SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ATROPINE SULPHATE OSEL 1 MG/1 ML I.M./I.V./S.C. AMPOULE CONTAINING SOLUTION FOR INJECTION

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each 1 ml ampoule contains;
Active substance: 1 mg atropine sulphate*
Excipient(s): 9 mg sodium chloride
For excipients, see section 6.1.
*1% excess dose is added.

3. PHARMACEUTICAL FORM

Ampoule.

Clear, colorless solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Due to the anticholinergic and spasmolytic effect of ATROPINE SULPHATE;

- In bradyarrhythmias due to increased vagal activity,
- In the elimination of vagal effects such as bradycardia, hypotension and arrhythmias which may occur during surgery, and cardiopulmonary resuscitation,
- To reduce or prevent respiratory tract secretions during anesthesia (as an antisialogogue in pre-anesthetic medication),
- In pylorus, small intestine and colon spasms (irritable bowel syndrome),
- In urethra and biliary colic,
- As an antidote in the treatment of the poisoning effects of cholinesterase inhibitors (neostigmine, pridostigmine, pilocarpine), muscarinic (inocyte and clitocyte type fungal intoxications) or organophosphate insecticides.

4.2. Posology and method of administration

Posology / frequency and duration of administration

- Dose and frequency of atropine sulphate in the treatment of bradycardia arrhythmias, depends on the severity of the condition.

Adults:

The usual starting doses are 0.5 - 1.0 mg (0.5 - 1 ml) intravenously (i.v.).

In less severe cases, the total dose may be repeated up to 0.03 mg/kg (about 2 mg) (2 ml). The recommended dose range may vary from 3-5 minutes to 1-2 hours.

In severe cases, a total dose of 0.04 mg/kg (approximately 3 mg) (3 ml) may be given.

Some experts recommend that this total dose should be divided to intervals of 3-5 minutes (1 mg), while others recommend that a total dose of 3 mg be administered in a single dose.

- Pre-anesthetic medication: In order to reduce the risk of vagal inhibition of the heart and to reduce the salivary and bronchial secretion prior to induction of general anesthesia, ATROPINE SULPHATE should be administered by subcutaneous (s.c.) or intramuscular (i.m.) route usually 30-60 minutes before administration at a dose of 0.3 - 0.6 mg (0.3 - 0.6 ml) (approximately 0.5 mg) (0.5 ml). Alternatively, the same dose can be given intravenously just before the induction of anesthesia.
- Gastrointestinal radiography: 1 mg (1 ml) is administered by i.m. route.
- As an antidote: Doses up to 1 - 2 mg (1 - 2 ml) via s.c. or i.m. route or up to 4 mg (4 ml) via i.v. route are administered for the treatment of overdose with parasympathomimetic agents. In the treatment of irreversible anticholinesterase intoxications such as organophosphate insecticides: Higher doses (at least 2-3 mg) may be required. These doses are repeated until the signs of cyanosis disappear or the heart rhythm is 80-90/min. Dose intervals are adjusted according to the patient's heart rate. This practice should be continued until a definite improvement is made. This period may be 2 days or more. It should be administered at doses sufficient to control parasympathomimetic symptoms before coma and cardiovascular collapse, in rapidly developing fungal intoxications.

Method of administration:

ATROPINE SULPHATE ampoules can be administered via i.m., i.v. or s.c. route.

Additional information regarding special populations

Renal impairment:

No data available.

Hepatic impairment:

No data available.

Pediatric population:

It should generally not exceed 0.4 mg in children younger than 12 years.

- In the treatment of bradycardia arrhythmias:

as i.v. administration 0.01 - 0.03 mg/kg (0.01 - 0.03 ml/kg).

- Pre-anesthetic medication:

as s.c. administration infants up to 3 kg 0.1 mg (0.1 ml),
children between 7-9 kg 0.2 mg (0.2 ml),
children between 12-16 kg, 0.3 mg (0.3 ml),
children between 20-27 kg, 0.4 mg (0.4 ml),
children weighing 32 kg, 0.5 mg (0.5 ml),
children weighing 41 kg, 0.6 mg (0.6 ml).

These doses are repeated every 4-6 hours when necessary.

Geriatric population:

The recommended dose for adults is applied.

4.3 Contraindications

ATROPINE SULPHATE is contraindicated in;

- Obstructive gastrointestinal disorders: Pyloro-duodenal stenosis, achalasia, cardio spasm, paralytic ileus, intestinal atony (especially in geriatric patients), ulcerative colitis and toxic megacolon, gastroesophageal reflux and hiatus hernia.
- Bladder neck obstruction, prostate hypertrophy, atonic or hypotonic bladder, other obstructive uropathies.
- Narrow-angle glaucoma (can be used with myotics in wide-angle glaucoma).
- Thyrotoxicosis and tachycardia associated with heart failure.
- Cardiovascular system instillation due to acute bleeding.
- Myasthenia gravis (as long as atropine is not used to treat side effects of an anticholinesterase drug)
- Hypersensitivity to atropine and belladonna alkaloids.

4.4 Special warnings and precautions for use

– Atropine should be used with caution in children and elderly, since they are more susceptible to side effects of atropine.

- Patients with Down syndrome (Trisomy 21 or mongolism) are more susceptible to atropine. In contrast, patients with albinism may be resistant to the effects of atropine.
- Atropine should not be used, especially in children, when the ambient temperature is elevated. There is a danger of hyperpyrexia. It should also be used with caution in patients with febrile illnesses.
- Atropine should be used with caution in cases such as thyrotoxicosis, heart failure and cardiac surgery which cause tachycardia. Tachycardia may worsen.
- Administration of atropine in acute myocardial infarction may aggravate ischemia and infarction.
- Atropine may reduce bronchial secretions in patients who are unable to report their condition, in children, in elderly people and in those with brain damage, resulting in the formation of mucus plugs and decreased respiratory function.
- Atropine dosage should be gradually reduced during dose escalation or switching to other drugs for the treatment of Parkinson's disease. Atropine should not be stopped suddenly.
- Atropine is contraindicated in narrow angle glaucoma. However, there may be patients over the age of 40, who have not been diagnosed with glaucoma. In this case, atropine can lead to an acute glaucoma crisis. If in doubt, intraocular pressure should be measured prior to administration of atropine.
- It may lead to ileus or megacolon in patients with regional arthritis and ulcerative colitis. Or it can increase the severity of reflux in the esophagus.
- Atropine can cause mental confusion, especially in elderly patients or patients with brain damage.

  It should be used with extreme caution in Myasthenia gravis.
- Amantadine, some antihistamines, tricyclic antidepressants such as butyrophenone, and phenothiazines, which have antimuscarinic properties, may enhance the effects of atropine.
- This group of drugs (atropine), which reduces gastric motility, can reduce the absorption of other drugs.
- It should be used with caution in patients with hyperthyroidism, hepatic or renal disease or in patients with hypertension.
- The reduction in bronchial secretions may cause bronchial plug formation and therefore it

should be used with caution in patients with chronic pulmonary disease.

- Antimuscarinic drugs should be used with extreme caution in autonomic neuropathic patients.
- This medicinal product contains less than 1 mmol (23 mg) of sodium per ampoule; it can be assumed that it is essentially sodium-free.

4.5 Interaction with other medicinal products and other forms of interaction

- Urinary alkalinization (citrate, bicarbonate, carbonic anhydrase inhibitors) complicates atropine elimination and increases its blood levels.
- Anti-acids and anti-diarrheals reduce the absorption of oral atropine.
- If anticholinergics are given with atropine, antimuscarinic effect may be enhanced and it may cause paralytic ileus.
- If atropine is given intravenously during cyclopropane anesthesia, it may cause ventricular arrhythmias.
- Atropine may reduce the antipsychotic effect of haloperidol.
- Atropine may slow the absorption of ketoconazole by raising the stomach pH.
- Atropine may antagonize the gastro kinetic effect of metoclopramide.
- Concomitant use of atropine and opioids may cause severe constipation, paralytic ileus and urinary retention.
- Atropine may increase the ulcerative effect of waxy-matrix based potassium preparations.

Laboratory Tests: Gastric secretions, gastric emptying time, should not be measured or phenolsulfonphthalein (PSP) test should not be conducted in patients given atropine. Atropine and PSP are excreted via the same tubular mechanism.

Additional information regarding special populations:

No data available.

Pediatric population:

No data available.

4.6 Pregnancy and lactation General recommendation

Pregnancy category: C

Women of child bearing potential/birth control (contraception)

No clinical data is available on exposure during pregnancy for atropine.

Animal studies are not sufficient for the effects on pregnancy and/or embryonic/fetal development and/or labor and/or postnatal development (see 5.3). The potential risk for humans is unknown.

ATROPINE SULPHATE should not be used during pregnancy, unless clearly indicated.

Pregnancy

There are no experimental and clinical studies on the teratogenic potential of atropine. However, until now, the teratogenic effect of atropine has not been clinically reported. Intravenous administration of atropine may cause fetal tachycardia.

Lactation period

Anticholinergics inhibit lactation. Atropine is excreted in breast milk in small amounts. It should not be used in breast-feeding mothers because babies are very sensitive to atropine.

Reproductivity / Fertility

No data available.

4.7 Effects on ability to drive and use machines

Atropine can cause side effects such as blurred vision, accommodation paralysis, mydriasis, photophobia, dizziness, drowsiness, excitation and confusion. Patients driving and using machines should be warned about such effects.

4.8 Undesirable effects

The side effects of atropine are dose dependent, and usually disappear when the treatment is stopped. At low doses it may reduce salivation, bronchial and sweat secretion thus causing anhydrous and dry mouth. These effects of atropine can be exacerbated with increasing doses. A decrease in the bronchial secretion may lead to the dehydration of residual secretion and may lead to the formation of a bronchial plug that is difficult to remove from the airways.

At high doses atropine may cause;

- Inhibition of eye accommodation by causing mydriasis,
- Increased heart rate and possible atrial arrhythmias by blocking the vagal impulses,

- Atrioventricular dissociation and many ventricular ectopic beats,
- Urinary retention due to the parasympathetic control of the bladder,
- Constipation due to the inhibition of the gastrointestinal system.

A further increase in dose inhibits gastric secretion. In some patients, anaphylaxis, urticaria and rarely redness in the skin which later progresses to skin exfoliation may be seen. Other effects include hallucinations, increased intraocular pressure, loss of taste sensation, headache, irritability, drowsiness, weakness, dizziness, flushing, insomnia, nausea, vomiting and swelling of the abdomen. Mental confusion and/or excitation may occur, especially in the elderly.

Reporting of the side effects:

If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose and treatment

Overdose symptoms are a burning sensation accompanied by distinct dry mouth, swallowing difficulties, distinct photophobia, facial flushing, skin dryness, fever, rash, nausea, vomiting, tachycardia and hypertension. Depending on the stimulation of the central nervous system irritability, tremors, confusion, excitation, hallucinations and delirium may occur, consequently generalized central depression may develop resulting in increase in sleepiness, unconsciousness, death due to circulatory and respiratory failure.

In severe cases, 1-4 mg of physostigmine should be administered intravenously, intramuscularly or subcutaneously, and the dose should be repeated if necessary, since physostigmine is rapidly eliminated from the body. Diazepam may be administered for sedative use in patients with delirium, but the administration of sedatives at high doses is contraindicated as the risk of central depression may occur in the late period of atropine poisoning. Adequate airway clearance must be provided. Respiratory insufficiency can be treated by inhalation of oxygen and carbon dioxide. Fever can be reduced with the application of cold. Adequate fluid intake is also important. Urethral catheterization may be necessary. If photophobia is present or likely to occur, treatment should be undertaken in a dark room.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimuscarinics (Systemic, parasympatholytic)

ATC code: A03BA01

Atropine (d and l-hyoscyamine) is a tertiary amine alkaloid with central and peripheral antimuscarinic activity. It shows its effect by competitively inhibiting the muscarinic receptors of acetylcholine. Atropine exhibits antimuscarinic effects in organs fed by parasympathetic nerves and tissues bearing acetylcholine receptors (smooth muscles). It has little effect on both autonomic ganglia and the nicotinic acetylcholine receptors in skeletal muscle. Atropine causes pharmacodynamic effects such as inhibition of saliva, bronchial and sweat secretions, mydriasis, loss of accommodation, tachycardia, relaxation in bladder detrusor smooth muscles, difficulty in urinating due to increased tonus in smooth muscles in the sphincter and trigon area, decrease in intestinal tonus and motility, decrease in gastric secretion, tonus and motility. Atropine also has a relaxant effect on the biliary tract. Atropine can also be effective against motion sickness, vertigo and vomiting by depressing the vestibular system at the cortex or vestibular nuclei level.

5.2 Pharmacokinetic properties

General properties

Absorption:

Atropine is well absorbed by i.m. route, reaching peak plasma concentration in 20 minutes. Its impact via the i.v. route is seen in 2-4 minutes.

Distribution:

Atropine passes through the cerebrospinal fluid and the fetal circulation in quantities close to its blood concentrations. The protein binding rate is 18% in vitro.

Biotransformation:

Atropine is metabolized in the liver and 77-94% of the administered i.m. dose is excreted in urine in 24 hours.

Elimination:

Elimination half-life is 2-3 hours, the elimination curve is biphasic. Approximately half of the atropine excreted in urine is unchanged atropine, the other is in the form of tropic acid esters and glucuronide conjugates.

Linearity/non-linearity:

No data available.

5.3 Pre-clinical safety data

Exceeding the therapeutic dose of atropine as a result of lack of attention or by mistake, results in signs of intoxication. These are the more generalized and severe occurrence of the pharmacodynamic effects of atropine. Especially in doses exceeding 3 mg, hallucinations, delirium and excitation are seen.

In humans, minimal lethal dose for adults has been reported as 100 mg atropine. A few milligrams may be toxic and lethal in children, with a minimal lethal dose for l-hyoscyamine being 10 mg in adults.

The acute dose toxicity as LD_{50} values were 622 mg/kg in rats, 400 mg/kg in mice and 600 mg/kg in rabbits. Chronic and repeated dose toxicity has not been investigated.

No data are available on the genotoxic, teratogenic, carcinogenic effects and the reproductive toxicity of atropine. However, there is no publication in the literature that atropine has such effects. Atropine is not included in the list of carcinogenic substances.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

Water for injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at room temperature between 15-30°C, protected from light.

6.5 Nature and contents of container

Colorless, 1 ml, type I glass ampoules, in cardboard boxes containing 10, 50 and 100 ampoules

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with "Regulation on Control of Medical Wastes" and "Regulation on Control of Packaging Wastes".

7.MARKETING AUTHORIZATION HOLDER

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8.MARKETING AUTHORIZATION NUMBER

192/11

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10. DATE OF REVISION OF THE TEXT
