ATROPINE SULPHATE-FRESENIUS 1MG/1ML
Atropine Sulphate 1.0MG/1ML solution for injection

Description
A clear colorless solution in a clear glass ampoule.

Composition
Each ml injection ampoule contains 1.0mg of Atropine Sulphate.

Pharmacodynamics
Atropine sulphate is an antimusculic agent. The major action is a competitive or surmountable antagonism to ACh (acetylcholine) and other muscarinic agents, the antagonism can therefore be overcome by increasing sufficiently the concentration of ACh at receptor sites of the effector organ, for example by anticholinesterase agents. The receptors affected are those on peripheral structures that are either stimulated or inhibited by muscarine, that is, exocrine glands and smooth and cardiac muscle. The medicine can block all muscaric actions of ACh, and other choline esters. Responses to postganglionic cholinergic nerve stimulation may also inhibited, but less readily than are responses to injected choline esters. The difference may be due to release of ACh by cholinergic nerve terminals so close to receptors that diffusion limits the concentration of antagonist that can be attained in the very narrow synaptic cleft. Atropine-induced parasympathetic block may be preceded by transient phase of mild stimulation. Atropine has a potent action on heart, intestine and bronchial muscle and has more prolonged action than scopolamine. It is absorbed rapidly from the gastrointestinal tract. It disappears rapidly from the blood and is distributed through the entire body. Atropine has a half-life of approximately 4 hours; hepatic metabolism accounts for the elimination of about half of a dose, and the remainder is excreted unchanged in the urine. Traces of atropine are found in various secretions, including breast milk.

Pharmacokinetics
Atropine is an antimuscarinic agent which competitively antagonizes acetylcholine at postganglionic nerve endings, thus affecting receptors of the exocrine glands, smooth muscle, cardiac muscle and the central nervous system. Peripheral effects include tachycardia, decreased production of saliva, sweat, bronchial, nasal, lachrymal and gastric secretions, decreased intestinal motility and inhibition of micturition. Atropine increases sinus rate and sinoatrial and AV conduction. Usually heart rate is increased but there may be an initial bradycardia. Atropine inhibits secretions throughout the respiratory tract and relaxes bronchial smooth muscle producing bronchodilatation. Following intravenous administration, the peak increase in heart rate occurs within 2 to 4 minutes. Peak plasma concentrations of atropine after intramuscular administration are reached within 30 minutes, although peak effects on the heart, sweating and salivation may occur nearer one hour after intramuscular administration. Plasma levels after intramuscular and intravenous injection are comparable at one hour. Atropine is distributed widely throughout the body and crosses the blood brain barrier. The elimination half-life is about 2 to 5 hours. Up to 50% of the dose is protein bound. It disappears rapidly from the circulation. Atropine is metabolised in the liver by oxidation and conjugation to give inactive metabolites. About 50% of the dose is excreted within 4 hours and 90% in 24 hours in the urine, about 30 to 50% as unchanged drug.

Indications
Atropine Sulphate-Fresenius injection is indicated for acute myocardial infarction with AV conduction block due to excess vagal tone (Wenkebach Type 1, second-degree AV block) and sinus bradycardia, with associated hypotension and increased ventricular irritability.
Atropine can also be used in cardiopulmonary resuscitation for the treatment of sinus bradycardia accompanied by hypotension, hypoperfusion or ectopic arrhythmias.
Parenteral atropine is indicated as an antisialogogue in anaesthetic premedication to prevent or reduce secretions of the respiratory tract. During anaesthesia, atropine may be used to prevent reflex bradycardia and restore cardiac rate and arterial pressure resulting from increased vagal activity associated with laryngoscopy, tracheal intubation and intra-abdominal manipulation.
It may also be administered to block muscarinic effects when neostigmine is used to counteract muscle relaxants such as tubocuratine.
Parenteral atropine is an antidote for cardiovascular collapse following overdose of anticholinesterases; in the treatment of poisoning from organophosphorous insecticides or from chemical warfare 'nerve' gases and in the treatment of mushroom poisoning.

Dosage and directions for use
Adults, children over 12 and the elderly:
Bradyarrhythmias: intramuscular or intravenous, 300 to 600 mcg (0.3 to 0.6 mg) every four to six hours to a total dose of 2 mg.
In cardiac resuscitation, intravenous 500 mcg (0.5 mg) repeated at 5 minute intervals until the desired heart rate is achieved. In asystole, 3 mg may be given intravenously as a once only single dose. If atropine cannot be administered intravenously during resuscitation, 2-3 times the intravenous dose may be administered via an endotracheal tube.
Premedication before anaesthesia: intramuscular or subcutaneous, 300 to 600 mcg (0.3 to 0.6 mg) 30-60 minutes before surgery or the same dose intravenously immediately before surgery.
To control muscarinic side effects of neostigmine: intravenous, 600 to 1200 mcg (0.6 - 1.2 mg).
Anticholinesterase poisoning: intramuscular or intravenous, 1 to 2 mg repeated every 5 to 60 minutes until signs and symptoms disappear, up to a maximum of 100 mg in the first 24 hours.

Children up to the age of 12 years:
The usual intramuscular, intravenous or subcutaneous dose in children is 10 mcg/kg (0.01 mg/kg), but generally not exceeding 400 mcg (0.4 mg). If necessary, these doses may be repeated every 4-6 hours.
Cardiac: for advanced cardiac life support: intravenous, 20mcg/kg (0.02 mg/kg) with a minimum dose of 10 mcg (0.01 mg) repeated at 5 minute intervals, to a maximum dose of 100 mcg (0.1 mg).
Premedication before anaesthesia: intramuscular or subcutaneous; 30-60 minutes before surgery.
Up to 3 kg - 100 mcg (0.1mg)
7 - 9 kg - 200 mcg (0.2mg)
12 - 16 kg - 300 mcg (0.3mg)
Over 20 kg - as for adults.
To control the muscarinic side effects of neostigmine: intravenous; neonates, infants and children - 20 mcg/kg (0.02 mg/kg). Maximum dosage 600 mcg.
Anticholinesterase poisoning: intramuscular or intravenous, 50 mcg/kg (0.05 mg/kg) every 10-30 minutes until muscarinic signs and symptoms disappear.

Route of Administration
Intramuscular (IM) / Intravenous (IV) / Subcutaneous (SC)

Incompatibility
Atropine Sulphate-Fresenius should not be combined with other aqueous solutions of medicaments except with water for injection. The injection should be freshly prepared and unused portions should be discarded.

Contraindications
Atropine Sulphate-Fresenius should not be given to patients with closed-angle glaucoma or to patients with narrow angle between the iris and the cornea, since it may increase the intra-ocular pressure and precipitate an acute attack. It is contraindicated in patients with prostatic enlargement, and in those with paralytic ileus, pyloric stenosis and status asthmaticus. It should not be given to patients with myasthenia gravis unless it is given to reduce adverse muscarinic effects of an anti-cholinesterase agent. Due to the risk of provoking hyperpyrexia Atropine Sulphate-Fresenius should not be given to patients, especially children, when the ambient temperature is high. It should also be

used cautiously in patients with fever. Atropine Sulphate-Fresenius should not be given to patients who are being treated with a monoamine-oxidase inhibitor, or within ten days of the discontinuation of such treatment.
Contraindications are not applicable to the use of atropine in life-threatening emergencies (eg. Asystole).

Warning and precaution
Caution should be observed in administering this medicine to patients with coronary insufficiency of cardiac failure. Atropine Sulphate-Fresenius should be used with caution in children and in geriatric patients, who may be more susceptible to its adverse effects. It is generally advisable to be cautious in giving atropine to any patient with diarrhoea. Atropine Sulphate-Fresenius and other antimuscarinic agents should be used with caution in conditions characterised by tachycardia such as throtoxicosis, cardiac insufficiency or failure, and in cardiac surgery, where it may further accelerate the heart-rate. Care is required in patients with acute myocardial infarction as ischaemia and infarction may be made worse. Atropine Sulphate-Fresenius should be given care to patients with hypertension. In patients with ulcerative colitis its use may lead to ileus or megacolon and its effects on the lower oesophageal sphincter may exacerbate reflux.

Interactions with Other Medications
The effects of Atropine Sulphate-Fresenius and other antimuscarinic agents may be enhanced by the concomitant administration of other agents with antimuscarinic properties, such as amantadine, some antihistamines, butyrophenones and phenothiazines and tricyclic antidepressants. The reduction in gastric motility caused by Atropine Sulphate-Fresenius may affect the absorption of other medicines. Additive anticholinergic adverse effects may also occur with antipsychotics, quinidine and disopyramide. The degree of absorption of digoxin may be increased.

Statement on usage during pregnancy and lactation
Atropine Sulphate-Fresenius pregnancy class C. Atropine crosses the placenta. Well-controlled studies in humans have not been done. Intravenous administration of Atropine Sulphate-Fresenius during pregnancy or near term may produce tachycardia in the foetus. Atropine is distributed into breast milk and use thereof should be avoided during breast feeding since infants are usually very sensitive to the effects of anticholinergics.

Adverse Effects/ Undesirable Effects
Atropine Sulphate-Fresenius injection is indicated for its parasympatholytic effects.
- Peri-operatively: to counteract the vagal effects that may frequently occur during anaesthesia.

Atropine Sulphate-Fresenius is commonly given with neostigmine to counteract the unwanted muscarinic effects which may accompany reversal of neuromuscular blockade with neostigmine.
- Atropine Sulphate-Fresenius is a specific antidote for the cardiovascular collapse that may result from the injudicious administration of a choline ester or an inhibitor of cholinesterase. It is also used to antagonize refex vagal cardiac slowing.

Atropine Sulphate-Fresenius may be of value in the initial treatment of patients with acute myocardial infarction in whom excessive vagal tone causes sinus or nodal bradycardia.
- In the treatment of muscarinic toxicity, and in poisoning caused by pesticides that are organophosphate cholinesterase inhibitors.

Atropine Sulphate-Fresenius is a specific antidote for the so-called rapid type of mushroom poisoning due to the cholinomimetic alkaloid muscarine, found in Amanita muscaria and a few other fungi.

Gastrointestinal disorders:
More frequent: Reduction in the tone and motility of the gastrointestinal tract, constipation.
The following side effects have been reported, but the frequency is unknown: ileus or megacolon may occur in patients with ulcerative colitis, and the effect on the lower eosophageal sphincter may exacerbate reflux.

Disorders of the eye:
Less frequent: Dilatation of the pupil with difficulty in accommodation of the eye, photophobia.
Cardiac disorders:
The following side effects have been reported, but the frequency is unknown: transient bradycardia followed by tachycardia with palpitations, arrhythmias.
Respiratory disorders:
The following side effects has been reported, but the frequency is unknown: formation of mucous plugs may result from reduced bronchial secretion.
Renal and urinary disorders:
Less frequent: Difficulty in micturition.
Neurological disorders:
Less frequent: Confusion.
General disorders:
Less frequent: Flushing and dryness of skin.
The following side effects have been reported, but the frequency is unknown: tolerance occurs to a limited extent; vomiting, malaise, sweating and salivation have been recorded in patients with parkinsonism upon sudden withdrawal of the large doses required for therapeutic effect. In treatment of parkinsonism, increases in dosages and transfer to other forms of treatment should be gradual and antimuscarinic agents should not be withdrawn abruptly.

Overdosage, symptoms and treatment
Delirium or toxic psychoses can occur after overdosage. Also hallucinatory effects. Symptoms develop promptly. Vision becomes blurred and photophobia is prominent. The skin is hot, dry and flushed. A rash may appear, especially over the face, neck and upper part of the trunk; desquamation may follow. The body temperature rises and the pulse is weak and very rapid. Palpitation is prominent, and the blood pressure may be elevated. Urinary urgency and difficulty in micturition are sometimes noted. Restlessness and confusion, giddiness and muscular inco-ordination occur.

Treatment
If marked excitement is present and more specific treatment is not available, diazepam is most suitable for sedation and for control of convulsions. Large doses should be avoided because the central depressant action may coincide with the depression occurring late in atropine poisoning. Artificial respiration with oxygen may be necessary.

Presentation
This injection is available in 1 ml ampoules
10 ampoules are packed into one folded outer carton.

Storage conditions
Protect from light and store below 30°Celcius. Keep out of reach of children.

Shelf-life
The injections can be used within 60 months from the date of manufacturer if kept as recommended. Discard any unused portion.

Manufactured by
Fresenius Kabi Manufacturing SA (Pty) Ltd
6 Gibaud Road
Port Elizabeth 6020
South Africa

Registration Holder/Importer:
Fresenius Kabi Malaysia Sdn Bhd
3-1 & 3-2, Axis Technology Centre,
Lot 13, Jalan 51A/225,
46100 Petaling Jaya
Selangor, Malaysia

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