CLEAN COPY OF THE PROPOSED PACKAGE INSERT

SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

Pharma-Q Atropine Injection 0,5 mg/1 ml solution for injection

Pharma-Q Atropine Injection 1,0 mg/1 ml solution for injection

COMPOSITION:

Pharma-Q Atropine Injection 0,5 mg/1 ml:

Each 1 ml ampoule contains 0,5 mg of atropine sulphate.

Pharma-Q Atropine Injection 1,0 mg/1 ml:

Each 1 ml ampoule contains 1,0 mg of atropine sulphate.

Excipients: Acid sulphate, sodium chloride, water for injection.

PHARMACOLOGICAL CLASSIFICATION:

A.5.4 Cholinolytics

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Atropine sulphate is an antimuscarinic agent with both central and peripheral actions. The major action is a competitive antagonism to Ach (acetylcholine) and other muscarinic agonists by blocking its binding to muscarinic cholinergic receptors at neuroeffector sites on smooth muscle, cardiac muscle and gland cells; in peripheral ganglia; and in the central nervous system. Since antagonism by atropine sulphate is competitive, this antagonism can therefore be overcome by

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sufficiently increasing the concentration of Ach at the receptor sites of the effector organ.

The receptors mainly affected are those on peripheral structures that are either stimulated or inhibited by muscarine, namely exocrine glands and smooth muscle and cardiac muscle.

Pharmacokinetic properties:

Absorption:

Atropine sulphate is readily absorbed from the gastro-intestinal tract. It crosses the blood brain barrier. It has a half-life of about 4 hours.

Distribution:

Atropine sulphate is rapidly cleared from the blood and is distributed throughout the entire body. The plasma binding is between 14 and 22 %.

Metabolism:

Atropine sulphate is incompletely metabolised in the liver.

Elimination:

Atropine sulphate is excreted in the urine as unchanged medicine and metabolites. Atropine sulphate crosses the placenta and traces appear in milk (see **PREGNANCY AND LACTATION**).

INDICATIONS:

Pharma-Q Atropine Injection is indicated:

- in the treatment of conditions where anticholinergic effects are required
- pre-operatively, to counteract the vagal effects that may frequently occur during anaesthesia and to counteract the unwanted muscarinic effects which may accompany reversal of neuromuscular blockade with neostigmine

- initial treatment of patients with acute myocardial infarction in whom excessive vagal tone causes sinus or nodal bradycardia
- treatment of muscarinic toxicity and in poisoning caused by pesticides that are organophosphate cholinesterase inhibitors.

CONTRAINDICATIONS:

Pharma-Q Atropine Injection is contraindicated in:

- patients who are hypersensitive to atropine sulphate or to any ingredients of this medicine
- patients with closed-angle glaucoma
- patients with a narrow angle between the iris and cornea, since it may increase the intra-ocular pressure
- patients with prostatic enlargement, in whom it may lead to urinary retention and in those with paralytic ileus or pyloric stenosis
- patients with myasthenia gravis, unless it is given to reduce adverse muscarinic effects of an anti-cholinesterase agent
- patients with coronary insufficiency or cardiac failure
- patients who are pregnant or lactating since safety in pregnancy and lactation has not been established (see **PREGNANCY AND LACTATION**).

WARNINGS and SPECIAL PRECAUTIONS:

Pharma-Q Atropine Injection should be used with caution in:

- children and geriatric patients since they are more susceptible to its adverse effects
- patients with ulcerative colitis as it may cause ileus or megacolon
- patients who have reflux since its effects on the lower oesophageal sphincter may also

exacerbate reflux

- patients who have diarrhoea
- patients who have a fever as it may provoke hyperpyrexia [~~(see **Special Precautions**)~~]
- patients who have conditions characterised by tachycardia such as thyrotoxicosis, cardiac insufficiency or cardiac failure
- patients undergoing cardiac surgery, as it may further accelerate the heart-rate
- patients with acute myocardial infarction as ischaemia and infarction of the heart may be aggravated
- patients with hypertension.

Pharma-Q Atropine Injection:

- high doses may cause postural hypotension
- due to the risk of provoking hyperpyrexia, it should not be given to patients, especially children, when the ambient temperature is high, or to patients who present with fever.
- in the treatment of Parkinsonism, increases in dosage and transfer to other forms of treatment should be gradual and anti-cholinergic agents should not be withdrawn abruptly. If higher doses provoke severe mental disturbances **Pharma-Q Atropine Injection** should be discontinued, but minor reactions can be controlled by reducing the dose until tolerance has developed
- patients with Down's syndrome appear to have an increased susceptibility to the action of **Pharma-Q Atropine Injection**, whereas those with albinism may be resistant.

Effects on the ability to drive and use machines:

Pharma-Q Atropine Injection may cause mental confusion, especially in the elderly. Patients should be advised not to drive or operate hazardous machinery because loss of concentration could lead to serious accidents.

INTERACTIONS:

Pharma-Q Atropine Injection:

The effects of ~~this medicine~~ **Pharma-Q Atropine Injection** may be enhanced by the concomitant administration of other medicines with antimuscarinic properties such as:

- amantadine
- some antihistamines
- butyrophenones
- phenothiazines
- tricyclic antidepressants.

The reduction in gastric mobility caused by these antimuscarinic medicines may also affect the absorption of other medicines.

PREGNANCY AND LACTATION:

Pharma-Q Atropine Injection:

- is contraindicated for use in pregnancy and lactation since safety during pregnancy and lactation has not been established (see **CONTRAINDICATIONS**).
- it may cross the placenta and may be excreted into breast-milk (see **Pharmacokinetic properties-Elimination**).

DOSAGE AND DIRECTIONS FOR USE:

Premedication prior to anaesthesia:

Pharma-Q Atropine Injection may be given before the induction of general anaesthesia to diminish the risk of vagal inhibition of the heart and to reduce salivary and bronchial secretions.

Adult doses of Pharma-Q Atropine Injection given as pre-medication:

- 0,3 to 0,6 mg may be given by subcutaneous or intramuscular injection, usually 30 to 60 minutes before anaesthesia
- it may also be given in conjunction with up to 10 mg morphine sulphate, by subcutaneous or intramuscular injection, about an hour before anaesthesia.
- **alternatively**, 0,3 to 0,6 mg may be given intravenously immediately before the induction of anaesthesia.

Paediatric pre-medication doses given subcutaneously are:

- Children weighing up to 3 kg: 100 µg subcutaneously
- Children weighing 7 to 9 kg: 200; µg
- Children weighing 12 to 16 kg: 300 µg
- Children weighing 20 to 27 kg: 400 µg
- Children weighing 32 kg: 500 µg
- Children weighing 41 kg: 600 µg

Other dosages of **Pharma-Q Atropine Injection:**

- **Arrhythmias:**

  In the management of arrhythmias, 400 µg to 1 mg given intravenously and repeated as needed to a total dose of 2 mg.

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- **Bradycardia:**

  In the treatment of bradycardia following cardiac infarction, it is given intravenously, in initial doses of 0,4 to 1 mg, subsequently increased up to 2 mg, according to the needs of the patient.

- **Reversal of non-depolarising muscle relaxants:**

  To reverse the effects of non-depolarising muscle relaxants, 0,6 to 1,2 mg can be given by slow intravenous injection in conjunction with neostigmine methylsulphate.

- **Organophosphate poisoning:**

  In the treatment of organophosphate poisoning, 2 mg should be given by subcutaneous, intravenous or intramuscular injection and administered together with pralidoxime. It should be repeated at intervals of 5 to 60 minutes until the patient shows signs of atropine toxicity. Atropinisation should then be maintained throughout the course of pralidoxime treatment which may continue for 48 hours or more.

  Considerably higher doses may be required in the treatment of poisoning, due to irreversible anti-cholinesterases such as organo-phosphorus insecticides.

SIDE EFFECTS

Pharma-Q Atropine Injection may have side effects but the frequencies are unknown.

Immune system disorders:

Frequency unknown: Hypersensitivity may occur.

Cardiovascular disorders:

Frequency unknown: Transient bradycardia followed by tachycardia with palpitations and arrhythmias.

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Eye disorders:

Frequency unknown: Dilatation of the pupils (mydriasis) with loss of accommodation (cycloplegia), increased intra-ocular pressure and photophobia.

Nervous system disorders:

Frequency unknown: Confusion, giddiness and staggering.

Gastro-intestinal disorders:

Frequency unknown: Dryness of the mouth with difficulty in swallowing and talking, thirst, vomiting, as well as reduction in the tone and mobility of the gastro-intestinal tract, leading to constipation. Increased retrosternal pain may occur due to increased gastric reflux.

Respiratory, thoracic and mediastinal disorders:

Frequency unknown: Reduced bronchial secretions.

Skin and subcutaneous tissue disorders:

Frequency unknown: Flushing and dryness of the skin.

Renal and urinary disorders:

Frequency unknown: Difficulty in micturition.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See **SIDE-EFFECTS** and **WARNINGS and SPECIAL PRECAUTIONS**.

Toxic doses of **Pharma-Q Atropine Injection** may cause:

- tachycardia and rapid respiration
- hyperpyrexia
- central nervous system stimulation marked by restlessness, confusion, excitement, paranoid and psychotic reactions, hallucinations and delirium and occasionally seizures or convulsions

- a rash may appear on the face or upper trunk.

In severe intoxication:

Central stimulation may give way to central nervous system depression, coma, circulatory and respiratory failure and death.

Treatment of **Pharma-Q Atropine Injection** overdose:

- symptomatic and supportive
- diazepam may be given to control marked excitement and convulsions
- phenothiazines should not be given as they may exacerbate antimuscarinic effects
- physostigmine salicylate may control the central and peripheral effects, but is not generally recommended.

IDENTIFICATION:

Pharma-Q Atropine Injection is a clear colourless solution filled into clear colourless glass ampoules.

PRESENTATION:

10 or 100 x 1 ml clear colourless glass ampoules.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from light.

Keep out of reach of children.

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REGISTRATION NUMBERS:

Pharma-Q Atropine Injection 0,5 mg/1 ml: 31/5.4/0206

Pharma-Q Atropine Injection 1,0 mg/1 ml: 31/5.4/0207

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

PHARMA-Q HOLDINGS (PTY) LTD

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