SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Atropine Sulfate Injection 1mg in 1 ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Atropine Sulfate 0.10% w/v

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear, Colourless Solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Atropine Sulfate Solution for Injection is used:

- As a preoperative medication for the reduction of salivary and bronchial secretions.
- During cardiopulmonary resuscitation to treat sinus bradycardia or asystole.
- For treatment of symptomatic sinus bradycardia induced by drugs or toxic substances such as pilocarpine, organophosphate pesticides, amanita muscaria mushrooms.
- For management of bradycardia of acute myocardial infarction.
- For prevention of cholinergic effects on the heart (e.g. arrhythmias, bradycardia) during surgery.
- In combination with neostigmine during reversal of effect of non-depolarising muscle relaxants.

4.2 Posology and method of administration

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 1mg in 1ml solution for injection is administered by intravenous, intramuscular or subcutaneous injection.

4.3 Contraindications

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.

4.4 Special warnings and precautions for use

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.

4.5 Interaction with other medicinal products and other forms of interaction

The effects of atropine may be enhanced by the concomitant administration of other drugs with antimuscarinic activity including phenothiazines, amantadine, tricyclic antidepressants, MAOI's, some antihistamines and disopyramide.

Reduced GI motility caused by atropine may affect the absorption of other drugs such as mexilitine and ketoconazole.

Atropine induced dry mouth may prevent dissolution of sublingual preparations such as the nitrates, reducing their effectiveness.

During anaesthesia, the heart rate responsiveness to IV atropine could be decreased (and not effectively overcome by a large dose of atropine) when the subject is receiving concomitant propofol; it could be due to propofol-induced suppression of the sympathetic nervous system.

4.6 Fertility, pregnancy and lactation

Atropine sulfate crosses the placenta. There is insufficient evidence to establish the safety of atropine in human pregnancy. It should therefore be used during pregnancy only if considered essential by the physician.

Atropine sulfate is excreted in breast milk, and infants of nursing mothers may exhibit some effects of the drug. Infants are usually very sensitive to the effects of anticholinergic drugs. Atropine should therefore only be used during breast feeding if considered essential by the physician.

4.7 Effects on ability to drive and use machines

Atropine sulfate may cause drowsiness or blurred vision and patients should be used advised accordingly.

4.8 Undesirable effects

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

Immune system disorders:
Anaphylaxis.

Nervous system/ Psychiatric disorders:
Dizziness, confusional states, especially in the elderly. At higher doses hallucinations, restlessness, delirium.

Eye disorders:
Dilatation of the pupils with loss of accommodation and photophobia, raised intraocular pressure.

Cardiac disorders:
Transient bradycardia followed by tachycardia, palpitations, arrhythmias.
There have been reports of paradoxical atrioventricular block, especially after heart transplantation (see section 4.4).

Vascular disorders:
Flushing.

Respiratory disorders:
Reduced bronchial secretion may result in the formation of thick bronchial plugs which are difficult to eject from the respiratory tract (see section 4.4).

Gastrointestinal disorders:
Dry mouth with difficulty in swallowing, nausea, vomiting, constipation. Inhibition of gastric secretion, retrosternal pain due to gastric reflux.

Skin & subcutaneous tissue disorders:
Dry skin, urticaria, rashes, skin exfoliation.

Renal & urinary disorders:
Difficulty with micturition.

General disorders:
Thirst, fever.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

Flushing and dryness of the skin, dilated pupils, dry mouth and tongue, tachycardia, rapid respiration, hyperpyrexia, hypertension, nausea, vomiting. A rash may appear on the face or upper trunk. Symptoms of CNS stimulation include restlessness, confusion, hallucinations, paranoid and psychotic reactions, incoordination, delirium and occasionally convulsions. In severe overdose, CNS depression may occur with coma, circulatory and respiratory failure and death.

Treatment

Treatment should be supportive. An adequate airway should be maintained. Diazepam may be administered to control excitement and convulsions but the risk of central nervous system depression should be considered. Hypoxia and acidosis should be corrected. Antiarrhythmic drugs are not recommended if dysrhythmias occur.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anticholinergic agents
ATC code: A03BA01

Atropine is an antimuscarinic agent which competitively antagonises acetylcholine at postganglionic nerve endings, thus affecting receptors if the exocrine glands, smooth muscle, cardiac muscle and the central nervous system.
Peripheral effects include decreased production of saliva, sweat, 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 bronchodilation

5.2 Pharmacokinetic properties

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.

It is incompletely metabolised in the liver and is excreted in the urine as unchanged drug and metabolites. About 50% of the dose is excreted within 4 hours and 90% in 24 hours.

5.3. Preclinical Safety Data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride

Water for Injections

The pH may be adjusted using Sodium Hydroxide or Sulfuric Acid.

6.2 Incompatibilities

Atropine sulfate injection is reported to be physically incompatible with bromides, iodides, alkalis, noradrenaline bitartrate, metaraminol bitartrate and sodium bicarbonate. A haze or precipitate may form within 15 minutes when atropine sulfate is mixed with methohexital sodium solutions.

6.3 Shelf Life

36 months.

6.4 Special precautions for storage

None.

6.5 Nature and contents of container

1ml (Type 1) clear glass ampoules.

Fusion sealed Packed into carton of 10 ampoules.

6.6 Special precautions for disposal

Use contents once opened.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 01883/6172R

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9 October1989

10 DATE OF REVISION OF THE TEXT

10/01/2017