Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Atropine Injection BP Minijet 100 microgram/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml contains 0.1 mg atropine sulfate. Each 5ml contains 0.5 mg atropine sulfate; each 10ml contains 1mg atropine sulfate; each 30 ml contains 3mg atropine sulfate.

Excipients: also includes sodium, not more than 0.22 mmol per 1ml.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection
A clear, colourless solution is contained in a USP Type 1 glass vial with an elastomeric closure. The container is specially designed for use with the IMS Minijet injector supplied.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Acute myocardial infarction with AV conduction block due to excess vagal tone (Wenkebach Type I, 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 tubocurarine.
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.

4.2 Posology and method of administration

Adults, children over 30kg 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 2mg.

In cardiac resuscitation, intravenous 500mcg (0.5mg) repeated at 5 minute intervals until the desired heart rate is achieved. In asystole 3mg 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 under 30kg:
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 10mcg (0.01 mg) repeated at 5 minute intervals, to a maximum dose of 100mcg (0.1mg).

Premedication before anaesthesia: intramuscular or subcutaneous; 30-60 minutes before surgery.
Up to 3 kg - 100 mcg (0.1 mg).
7 - 9 kg - 200 mcg (0.2 mg).
12 - 16 kg - 300 mcg (0.3 mg).
Over 20 kg - as for adults.

To control the muscarinic side effects of neostigmine: neonates and infants and children – 20 mcg/kg (0.02 mg/kg).
Anticholinesterase poisoning: intramuscular or intravenous, 50 mcg/kg (0.05 mg/kg) every 10-30 minutes until muscarinic signs and symptoms disappear.

4.3 Contraindications

Contraindications are not applicable to the use of atropine in life-threatening emergencies (eg. asystole).
Atropine is contraindicated in patients with known hypersensitivity to the drug, obstruction of the bladder neck e.g. due to prostatic hypertrophy, reflux oesophagitis, closed angle glaucoma, myasthenia gravis (unless used to treat the adverse effects of an anticholinesterase agent), paralytic ileus, severe ulcerative colitis and obstructive disease of the gastrointestinal tract.

4.4 Special warnings and precautions for use

Antimuscarinic agents should be used with caution in the elderly and children since these patients may be more susceptible to adverse effects. Atropine should also be used with caution in patients with hyperthyroidism, hepatic or renal disease or hypertension. Use with caution in febrile patients or when ambient temperature is high since antimuscarinics may cause an increase in temperature. Antimuscarinics block vagal inhibition of the SA nodal pacemaker and should thus be used with caution in patients with tachyarrhythmias, congestive heart failure or coronary heart disease. Parenterally administered atropine should be used cautiously in patients with chronic pulmonary disease since a reduction in bronchial secretions may lead to formation of bronchial plugs. Antimuscarinics should be used with extreme caution in patients with autonomic neuropathy. Antimuscarinics decrease gastric motility, relax the lower oesophageal sphincter and may delay gastric emptying; they should therefore be used with caution in patients with gastric ulcer, oesophageal reflux or hiatus hernia associated with reflux oesophagitis, diarrhoea or GI infection.

4.5 Interaction with other medicinal products and other forms of interactions

The effects of atropine may be enhanced by the concomitant administration of other drugs with anticholinergic activity e.g. tricyclic antidepressants, antispasmodics, anti-parkinsonian drugs, some antihistamines, phenothiazines, disopyramide and quinidine. By delaying gastric emptying, atropine may alter the absorption of other drugs.

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 concomitantly propofol; it could be due to propofol-induced suppression of the sympathetic nervous system.

An extreme caution should be observed when dobutamine-atropine stress echocardiography or the concomitant administration of a cetecholamine with atropine has to be performed in patients who seem already extremely stressed or are in an underlyine hyperadrenergic state (risk of Tako-tsubo syndrome).

4.6 Fertility, pregnancy and lactation

Atropine crosses the placenta. Studies in humans have not been done and only limited information is available from animal studies. Intravenous administration of atropine during pregnancy or at term may cause tachycardia in the foetus. Atropine should only be administered to pregnant women if the benefits outweigh the risks to the foetus. Trace amounts of atropine appear in the breast milk and may cause antimuscarinic effects in the infant; lactation may be inhibited.

4.7 Effects on ability to drive and use machines

Not applicable; this preparation is intended for use only in emergencies.

4.8 Undesirable effects

Adverse effects are dose-related and usually reversible when therapy is discontinued.

In relatively small doses, atropine reduces salivary, bronchial and sweat secretions; dry mouth and anhidrosis may develop, these effects being intensified as the dosage is increased.

Psychiatric disorders:
Hallucinations, mental confusion and/or excitement especially in the elderly.

Nervous system disorders:
Headache, nervousness, drowsiness, dizziness, insomnia.

Eye disorders:
Increased ocular tension, larger doses dilate the pupil and inhibit accommodation of the eye.

Cardiac disorders:
Larger doses block vagal impulses with consequent increase in heart rate with possible atrial arrhythmias, A-V dissociation and multiple ventricular ectopics, ST elevation, acute myocardial infarction. There have been cases where severe bradycardia due to hyperkalaemia could not be resolved with atropine.

Vascular disorders:
Flushing.

Respiratory, thorasic and mediastinal disorders:
Reduced bronchial secretion may cause dehydration of residual secretion and consequent formation of thick bronchial plugs that are difficult to eject from the respiratory tract.

Gastrointestinal disorders:
Reduction of salivary secretions, parasympathetic inhibition of gastrointestinal tract, constipation, inhibition of gastric secretion, loss of taste, nausea, vomiting, bloated feeling.

Skin and subcutaneous tissue disorders:
Anaphylaxis, anhidrosis, urticaria and rash occasionally progressing to exfoliation.

Musculoskeletal, connective tissue and bone disorders:
Weakness.

Renal and urinary disorders:
Inhibition of the parasympathetic control of the urinary bladder, urinary retention.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 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, nausea, vomiting, tachycardia and hypertension. 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. Treatment: 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

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.
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.

5.3 Preclinical safety data

Not applicable since atropine has been used in clinical practice for many years and its effects in man are well known.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Citrate
Citric Acid Monohydrate
Sodium Chloride
Water for Injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened: 3 years.
Once opened: Use immediately. Discard any unused portion.

6.4 Special precautions for storage

Do not store above 25°C. Keep vial in outer carton.

6.5 Nature and contents of container

The solution is contained in a USP type I glass vial with an elastomeric closure which meets all the relevant specifications. The container is specially designed for use with IMS Minijet injector supplied. The injector is manufactured from polypropylene resin with a central stainless steel canula and polyethylene end caps. It is fitted at the end with a Luer lock/Clave connector. The product is available either as 5, 10 or 30ml. Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

The container is specially designed for use with the IMS Minijet injector.
No special requirements.

7 MARKETING AUTHORISATION HOLDER

DLRC Pharma Services Limited
Chesterfield House
Clonmannon
Ashford
Wicklow
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22684/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08 September 1977

Date of last renewal: 08 September 2007

10 DATE OF REVISION OF THE TEXT

May 2019