SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Atropine Sulfate 600 micrograms/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 600 micrograms of Atropine Sulfate.

Each 1 ml ampoule contains 600 micrograms of Atropine Sulfate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Atropine Sulfate 600 micrograms/ml solution for injection is used in adults and children aged 0 years to 17 years:

- as a pre-medication for the reduction of salivary and bronchial secretions and to prevent vagal reactions associated with tracheal intubation and surgical manipulation.

- for treatment of symptomatic sinus bradycardia induced by drugs or toxic substances such as pilocarpine, and as antidote to cholinesterase inhibitors, organophosphate pesticides or amanita muscaria mushrooms poisoning.

- in combination with neostigmine during reversal of effect of non-depolarising muscle relaxants.

- for treatment of bradycardia of various origins e.g. peri-arrest bradycardia with life-threatening signs caused by acute myocardial infarction, and intra-operative bradycardia.

4.2 Posology and method of administration

Posology

As a pre-medication

Adults:
300-600 micrograms IM or SC about 30-60 minutes before induction of anaesthesia or 300-600 micrograms IV immediately before induction.

Paediatric population:

Paediatric age group	by IV injection immediately before induction of anaesthesia	by SC or IM injection 30-60 minutes before induction of anaesthesia
Neonate	10 micrograms/kg body weight	10 micrograms/kg body weight
Child (1 month to 11 years)	20 micrograms/kg body weight (maximum 600 micrograms)	*10-30 micrograms/kg* (maximum 600 micrograms)
Child (12 years to 17 years)	the adult dose	the adult dose

As an antidote to cholinesterase inhibitors

The UK National Poisons Information Service (NPIS) should be consulted for further specific advice.

As an antidote to organophosphate pesticides and in muscarinic mushroom poisoning

The UK National Poisons Information Service (NPIS) should be consulted for further specific advice.

Adults:
2mg IV every 5 minutes until muscarinic effects disappear or signs of atropine toxicity are seen. In severe poisoning, some sources have suggested doubling the dose of atropine every 5 to 10 minutes until improvement is seen. Continuous infusion has also been used.

Paediatric population (from 1 month to 17 years):
20 micrograms/kg body weight IV (maximum per dose 2 mg) given every 5-10 minutes until the skin becomes flushed and dry, the pupils dilate, and

bradycardia is abolished. The frequency of administration depends on the severity of poisoning.

Treatment of symptomatic sinus bradycardia induced by pilocarpine

The UK National Poisons Information Service (NPIS) should be consulted for further specific advice.

Reversal of effects of non-depolarising muscle relaxants

Adults:
0.6 –1.2 mg given IV in conjunction with neostigmine methylsulfate.

Paediatric population:
Neonate
20 micrograms/kg body weight given IV in conjunction with neostigmine methylsulfate.

Child (1 month to 11 years)
20 micrograms/kg body weight (max. per dose 1.2 mg) given IV in conjunction with neostigmine methylsulfate.

Child (12 years to 17 years)
The adult dose should be given.

Bradycardia of various origins

- Peri-arrest bradycardia with life threatening signs (e.g. shock, myocardial ischemia, severe heart failure, syncope)

Adults:
500 micrograms by IV injection every 3-5 minutes, maximum 3 mg per course.

- Bradycardia caused by excessive vagal tone (e.g. after insertion of nasogastric tube) if no response to oxygenation

Paediatric population:
Neonate and child (1 month to 11 years)
20 micrograms/kg body weight IV.

Child (12 years to 17 years)
300-600 micrograms IV, larger doses may be used in emergencies.

- Intraoperative bradycardia

Adults:
300-600 micrograms by IV injection, larger doses may be used in emergencies.

Paediatric population:
Neonate and child (1 month to 11 years)
10-20 micrograms/kg body weight by IV injection.

Child (12 years to 17 years)
The adult dose should be given.

Method of administration
For intramuscular, intravenous and subcutaneous use.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Angle-closure glaucoma or narrow angle glaucoma,
- Prostatic enlargement as may lead to urinary retention,
- Significant bladder outflow obstruction,
- Myasthenia gravis (unless given in conjunction with anticholinesterase),
- Paralytic ileus,
- Pyloric stenosis,
- Gastro-intestinal obstruction, intestinal atony,
- Severe ulcerative colitis,
- Toxic megacolon.

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 who may be more susceptible to its adverse effects. It should be given with caution to patients with diarrhoea, urinary retention. Due to the risk of hyperthermia it should not be given to patients, especially children, when the ambient temperature is high. It should be used with caution in patients with fever. Care is required in patients with acute myocardial infarction as ischaemia and infarction may be exacerbated and in patients with hypertension.

Caution is also required when using the drug in patients with conditions characterised by tachycardia such as thyrotoxicosis, tachyarrhythmias, heart failure, coronary heart disease 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 mucous 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.

Caution is advised for patients with renal or hepatic insufficiency.

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 (risk of antimuscarinic toxicity) including phenothiazines, clozapine, 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 may also antagonise the gastrointestinal effects of cisapride, domperidone, and metoclopramide.

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.

Atropine increases the risk of severe hypertension when given with phenylephrine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Studies of the pharmacokinetics of atropine in mother and foetus in late pregnancy indicated that atropine rapidly crosses the placenta. However, where peak concentrations of atropine in foetal cord blood were reached about 5 minutes after intravenous doses, the maximum effect on foetal heart rate occurred after about 25 minutes.

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.

Breast-feeding

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.

Following a single dose exposure from atropine sulfate injection given as premedication to reduce secretion and if injection is repeated for intraoperative bradycardia, limited transfer of atropine into the breast milk and subsequent exposure to the infant is expected. Single dose use and delayed resumption of breast-feeding until the mother has sufficiently recovered from general anaesthesia should mitigate the risk of increased sensitivity to anticholinergics in infants.

Long-term use of atropine might reduce milk production or milk letdown, however a single systemic dose is not likely to interfere with breastfeeding.

4.7 Effects on ability to drive and use machines

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

The undesirable effects are listed according to system organ class and following frequency:

Not known (cannot be estimated from the available data)

System Organ Class (SOC)	Undesirable effects
Immune system disorders	Anaphylaxis
Psychiatric disorders	Confusional states, especially in the elderly. At higher doses hallucinations, restlessness, delirium.
Nervous system disorders	Dizziness
Eye disorders	Dilatation of the pupils with loss of accommodation and photophobia, raised intraocular pressure.
Cardiac disorders	Transient bradycardia followed by tachycardia, palpitations, arrhythmias.*
Vascular disorders	Flushing
Respiratory, thoracic and mediastinal 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 and subcutaneous tissue disorders	Dry skin, urticaria, rashes, skin exfoliation.
Renal and urinary disorders	Difficulty with micturition
General disorders and administration site conditions	Thirst, fever.

*There have been reports of paradoxical atrioventricular block, especially after heart transplantation (see section 4.4 Special warnings and precautions for use).

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, hyperthermia, 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: Belladonna alkaloids, tertiary amines
ATC code: A03BA01

Mechanism of action

Atropine is an antimuscarinic agent which competitively antagonises acetylcholine at postganglionic nerve endings, thus affecting receptors in the exocrine glands, smooth muscle, cardiac muscle and the central nervous system.

Pharmacodynamic effects

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

Absorption

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.

Distribution

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

Biotransformation

It is incompletely metabolised in the liver and is excreted in the urine as unchanged drug and 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.

5.3 Preclinical safety data

No further information other than that which is included in the Summary of product characteristics.

6.1 List of excipients

Water for Injections Ph. Eur.
Sulfuric acid 1N (for pH adjustment)

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

Do not store above 25°C. Keep the ampoules in the outer carton in order to protect from light.

6.5 Nature and contents of container

Type I clear glass ampoule, 1ml

Packed in cardboard cartons to contain 10 ampoules x 1ml

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

hameln pharma ltd
Nexus, Gloucester Business Park
Gloucester, GL3 4AG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 01502/0016R

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24/08/2008

10 DATE OF REVISION OF THE TEXT

17/03/2025