metabolism and nutrition disorders: Decreased appetite.

Psychiatric disorders: Anxiety, fear, irritability, psychotic disorder.

Nervous system disorders: Headache, tremor, restlessness, insomnia, confusional state

Cardiac disorders: Palpitation, arrhythmia.

Vascular disorders: Hypertension, peripheral coldness.

Respiratory, thoracic and mediastinal disorders: Dyspnoea.

Gastrointestinal disorders: Dry mouth, salivary hyper-secretion, vomiting.

Skin and subcutaneous tissue disorders: Hyperhidrosis.

Renal and urinary disorders: Dysuria, urinary retention.

General disorders and administration site conditions: Asthenia.

Hypertension and cardiac arrhythmias, including ventricular fibrillation, may result from interaction between adrenaline (epinephrine) and certain other medicines (see section 4.5 Interactions).

4.9 OVERDOSE

Possible signs of overdosage include restlessness, confusion, pallor, tachycardia, bradycardia, cardiac arrhythmias and cardiac arrest. Treatment is primarily symptomatic and supportive. Prompt injection of a rapid acting alpha-adrenoceptor blocking agent such as phentolamine followed by a beta-blocker such as propranolol, has been tried to counteract the pressor and arrhythmogenic effects of adrenaline (epinephrine). A rapidly-acting vasodilator such as glyceryl trinitrate has also been used.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

ATC Code: R03AK01 Group: Epinephrine and other drugs for obstructive airway disease Adrenaline (epinephrine) is a direct-acting sympathomimetic agent. It has more pronounced effects on beta- than on alpha- adrenergic receptors, although alpha effects prevail at high dose.

The effects of adrenaline (epinephrine) include increased rate and force of cardiac contraction, cutaneous vasoconstriction and broncho-dilatation. With higher doses, stimulation of peripheral alpha-receptors results in an increase in peripheral resistance and in blood pressure.

5.2 PHARMACOKINETIC PROPERTIES

As a result of enzymatic degradation in the gut and first-pass metabolism in the liver, adrenaline (epinephrine) is almost totally inactive when given by mouth. It acts rapidly following subcutaneous or intramuscular injection; although absorption is slowed by local vasoconstriction, it can be hastened by massaging the injection site.

Most adrenaline (epinephrine) that is either injected into the body or released into the circulation from the adrenal medulla, is very rapidly inactivated by processes which include uptake into the adrenergic neurones, diffusion, and enzymatic degradation in the liver and body tissues. The enzymes responsible for the chemical inactivation of exogenous or hormonal adrenaline are catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO). In general, adrenaline (epinephrine) is methylated to metanephrine by COMT followed by oxidative deamination by MAO to 4-hydroxy-3-methoxymandelic acid (formerly termed vanillylmandelic acid: VMA), or oxidatively deaminated by MAO to 3,4-dihydroxymandelic acid which, in turn, is methylated by COMT, once again to 4-hydroxy-3-methoxymandelic acid; the metabolites are excreted in the urine mainly as their glucuronide and ethereal sulphate conjugates.

The ability of catechol-O-methyltransferase to effect introduction of a methyl group is an important step in the chemical inactivation of adrenaline (epinephrine) and similar catecholamines (in particular, noradrenaline/norepinephrine). It means that the termination of the pharmacological response of catecholamines is not simply dependent upon monoamine oxidase. In its role of neurotransmitter, intraneuronal catecholamine (mainly noradrenaline/norepinephrine) is, however, enzymatically regulated by monoamine oxidase. Adrenaline (epinephrine) crosses the placenta to enter foetal circulation.

5.3 PRECLINICAL SAFETY DATA

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium Metabisulphite
Sodium Chloride
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

2 years

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25°C.

Keep the container in the outer carton in order to protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

Ph.Eur. Type 1 colourless glass ampoules, 1 ml.

Pack size: 10 x 1 ml ampoules.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND HANDLING

If only part of an ampoule is used, discard the remaining solution.

7 MARKETING AUTHORISATION HOLDER

Taro Pharmaceuticals Ireland Ltd.,

Lourdes Road,

Roscrea,

County Tipperary,

Ireland.

8 MARKETING AUTHORISATION NUMBER(S)

PL 20910/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/10/2007

10 DATE OF REVISION OF THE TEXT

23/10/2007

PATIENT INFORMATION LEAFLET

Patient Information Leaflet

Adrenaline (epinephrine) 1:1000 Injection BP

Please read all of this leaflet carefully before you start using this medicine.

Keep this leaflet. You may need to read it again.

If you have further questions, please ask your doctor or pharmacist.

This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

WHAT IS ADRENALINE (EPINEPHRINE) 1:1000 INJECTION BP

Adrenaline (epinephrine) 1:1000 Injection BP is a colourless sterile solution for injection. Each ml of solution for injection contains 1 mg adrenaline (epinephrine) as the acid tartrate.

It also contains the inactive ingredients sodium metabisulphite, sodium chloride and water for injections.

Type of medicine: Adrenaline (epinephrine) is one of a group of medicines called sympathomimetics.

Pack sizes: Ten 1 ml ampoules.

Manufacturer and Marketing Authorisation Holder: Taro Pharmaceuticals Ireland Ltd., Lourdes Rd., Roscrea, Co. Tipperary, Ireland. PL 20910/0002

WHAT IS THIS MEDICINE USED FOR

Adrenaline (epinephrine) may be used to provide rapid relief of severe allergic reactions. It may also be used in the treatment of shock due to an allergic reaction.

BEFORE YOU RECEIVE YOUR MEDICINE

Before you are given this medicine, please read the following statements:

When must you not take this medicine

You must not receive this medicine:

- if you are allergic (hypersensitive) to adrenaline (epinephrine) or to any of the ingredients in this medicine
- during childbirth
- if the solution is discoloured.

You must not receive this medicine:

- if you have heart failure
 - if you suffer from angina (chest pain)
 - if you have hardening of the arteries,
- unless in emergencies where your doctor considers that the possible benefit clearly outweighs the risk.

When to take special care using this medicine

- if you are elderly
- if you have high blood pressure or angina
- if you have an overactive thyroid gland
- if you have long-standing asthma or emphysema
- if you suffer from diabetes
- if you have glaucoma (abnormally high pressure in the eye)
- if you are receiving repeated doses of this medicine
- if you are being given an inhaled anaesthetic.

If any of these statements apply to you, now or in the past, please consult your doctor.

Take special care if you are using any other medicines

Please tell your doctor, nurse or pharmacist if you are taking any other medicines, including those bought without a prescription. This applies to medicines used some time ago and ones you are due to receive. The following medicines may increase the effects of adrenaline (epinephrine), resulting in high blood pressure and/or irregular heart beats:

- tricyclic antidepressants (for example imipramine or amitriptyline), used to treat depression
- cardiac glycosides (for example digoxin) used to treat a heart problem
- diuretics (water tablets)
- guanethidine, methyldopa or reserpine to treat high blood pressure
- beta-blocker medicines (for high blood pressure and angina)

If you are pregnant or if you are breast-feeding

If you are pregnant or if you are breast-feeding, tell your doctor or nurse before you receive adrenaline (epinephrine).

HOW SHOULD THIS MEDICINE BE GIVEN

Your medicine will be given to you by a doctor or nurse. This is because it can only be given by injection. The injection may be given into a muscle or beneath the skin. If you ask the person giving you the injection they will tell you

- how much of this medicine has been prescribed for you
- how often it is to be given
- how long your treatment will last.

Adults: The usual dose is 500 micrograms (0.5 ml), by injection into a muscle. If necessary, this dose may be repeated several times at periodic

intervals, depending on your need.

If you are taking imipramine or amitriptyline for depression, or a beta-blocker medicine, your doctor or nurse may decide to reduce the dose of adrenaline (epinephrine) by one half.

Children:

Over 12 years: The usual dose is 500 micrograms (0.5 ml). If necessary, this dose may be repeated several times at periodic intervals depending on the need. The dose may be reduced to 250 micrograms (0.25 ml) if the child is small or has not reached puberty.

6 to 12 years: The usual dose is 250 micrograms (0.25 ml). If necessary, this dose may be repeated several times at periodic intervals depending on the need.

6 months to 6 years: The usual dose is 120 micrograms (0.12 ml). If necessary, this dose may be repeated several times at periodic intervals depending on the need.

Under 6 months: The usual dose is 50 micrograms (0.05 ml). If necessary, this dose may be repeated several times at periodic intervals depending on the need.

If you receive too much of this medicine

It is most unlikely that you will be given too much of this medicine by the nurse or doctor. Symptoms of an overdose could include restlessness, confusion, abnormal paleness of the skin, an abnormally slow or fast heartbeat, palpitations and an irregular heart beat. If you notice these or any other symptoms after you receive your injection, tell the doctor or nurse.

If you miss a dose of your medicine

If you think you may have missed a dose, tell the doctor or nurse.

POSSIBLE SIDE EFFECTS

Like all medicines, Adrenaline (epinephrine) 1:1000 Injection BP can have side effects. If you become aware of any of the following effects, tell the doctor or nurse immediately:

- headache
- palpitations or irregular heart beats
- high blood pressure
- difficulty passing water
- coldness of the arms or legs
- feeling breathless
- too much sugar in your blood
- feeling irritable or confused, or having abnormal thoughts
- feeling anxious, nervous or restless
- weakness or tremor (shaking)
- nausea (feeling sick) or vomiting (being sick)
- dry mouth or watering of the mouth
- sweating
- insomnia
- loss of appetite.

If you notice any side effects that are not mentioned in this leaflet, please tell your doctor or nurse.

STORING ADRENALINE (EPINEPHRINE) 1:1000 INJECTION BP

Keep this medicine out of reach and sight of children.

Do not store above 25° C.

Keep the container in the outer carton in order to protect from light.

This medicine should not be used after the expiry (EXP) date printed on the pack.

FURTHER INFORMATION

For any further information about this medicine, please contact Taro Pharmaceuticals Ireland Ltd.,

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info@taro.ie



This leaflet was last approved in MM/YYYY.

LABELLING

