PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE

PHARMA-Q ADRENALINE INJECTION 1 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml contains 1 mg adrenaline (epinephrine) base as tartrate

Excipients with known effect:

Antioxidant: sodium metabisulphite 0,1 % *m/v*.

For full list of excipients, see section 6.1

Sugar free.

3 PHARMACEUTICAL FORM

Solution for injection

A clear, practically colourless, slightly acid liquid. Gradually turns dark on exposure to light and air.

The pH of the solution is between 2,2 to 5,0.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

PHARMA-Q ADRENALINE INJECTION 1 mg/ml may be used in the treatment of acute allergy and anaphylactic shock.

4.2 Posology and method of administration

Posology

Discard contents if discoloured.

The dosage of PHARMA-Q ADRENALINE INJECTION 1 mg/ml is:

By subcutaneous or intramuscular injection.

Adults: 0,2 to 0,5 ml

Children: 0,1 to 0,3 ml

Adults

Bronchodilator: Subcutaneous injection: 0,2 to 0,5 mg every 20 minutes to 4 hours if necessary (maximum of 1 mg per dose).

Anaphylactic reaction: Intramuscular or subcutaneous injection: 0,2 to 0,5 mg repeated every 10 to 15 min if necessary (maximum 1 mg per dose).

Children

Bronchodilator or anaphylactic reactions: Subcutaneous 0,01 mg per kg body weight (maximum of 0,5 mg per dose) every 15 min for 2 doses and then every 4 hours as needed.

The patient must be continuously monitored.

Adults

Vasopressor (anaphylactic shock): 0,1 mg to 0,25 mg (base) administered slowly. May be repeated every five to fifteen minutes as needed.

Children

Vasopressor (anaphylactic shock): 0,01 mg (base) per kg of body weight every five to fifteen minutes as needed, if an inadequate response to IM or SC administration.

Method of administration

By subcutaneous or intramuscular injection.

The best site for IM injection is the anterolateral aspect of the middle third of the thigh. The needle used for injection needs to be sufficiently long to ensure that the adrenaline (epinephrine) is injected into muscle. Intramuscular injections of

PHARMA-Q ADRENALINE INJECTION 1 mg/ml into the buttocks should be avoided because of the risk of tissue necrosis.

The intramuscular (IM) route is generally preferred in the initial treatment of anaphylaxis, the IV route is generally more appropriate in the Intensive Care Unit or Emergency Department setting. Adrenaline (epinephrine) 1 mg/ml (1:1 000) solution for injection is not suitable for IV use. If the adrenaline (epinephrine) 0,1 mg/ml (1:10 000) injection is not available, adrenaline (epinephrine) 1 mg/ml (1:1 000) solution must be diluted to 0,1 mg/ml (1:10 000) before IV use.

The IV route for injection of adrenaline (epinephrine) must be used with extreme caution and is best reserved for specialists familiar with IV use of adrenaline (epinephrine).

4.3 Contraindications

- Hypersensitivity to sympathomimetics, including adrenaline (epinephrine), or to any of the other ingredients of PHARMA-Q ADRENALINE INJECTION 1 mg/ml (see section 6.1).
- PHARMA-Q ADRENALINE INJECTION 1 mg/ml should not be used in fingers, toes, ears, nose, or genitalia owing to the risk of ischaemic tissue necrosis.
- Adrenaline (epinephrine) is frequently used in emergency situations and any contraindications are therefore relative.
- PHARMA-Q ADRENALINE INJECTION 1 mg/ml interacts with monoamine oxidase inhibitors and should not be given to patients receiving such treatment or within 14 days of its termination.

4.4 Special warnings and precautions for use

PHARMA-Q ADRENALINE INJECTION 1 mg/ml should be used with caution in patients with:

- Parkinson's disease, hyperthyroidism, psychoneurosis, phaeochromocytoma (diagnosed or suspected), narrow angle glaucoma (or predisposition to), diabetes mellitus, hypokalaemia or hypercalcaemia;
- severe renal impairment, prostatic hypertrophy or urination difficulty;
- cerebrovascular disease, organic brain damage or arteriosclerosis;
- autonomic dysreflexia (hyperreflexia), particularly in spinal cord injury (e.g., tetraplegics);
- shock (other than anaphylactic shock; cardiogenic, traumatic, or haemorrhagic);
- organic heart disease, cardiovascular disease, or cardiac dilatation (severe angina pectoris, obstructive cardiomyopathy, hypertension) as well as most patients with dysrhythmias. Anginal pain may be induced when coronary insufficiency is present;
- congestive heart failure, coronary artery disease, degenerative heart disease, ischaemic heart disease, phenothiazine-induced circulatory collapse or hypotension.

PHARMA-Q ADRENALINE INJECTION 1 mg/ml should be used with caution in older patients.

Adrenaline (epinephrine) should be used with extreme caution in patients with long-standing bronchial asthma and emphysema who have developed degenerative heart disease.

PHARMA-Q ADRENALINE INJECTION 1 mg/ml should be avoided or used with caution in patients undergoing anaesthesia with cyclopropane, halothane, or other halogenated anaesthetics, as they may induce ventricular fibrillation (see section 4.5).

PHARMA-Q ADRENALINE INJECTION 1 mg/ml should not be used during the second stage of labour (see section 4.6).

Accidental intravascular (IV) injection may result in cerebral haemorrhage due to the sudden rise in blood pressure.

The IV route for injection of adrenaline (epinephrine) must be used with extreme caution and is best reserved for specialists familiar with IV use of adrenaline (epinephrine). Monitor the patient as soon as possible (pulse, blood pressure, electrocardiogram (ECG), pulse oximetry) in order to assess the response to adrenaline (epinephrine). Intramuscular injections of PHARMA-Q ADRENALINE INJECTION 1 mg/ml into the buttocks should be avoided because of the risk of tissue necrosis.

Prolonged use of PHARMA-Q ADRENALINE INJECTION 1 mg/ml can result in severe metabolic acidosis (because of elevated blood concentrations of lactic acid), renal necrosis and tachyphylaxis.

PHARMA-Q ADRENALINE INJECTION 1 mg/ml contains sodium metabisulphite, which can rarely cause severe hypersensitivity reactions and bronchospasm.
The presence of sodium metabisulphite in parenteral PHARMA-Q ADRENALINE INJECTION 1 mg/ml and the possibility of allergic-type reactions should not deter

use of the medicine when indicated for the treatment of serious allergic reactions or for other emergency situations.

4.5 Interaction with other medicines and other forms of interaction

Sympathomimetic medicines

PHARMA-Q ADRENALINE INJECTION 1 mg/ml should not be administered concomitantly with other sympathomimetic medicines because of the possibility of additive effects and increased toxicity.

Alpha-adrenergic medicines

The vasoconstrictor and pressor effects of adrenaline (epinephrine), mediated by its alpha-adrenergic action, may be enhanced by concomitant administration of medicines with similar effects, such as ergot alkaloids or oxytocin.

Alpha-adrenergic blocking medicines

Alpha-blockers, such as phentolamine, antagonise the vasoconstriction and hypertension effects of adrenaline (epinephrine). This effect may be beneficial in adrenaline (epinephrine) overdose (see section 4.9). PHARMA-Q ADRENALINE INJECTION 1 mg/ml specifically reverses the antihypertensive effects of adrenergic neurone blockers, such as guanethidine with the risk of severe hypertension.

Beta-adrenergic blocking medicines

Severe hypertension and reflex bradycardia may occur with non-cardio selective beta-blocking medicines, such as propranolol, due to alpha-mediated vasoconstriction.

Beta-blockers, especially non-cardio selective medicines, also antagonise the cardiac and bronchodilator effects of adrenaline (epinephrine). Patients with

severe anaphylaxis who are taking non-cardio selective beta-blockers may not respond to PHARMA-Q ADRENALINE INJECTION 1 mg/ml treatment.

General anaesthetics

Administration of PHARMA-Q ADRENALINE INJECTION 1 mg/ml in patients receiving halogenated hydrocarbon general anaesthetics that increase cardiac irritability and seem to sensitise the myocardium to adrenaline (epinephrine) may result in dysrhythmias including ventricular premature contractions, tachycardia or fibrillation (see section 4.4).

Antihypertensive medicines

Adrenaline (epinephrine) specifically reverses the antihypertensive effects of adrenergic neurone blockers, such as guanethidine, with the risk of severe hypertension. PHARMA-Q ADRENALINE INJECTION 1 mg/ml increases blood pressure and may antagonise the effects of antihypertensive medicines.

Antidepressant medicines

Tricyclic antidepressants, such as imipramine, inhibit reuptake of directly acting sympathomimetic medicines, and may potentiate the effect of adrenaline, increasing the risk of development of hypertension and cardiac dysrhythmias.
Concurrent use or use within 2 weeks of a monoamine oxidase inhibitor increases the risk of adverse events (see section 4.3).

Phenothiazines

Phenothiazines block alpha-adrenergic receptors (see above).
PHARMA-Q ADRENALINE INJECTION 1 mg/ml should not be used to counteract circulatory collapse or hypotension caused by phenothiazines; a reversal of the

pressor effects of PHARMA-Q ADRENALINE INJECTION 1 mg/ml may result in further lowering of blood pressure.

Other medicines

PHARMA-Q ADRENALINE INJECTION 1 mg/ml should not be used in patients receiving high dosage of other medicines (e.g. cardiac glycosides) that can sensitise the heart to dysrhythmias. Some antihistamines (e.g. diphenhydramine) and thyroid hormones may potentiate the effects of PHARMA-Q ADRENALINE INJECTION 1 mg/ml, especially on heart rhythm and rate. PHARMA-Q ADRENALINE INJECTION 1 mg/ml increases the risk of cardiac adverse effects of levodopa. Use of entacapone may potentiate the chronotropic and dysrhythmogenic effects of adrenaline (epinephrine).

Hypokalaemia

The hypokalaemic effect of adrenaline (epinephrine) may be potentiated by other medicines that cause potassium loss, including corticosteroids, potassium-depleting diuretics, aminophylline, and theophylline.

Hyperglycaemia

Adrenaline (epinephrine)-induced hyperglycaemia may lead to loss of blood-sugar control in diabetic patients treated with insulin or oral hypoglycaemic medicines.

4.6 Fertility, pregnancy and lactation

Pregnancy

Adrenaline (epinephrine) crosses the placenta. There is some evidence of a slightly increased evidence of congenital abnormalities.

Injection of adrenaline (epinephrine) may cause anoxia to the fetus, fetal

tachycardia, cardiac irregularities, extrasystoles and louder heart sounds.

Adrenaline (epinephrine) usually inhibits spontaneous, or oxytocin induced contractions of the pregnant human uterus and may delay the second stage of labour. In dosage sufficient to reduce uterine contractions, the medicine may cause a prolonged period of uterine atony with haemorrhage. For this reason, parenteral adrenaline (epinephrine) should not be used during the second stage of labour (see section 4.4).

PHARMA-Q ADRENALINE INJECTION 1 mg/ml should only be used during pregnancy if the potential benefits justify the possible risks to the foetus.

Lactation

Adrenaline (epinephrine) is distributed into breast milk. Breastfeeding should be avoided in mothers receiving PHARMA-Q ADRENALINE INJECTION 1 mg/ml.

4.7 Effects on ability to drive and use machines

The ability of a patient to drive and use machines may be affected by the anaphylactic reaction, as well as by possible adverse reactions to adrenaline (epinephrine) (see section 4.8).

4.8 Undesirable effects

a. Summary of the safety profile

The adverse events of PHARMA-Q ADRENALINE INJECTION 1 mg/ml mainly relate to the stimulation of both alpha- and beta-adrenergic receptors. The occurrence of undesirable effects depends on the sensitivity of the individual patient and the dose involved.

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Adverse reactions**
Immune system disorders	Frequency unknown	Anaphylaxis, possibly with severe bronchospasm (see section 4.4).
Metabolism and nutrition disorders	Frequency unknown	Hypokalaemia, metabolic acidosis (see section 4.4), disturbances of glucose metabolism, inhibition of insulin secretion and hyperglycaemia even with low doses, gluconeogenesis, glycolysis, lipolysis and ketogenesis.
Psychiatric disorders	Frequency unknown	Psychotic states, anxiety, fear, confusion, irritability, insomnia, restlessness, hallucinations, nervousness.
Nervous system disorders	Frequency unknown	Headache, tremors, dizziness, In patients with Parkinsonian syndrome, PHARMA-Q ADRENALINE INJECTION 1 mg/ml increases rigidity and tremor, syncope. Subarachnoid haemorrhage and hemiplegia have resulted from hypertension, even following subcutaneous administration of

MedDRA system organ class	**Frequency**	**Adverse reactions**
		usual doses of PHARMA-Q ADRENALINE INJECTION 1 mg/ml.
Eye disorders	Frequency unknown	Mydriases.
Cardiac disorders	Less frequent	Stress cardiomyopathy
	Frequency unknown	Palpitations, cardiac arrest, rapid pulse, anginal pain, acute angina attacks, tachycardia, reflex bradycardia, cardiac dysrhythmias, potentially fatal ventricular dysrhythmias including fibrillation, especially in patients with organic heart disease or those receiving other medicines that sensitise the heart to dysrhythmias, myocardial ischaemia and myocardial infarction, electrocardiogram (ECG) changes including a decrease in T-wave amplitude in all leads in normal subjects.
Vascular disorders	Frequency unknown	Bowel necrosis, hypotension with dizziness, flushing and fainting, stimulation of α-adrenergic

MedDRA system organ class	**Frequency**	**Adverse reactions**
		receptors produces vasoconstriction with resultant hypertension. This vasoconstriction is sometimes sufficiently severe to produce gangrene when PHARMA-Q ADRENALINE INJECTION 1 mg/ml is infiltrated into the digits. The rise in blood pressure may produce cerebral haemorrhage and pulmonary oedema, coldness of extremities may occur even with small doses.
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Dyspnoea, pulmonary oedema may occur after excessive doses or in extreme sensitivity.
Gastrointestinal disorders	Frequency unknown	Reduced appetite, nausea, vomiting, hypersalivation, dry mouth
Renal and urinary disorders	Frequency unknown	Difficulty in micturition, urinary retention
General disorders and administration site conditions	Frequency unknown	Weakness, sweating, pallor, extravasation of parenterally administered catecholamines may result in tissue necrosis and

MedDRA system organ class	Frequency	Adverse reactions
		sloughing, repeated injections can cause necrosis as a result of vascular constriction at the injection site, tissue necrosis may also occur in the extremities, kidneys and liver.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms

See section 4.8.

After overdosage or inadvertent intravenous administration of usual intramuscular subcutaneous doses of PHARMA-Q ADRENALINE INJECTION 1 mg/ml, systolic and diastolic blood pressure rise sharply; venous pressure also rises. Cerebrovascular or other haemorrhages and hemiplegia may result, especially in elderly patients. Pulmonary oedema may occur.

PHARMA-Q ADRENALINE INJECTION 1 mg/ml overdosage causes transient bradycardia followed by tachycardia and may cause other potentially fatal cardiac

dysrhythmias. Kidney failure, metabolic acidosis and cold white skin may also occur.

Treatment

Treatment of overdosage is symptomatic and supportive.

Because of the short duration of the adverse effects of PHARMA-Q ADRENALINE INJECTION 1 mg/ml, due to inactivation in the body, treatment of severe toxic reactions in hypersensitive patients or after overdose is primarily supportive. Prompt injection of a rapidly acting alpha-adrenoceptor blocking medicine, such as phentolamine, followed by a beta blocker, such as propranolol, has been tried to counteract the pressor and dysrhythmogenic effects of PHARMA-Q ADRENALINE INJECTION 1 mg/ml; rapidly-acting vasodilators, such as glyceryl trinitrate have also been used.

5 PHARMACOLOGICAL PROPERTIES

Category and class: A 5.1 Adrenomimetics (sympathomimetics)

ATC code: C01 CA 24 Pharmacotherapeutic group: adrenergic and dopaminergic agents, adrenaline.

5.1 Pharmacodynamic properties

Adrenaline (epinephrine) is an adrenomimetic hormone.

5.2 Pharmacokinetic properties

Absorption

Adrenaline has a rapid onset of action after intramuscular administration and in the shocked patient its absorption from the intramuscular site is faster and more reliable than from the subcutaneous site. The plasma half-life is about 2- 3minutes. 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.

Biotransformation

Adrenaline is rapidly inactivated in the body, mostly in the liver by the enzymes catechol-O-methyltransferase (COMT) and monoamine oxidase (MAO).

Elimination

Much of a dose of adrenaline is excreted as metabolites in urine. The onset of action and peak effect after injection is rapid, and the duration short (1 - 2 hours). Elimination is mainly via metabolism of the liver and sympathetic nerve endings, with a small amount excreted unchanged in the urine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulphite (anti-oxidant) (E223)

Sodium chloride

Nitrogen

Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light.

6.5 Nature and contents of container

A clear, practically colourless, slightly acid liquid. Gradually turns dark on exposure to light and air.

1 ml clear or amber, type I glass ampoules in single pack (with syringe) or packs of 10 and 100.

6.6 Special precautions for disposal and other handling

PHARMA-Q ADRENALINE INJECTION 1 mg/ml is not to be used if its colour is pinkish or darker than slightly yellow or if it contains a precipitate.

7 HOLDER OF CERTIFICATE OF REGISTRATION

PHARMA-Q HOLDINGS (PTY) LTD.

50 Commando Road

Industria West, 2093

Johannesburg

8 REGISTRATION NUMBER

30/5.1/0395

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12 February 2002

10 DATE OF REVISION OF THE TEXT

13 November 2024