1.4	**Product Information**
1.4.1	**Summary of Product Characteristics**

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE PRODUCT:

CIRATRO (Atropine Injection BP, 1 mg/ml)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Each ml contains:

Atropine Sulphate BP 1 mg

3. **PHARMACEUTICAL FORM:**

Liquid Injection

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:

Posology

The drug is used for intramuscular injection, five days course with the initial dose of 3.2mg/kg, followed by 1.6mg/kg for the following 4 days.

For children, the dose should be chosen as follows:

Age (Year)	Weight	Total Dose	Day 1	Day 2	Day 3	Day 4	Day 5
< 1	< 8kg	75mg	25mg	12.5mg	12.5mg	12.5mg	12.5mg
1-3	8-12.5kg	120mg	40mg	20mg	20mg	20mg	20mg
3-6	12.5-17.5kg	150mg	50mg	25mg	25mg	25mg	25mg

6-9	17.5-25kg	240mg	80mg	40mg	40mg	40mg	40mg
9-12	25-32kg	300mg	100mg	50mg	50mg	50mg	50mg
12-16	32-47kg	360mg	120mg	60mg	60mg	60mg	60mg

The dose for the children out of the above ranges should be decreased or increased on the basis of individual weight or under the doctor's prescription.

Method of administration
Intramuscular Injection

4.3 CONTRAINDICATIONS:

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.

4.5INTERACTION 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 PREGNANCY & 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.

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.

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.

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 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.

6.2 Shelf Life:

36 months from the date of manufacturing.

6.3 Special Precaution for Storage:

Store below 30°C. Keep container in the outer carton and protect from light.

6.4 Nature and contents of container:

1 ml Amber USP type I Ampoule.

6.5 Special precautions for disposal and other handling:

For single use only.

If only part of the contents of an ampoule is used, the remaining solution should be discarded.

Do not use if the solution is cloudy, discoloured or if there are any particles present.

7. MARKETING AUTHORISATION HOLDER

CIRON DRUGS & PHARMACEUTICALS PVT.LTD.

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8. MARKETING AUTHORISATION NUMBER(S)

None

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not applicable