SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Atropine Sulphate Injection BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Atropine Sulphate 0.03% w/v active substance BP
Water for Injections diluent BP
Sulphuric Acid BP pH adjustment
Nitrogen NF gassing agent

3. PHARMACEUTICAL FORM

A sterile aqueous solution for injection in pack sizes of one syringe (10ml).

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Cardiopulmonary resuscitation - in the treatment of asystole by intravenous injection. As an antidote to cholinesterase inhibitors by intravenous or intramuscular injection.

As an antidote to organophosphate pesticides and in mushroom poisoning. By intravenous or intramuscular injection.

In arrhythmias - Bradycardia associated with acute myocardial infarction.

4.2. Posology and method of administration

Cardiopulmonary Resuscitation in Adults and Children over 12 years of age: 3mg Intravenous Injection once only.

As an Antidote to Cholinesterase Inhibitors in Adults and Children over 12 years of age: 2mg intramuscular or Intravenous Injection, repeat dose every 5 - 10 minutes until signs of atropinisation appear.

As an Antidote to Organophosphate Pesticides and in Mushroom Poisoning in Adults and Children over 12 years of age: 2mg Intramuscular or Intravenous Injection, repeat dose every 10 - 30 minutes until muscarinic signs and symptoms subside.

Bradycardia associated with acute myocardial infarction in Adults and children over 12 years of age: 300 micrograms initially, increasing to 1mg if necessary

Children under 12 years of age: Not recommended.
Elderly: As for Adults

4.3. Contraindications

Known hypersensitivity to atropine, closed angle glaucoma, prostatic enlargement, paralytic ileus or pyloric stenosis, myasthenia gravis, severe ulcerative colitis.

4.4. Special warnings and precautions for use

Atropine Sulphate 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, acute myocardial infarction, hypertension or fever, and when the ambient temperature is high. 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.

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 antidepressant, 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.

4.6. Pregnancy and lactation

Atropine Sulphate crosses the placenta. There is insufficient evidence as to drug safety in pregnancy and lactation. This product should not be used during pregnancy unless considered essential by the physician. Atropine Sulphate 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 the drug. Atropine Sulphate, therefore, should only be used during breast feeding if considered essential by the physician.

4.7. Effects on ability to drive and use machines

This may be affected during treatment with Atropine. The time after which the patient can resume such activities must be decided by the physician.

4.8. Undesirable effects

Side effects which are common include, dry mouth with difficulty in swallowing, difficulty with micturition and constipation, thirst, dilation of the pupils with loss of accommodation and photophobia, flushing, dryness of the skin, bradycardia followed by tachycardia, palpitations and arrhythmias, vomiting, fever, rashes and confusional states may occur especially in the elderly.

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.

4.9. Overdose

Overdosage of Atropine Sulphate produces tachycardia, rapid respiration, hyperpyrexia and CNS stimulation marked by restlessness, confusion, hallucinations, paranoia, incoordination, delirium. In severe overdosage CNS depression may occur with coma, circulatory and respiratory failure, and death.

Treatment of overdosage with Atropine Sulphate injection consists of symptomatic and supportive therapy. General measures include: reduction of body temperature, administration of fluids orally or intravenously, monitoring of EGG, control of delirium or excitement with diazepam, urinary catheterisation to avoid urinary retention. The use of physostigmine as an antidote to atropine is controversial.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Atropine acts as an antimuscarinic and a competitive antagonist of acetylcholine at postganglionic cholinergic nerve endings. The receptors affected are those of exocrine glands, smooth muscle and cardiac muscle and the central muscle and the central nervous system. Atropine does not discriminate between the muscarinic receptor subtypes M1 and M2.

5.2. Pharmacokinetic properties

Absorption:
Atropine is well absorbed from the small bowel and not at all from the stomach. Thus the effects of oral dosing are much slower in onset than after parental dosing. Atropine is also absorbed by mucous membranes but less readily from the eye and skin, although significant toxicity can sometimes occur through absorption of excessive eye drops. Peak plasma concentrations after intramuscular injection are achieved within 30 minutes. After parental injection Atropine disappears rapidly from the circulation and plasma concentrations after the drug is given by intramuscular and intravenous routes are comparable at one hour.

Distribution:
Atropine has a volume of distribution of *1-6* I/kg. Protein binding is moderate, with approximately 50% of the drug bound in plasma. Its plasma clearance is 8 mI/mm/kg.

Only traces of atropine are found in breast milk. The drug readily crosses the blood-brain barrier and may cause confusion and delirium postoperatively. It crosses the placenta readily but the foetus is rarely affected by premedication doses.

Elimination:
The half life of elimination appears to be between two and five hours. Half of a single parenteral dose appears in the urine within four hours and about 90% within 24 hours with about 30% of the dose excreted as unchanged drug. Early studies with radioactive atropine had suggested a long half life of 12-36 hours, but recent studies with RIA and RRA have shown much more rapid elimination, with half lives of 4.3 $\pm$ 1.7 hours (by RIA) and 3.7 $\pm$ 2.3 hours (by RRA).

The differences in the two methods are probably due to the preferential tissue uptake of the l-isomer (l-hyoscamine) as the RRA ensures only the active l-form while RIA measures both l- and d- isomers.

5.3. Preclinical safety data

No further information, other than that which is included in the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Water for Injections, Sulphuric Acid and Nitrogen

6.2. Incompatibilities

Atropine Sulphate 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 Sulphate is mixed with methohexital sodium solutions.

6.3. Shelf life

36 Months.

6.4. Special precautions for storage

Store below 25°C.

Protect from light.

6.5. Nature and contents of container

Sterile aqueous solution for injection in Glass (Type I) 10ml prefilled syringe.

6.6. Instructions for use/handling

Use once and discard any remaining. Do not use if packaging is damaged.

7 MARKETING AUTHORISATION HOLDER

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Nexus, Gloucester Business Park
Gloucester, GL3 4AG
United Kingdom

8. MARKETING AUTHORIZATION NUMBER

PL 01502/0055

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

18th July 1995

10 DATE OF REVISION OF THE TEXT

11/08/2020