For the use of Registered Medical Practitioner of Hospital or a Laboratory only

Atropine Injection BP 0.6mg/ml
Atropine Injection BP 1mg/ml

COMPOSITION

Each ml contains:

Atropine Sulfate	BP	0.6mg/1mg
Water for Injection	BP	q.s.

CLINICAL PHARMACOLOGY

Pharmacodynamic properties

Pharmacotherapeutic group: Anticholinergic agents.

ATC code: A03BA01.

Mechanism of action

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.

Pharmacodynamic effects

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.

Pharmacokinetic properties

Absorption

Following intravenous administration, the peak increase in heart rate occurs within 2 to 4 minutes. Plasma levels after intramuscular and intravenous injection are comparable at one hour.

Distribution

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. Atropine is distributed widely throughout the body and crosses the blood brain barrier.

Biotransformation

Atropine is metabolised in the liver by oxidation and conjugation to give inactive metabolites.

Elimination

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.

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.

INDICATION AND USAGE

- In anaesthesia, to reduce the risk of vagal inhibition of the heart and to reduce salivary and bronchial secretions.
- In the treatment of cholinergic crisis of myasthenia gravis.
- In conjunction with neostigmine used to reverse the effects of non-depolarising muscle relaxants.
- In the treatment of poisoning by certain cholinesterase inhibitors e.g. organo-phosphorous compounds.
- During cardiopulmonary resuscitation to counteract excessive vagal tone on the heart.

CONTRA-INDICATION

Hypersensitivity to Atropine Sulfate or to any of the excipients listed in section 6.1.

Known hypersensitivity to the drug, closed-angle glaucoma, prostatic enlargement, myasthenia gravis (unless given in conjunction with anticholinesterase), paralytic ileus or pyloric stenosis and severe ulcerative colitis.

DRUG INTERACTIONS

Drugs with anticholinergic effects including antihistamines, tricyclic antidepressants, monoamine oxidase (MAO) inhibitors, disopyramide, domperidone, phenothiazines, amantadine, butyrophenones, antispasmodics, anti-parkinsonian drugs, quinidine	Enhanced antimuscarinic effects of atropine.
Beta-blockers	Reduced cardioacceleratory effect of atropine.
Ketoconazole, chlorpromazine, olanzepine, clozapine, mexilitine	Antimuscarinic drugs may alter the absorption of orally administered drugs by slowing GIT motility.
Sublingual medication such as nitrates	May have reduced absorption due to dry mouth.
Gastrointestinal prokinetic drugs such as metoclopromide, neostigmine	Antimuscarinic drugs including atropine antagonise effects of metoclopromide on gastric motility.

WARNINGS AND PRECAUTIONS

Atropine sulfate should be used with caution in children, the elderly and those with Down's syndrome. It should be given with caution to patients with diarrhoea, urinary retention or fever, and when the ambient temperature is high. Care is required in patients with acute myocardial infarction as ischaemia, and infarction may be exacerbated in patients with hypertension.

Caution is also required when using the drug in patients with conditions characterised by tachycardia such as thyrotoxicosis, cardiac insufficiency or failure and during cardiac surgery.

Paradoxical atrioventricular block or sinus arrest has been reported following administration of atropine in a few patients after heart transplantation. The use of atropine for therapeutic or diagnostic procedures in heart transplant patients should be undertaken with extreme caution, and ECG monitoring and equipment for immediate temporary pacing should be available.

Caution is required when atropine is administered systemically to patients with chronic obstructive pulmonary disease, as a reduction in bronchial secretions may lead to the formation of bronchial plugs.

Antimuscarinics such as atropine may delay gastric emptying, decrease gastric motility and relax the oesophageal sphincter. They should be used with caution in patients whose conditions may be aggravated by these effects e.g. reflux oesophagitis.

SIDE EFFECTS

Adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention: Very common: (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000); Not known: cannot be estimated from the available data.

The most commonly reported adverse events are due to the action of atropine on muscarinic receptors and at high doses, nicotinic receptors. These effects are dose related and usually reversible when therapy is discontinued.

System organ class	Frequency	Adverse reactions
Immune system disorders	Very rare	Anaphylaxis
Psychiatric disorders	Not known	Confusion state, especially in the elderly. At higher doses hallucinations, restlessness, delirium.
Nervous system disorders	Not known	Dizziness
Eye disorders	Not known	Dilatation of the pupils with loss of accommodation and photophobia, raised intraocular pressure.
Cardiac disorders	Very rare	Paradoxical atrioventricular block, especially after heart transplantation.
	Not known	Transient bradycardia followed by tachycardia, palpitations, arrhythmias. Exacerbation of myocardial ischaemia or myocardial infarction.
Vascular disorders	Not known	Flushing
Respiratory, thoracic and mediastinal disorders	Not known	Reduced bronchial secretion may result in the formation of thick bronchial plugs which are difficult to eject from respiratory tract
Gastrointestinal disorders	Not known	Dry mouth with difficulty in swallowing, constipation, nausea, vomiting, inhibition of gastric secretion, retrosternal pain due to gastric reflux.
Skin and subcutaneous tissue	Not known	Dry skin, urticaria, rashes, skin exfoliation.
Renal and urinary disorders	Not known	Urinary retention, difficulty with micturition.
General disorders and administration site conditions	Not known	Thirst, fever.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Atropine may cause blurred vision, drowsiness, confusion, hallucinations and other neuro-psychiatric effects. Patients should be advised that they should not drive, operate machinery or take part in any activities that could, if they are affected, put them or others at risk.

OVERDOSE

Symptoms

Marked dryness of the mouth accompanied by a burning sensation, difficulty in swallowing, pronounced photophobia, flushing and dryness of the skin, raised body temperature, rash, tachycardia, hypertension, nausea, and vomiting. Restlessness, tremor, confusion, excitement, hallucinations and delirium may result from CNS stimulation; this is followed by increasing drowsiness, stupor and general central depression terminating in death from circulatory and respiratory failure.

Management:

In severe cases, physostigmine, 1 to 4 mg, should be administered intravenously, intramuscularly or subcutaneously, the dose may be repeated if necessary since it is rapidly eliminated from the body. Diazepam may be administered for sedation of the delirious patient but the risk of central depression occurring late in the course of atropine poisoning contraindicates large doses of sedative. An adequate airway should be maintained and respiratory failure may be treated with oxygen and carbon dioxide inhalation. Fever is reduced by the application of cold packs or sponging with tepid water. Adequate fluid intake is important. Urethral catheterisation may be necessary. If photophobia is present or likely, the patient should be nursed in a darkened room.

DOSAGE & MODE OF ADMINISTRATION

Posology

Pre-oeprativemedication.

Adults:	By the intravenous route: 300 - 600 micrograms immediately before induction of anaesthesia. By the intramuscular or subcutaneous route: 300 - 600 micrograms, one hour before induction of anaesthesia.
Children:	**By the subcutaneous route 30 minutes before induction of anaesthesia**
Premature infants:	65 micrograms;
Children up to 3kg:	100 micrograms;
children 7-9kg::	200 micrograms;
Children 12-16kg:	300 micrograms;
Children 20-27kg:	400 micrograms;
Children 32kg:	500 micrograms;
Children 41kg:	600 micrograms;

By the intramuscular route 30-60 minutes before induction of anaesthesia.

Alternative dosage statement for children over 1 year:

10-20 micrograms/kg 30-60 minutes before induction of anaesthesia..

As an antidote to cholinesterase inhibitors

Adults:

2mg, preferably IV.

Children:

50 micrograms/kg IV or IM.

Repeat dose every 5-10 minutes until signs of atropinisation appear.
As an antidote to organophosphate pesticides and in mushroom poisoning
Adults:
2mg IV or IM.
Children:
50 micrograms/kg IV or IM
Repeat dose every 10-30 minutes until muscarinic signs and symptoms subside.
Reversal of effects of non-depolarising muscle relaxants
Adults:
0.6 –1.2 mg given IV in conjunction with neostigmine methyl- sulfate.
In cardiopulmonary resuscitation
Adults:
3mg IV once
Children:
20 micrograms/kg IV once
In arrhythmias
Bradycardia, particularly if complicated by hypotension, 300 micrograms IV initially, increasing to 1mg if necessary.

Method of Administration

Atropine sulfate solution for injection is administered by intravenous, intramuscular or subcutane

PREGNANCY AND LACTATION

Pregnancy

Atropine Sulfate crosses the placenta. Studies in humans have not been done and only limited information is available from animal studies. Animal studies are insufficient with respect to reproductive toxicity.

Intravenous administration of atropine during pregnancy or at term may cause tachycardia in foetus. Atropine should only be administered to pregnant women if the benefits outweigh the *risks to the foetus.*

Breast-feeding

Trace amounts of atropine appear in the breast milk and may cause antimuscarinic effects in the infant; lactation may be inhibited.

Fertility

There are no adequate preclinical fertility data with atropine, and no epidemiological data.

STORAGE CONDITION

Store protected from light.

KEEP OUT OF REACH OF CHILDREN

PRESENTATION

5x1ml ampoules packed in Tray.
Such 5 Tray packed in Carton along with package insert.

MANUFACTURED IN INDIA

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