PATIENT INFORMATION LEAFLET

ATROPINE SULPHATE Osel 0.5 mg/1 mL I.V./I.M./S.C. Ampoule Containing Solution for Injection
Intramuscular, subcutaneous, intravenous administration.

Each 1 mL ampoule contains;

- ***Active Substance*** **:** 0.5 mg atropine sulphate.
- ***Excipients*** **:** Sodium Chloride and water for injection

Read all of this PATIENT INFORMATION LEAFLET carefully before you start taking this medicine because it contains important information for you.

- *Keep this leaflet. You may need to read it again.*
- *If you have any further questions, ask your doctor or pharmacist.*
- *This medication is prescribed solely for you, do not offer it to others.*
- *If you go to doctor or hospital while using this medicine, tell your doctor that you are using this medicine.*
- *Follow the recommendations on this leaflet exactly as described. Do not use* ***higher or lower dose*** *except the dose you have been recommended for the medicine.*

In this Information Leaflet:

1. ***What ATROPINE SULPHATE is and what is it used for?***
2. ***What you need to to know before you use ATROPINE SULPHATE?***
3. ***How to use ATROPINE SULPHATE?***
4. ***What are the possible side effects?***
5. ***How to store ATROPINE SULPHATE?***

Headings are included.

1. What ATROPINE SULPHATE is and what is it used for?

ATROPINE SULPHATE is presented in boxes containing 10, 50 and 100 ampoules, each ampoule contains 0.5 mg atropine sulphate. The ampoules contain a clear, colorless solution. ATROPINE SULPHATE is used in;

– Bradyarrhythmias (heart rate below 60 per minute) due to increased vagal activity (stimulation of the vagus nerve),

– Elimination of vagal effects such as bradycardia, hypotension (low blood pressure) and arrhythmias (rhythm disorder) that may occur during operations, and cardiopulmonary resuscitation,

– To reduce or prevent the secretion of respiratory tract during anesthesia (as a saliva-reducing medication prior to anesthesia),

– Pylorus (the hole opening from the stomach to the duodenum), small intestine and large intestinal spasms (contractions) (irritable bowel syndrome),

– Urethra (urinary tract) and biliary colic (pain associated with the inflammation of the bile duct),

– 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.

2. What you need to know before you use ATROPINE SULPHATE?

DO NOT USE ATROPINE SULPHATE if;

- Obstructive gastrointestinal diseases (Diseases associated with obstructions in the digestive system): Pyloro-duodenal stenosis (constriction where the stomach opens into duodenum), achalasia (continuous closing of the valve at the lower end of the esophagus), cardio spasm (contraction of the constrictor muscular between the esophagus and the stomach), paralytic ileus (cessation of intestinal motility due to the paralysis of intestinal muscles), intestinal atonia (loss of the innate tension of the intestinal muscles), ulcerative colitis (inflammatory bowel disease) and toxic megacolon (sudden enlargement of the large intestine), gastroesophageal reflux (escaping of food and acid from the stomach to the esophagus) and hiatus hernia (gastric hernia).
- Bladder neck obstruction (bladder neck stenosis), prostatic hypertrophy (overgrowth of the prostate gland), atonic or hypotonic bladder (loss or decrease of the tension in the muscles of the bladder), other obstructive uropathies (diseases related to the obstruction of the urinary tract).
- Narrow angle glaucoma (an eye disease that causes sudden blurred vision, pain, and redness) (can be used with myotics in wide-angle glaucoma).
- Thyrotoxicosis (overactive thyroid gland) and tachycardia due to heart failure (heart palpitation).
- Cardiovascular system instillation due to acute bleeding.
- It should not be used in hypersensitivity to atropine and belladonna alkaloids.

USE ATROPINE SULPHATE CAREFULLY if;

– 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, albino patients (people who congenitally do not have the melanin pigment normally found in the body) 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 (high fever). 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 (death of tissues of the heart with insufficient blood supply) may cause ischemia (insufficient blood supply) and infarction to worsen.
- 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 should not be used 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.
- In patients with regional arthritis and ulcerative colitis, it may lead to ileus or megacolon, or it may increase the reflux severity 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 (a disease of the muscular system that manifests itself in advanced muscle fatigue).
- 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.

"If these warnings are applicable to you even for any period of time in the past, please consult your doctor."

Use of ATROPINE SULPHATE with food and drinks

There is no interaction with food and drinks in terms of the method of administration.

Pregnancy

Consult your doctor or your pharmacist before using the drug.

There are no adequate data from the use of atropine in pregnant women. Do not use

ATROPINE SULPHATE when you are pregnant unless it is deemed necessary by your doctor.

If you notice that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Breast-feeding

Atropine is excreted in breast milk in small amounts. Since babies are very sensitive to the effect of atropine, you should not use this drug while you are breastfeeding.

Consult your doctor or your pharmacist before using the drug.

Driving and using machines

Atropine may cause side effects such as blurred vision, adaptation paralysis (paralysis of the muscles that adjust the eye), pupillary growth, sensitivity to light, dizziness, drowsiness, excitation (arousal state), and confusion (blurring of consciousness). You should not drive and use machines when you are under the effects of the drug.

Important information about some excipients present in ATROPINE SULPHATE

This medicinal product contains less than 1 mmol (23 mg) of sodium per ampoule; it can be assumed that it is essentially sodium-free.

Use with other medicines

- Urinary alkalinization (basic) (citrate, bicarbonate, carbonic anhydrase inhibitors) complicates atropine elimination and increases its blood levels.
- Antacids (drugs used against excess stomach acid) and antidiarrheals (drugs used in the treatment of diarrhea) 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 (rhythm disturbance originating from the ventricles of the heart).
- Atropine can reduce the anti-psychotic effect of haloperidol (drugs used in mental conditions where thoughts and hearing are heavily impaired).
- Atropine may slow the absorption of ketoconazole by raising the stomach pH.
- Atropine may antagonize the gastro kinetic effect of metoclopramide (effect on the digestive system).
- The concomitant use of atropine and opioids (name given to morphine-like compounds including morphine) may cause severe constipation, paralytic ileus and urinary retention

(ability to urinate diminished or lost).

- 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.

If you are using or have recently used any type of prescription or non-prescription drugs, please inform your physician or your pharmacist.

3. How to use ATROPINE SULPHATE?

Since the ATROPIN SULPHATE is administered by your doctor or a healthcare professional, the following section is intended for your doctor or a healthcare professional.

Instructions for appropriate use and dose / administration frequency:

- 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 (1 - 2 mL) intravenously (i.v.).

In less severe cases, the total dose may be repeated up to 0.03 mg/kg (about 2 mg) (4 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) (6 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 (0.6 - 1.2 mL) (approximately 0.5 mg) (1 mL). Alternatively, the same dose can be given intravenously just before the induction of anesthesia.
- Gastrointestinal radiography: 1 mg (2 mL) is administered by i.m. route.
- As an antidote: Doses up to 1 - 2 mg (2 - 4 mL) via s.c. or i.m. route or up to 4 mg (8 mL) by 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.

Route and method of administration:

ATROPIN SULPHATE ampoules can be administered intramuscularly, subcutaneously or intravenously.

Various age groups

Use in children:

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

- In the treatment of bradycardia arrhythmias:

0.01 - 0.03 mg/kg (0.02 - 0.06 mL/kg) is administered intravenously.

- Pre-anesthetic medication:

Subcutaneous injection;

infants up to 3 kg, 0.1 mg (0.2 mL),
children between 7-9 kg, 0.2 mg (0.4 mL),
children between 12-16 kg, 0.3 mg (0.6 mL),
children between 20-27 kg, 0.4 mg (0.8 mL),
children weighing 32 kg, 0.5 mg (1.0 mL),
children weighing 41 kg, 0.6 mg (1.2 mL).

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

Use in elderly:

The recommended dose for adults is administered.

Special conditions

Renal impairment:

No data available.

Hepatic impairment:

No data available.

If you have the impression that the effect of ATROPINE SULPHATE is too strong or too weak, talk to your doctor or pharmacist.

If you have used more ATROPINE SULPHATE than you should

Overdose symptoms are a burning sensation accompanied by distinct dry mouth, swallowing difficulties, light hypersensitivity, facial flushing, skin dryness, fever, rash, nausea, vomiting, heart palpitations and increase in blood pressure. Depending on the stimulation of the central nervous system irritability, tremors, confusion, excitation, hallucinations and delirium may occur, consequently increase in sleepiness, unconsciousness, death due to circulatory and respiratory failure may occur.

In severe cases, 1-4 mg of physostigmine should be administered subcutaneously, intravenously or intramuscularly, 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 sedatives at high doses should not be administered, as the risk of deterioration of brain function 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. Urinary catheter may be necessary. If light sensitivity is present or likely to occur, treatment should be undertaken in a dark room.

If you have used more ATROPINE SULPHATE than you should, talk a doctor or pharmacist.

If you forget to use ATROPINE SULPHATE

Since your medication will be administered by a healthcare professional, dose skipping is not expected. However, if you think that your dose may not have been given to you, you should inform the healthcare personnel.

Do not take a double dose to make up for forgotten doses.

Effects which may occur when treatment with ATROPINE SULPHATE is discontinued

When treatment with ATROPINE SULPHATE is terminated, no adverse effects are expected.

4. What are the possible side effects?

Side effects are likely to occur at high doses, but these side effects usually disappear when the treatment is stopped.

Rarely, an allergic reaction can develop. This can cause skin rashes, severe itching, peeling, swelling of the face (especially around the lips and eyes), tension in the throat, difficulty in breathing or swallowing, fever, water loss, shock and fainting.

All of these are very serious side effects. If you notice any of these side effects, tell your doctor immediately.

Possible side effects include, decrease in saliva, sweat and mucus secretion (disposal of mucus with a cough may be difficult), dilation in pupillas (causing blurred vision), rapid or irregular heartbeat, difficulty in urination, constipation, hallucinations, increase in intraocular pressure, loss of taste sensation, headache, anxiety, dizziness, weakness, flushing of the face, insomnia and swelling in the abdomen. In addition, mental confusion and/or restlessness (especially in the elderly), nausea, vomiting and dizziness can be rarely seen.

If you experience any side effect not mentioned in this patient information leaflet, inform your doctor or your pharmacist.

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.

5. How to store ATROPINE SULPHATE

Keep ATROPINE SULPHATE out of the sight and reach of children, and in its packaging.

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

Use in compliance with the expiry date.

Do not use ATROPINE SULPHATE after the expiration date stated on the packaging.
Do not throw away expired or unused medicines! Unused products or waste materials must be disposed of in accordance with the local regulations.

Marketing Authorization Holder and Manufacturer:
OSEL İlaç San.ve Tic. A.Ş.
Akbaba Mah. Maraş Cad. No.:52
34820 Beykoz / ISTANBUL

This patient information leaflet is approved on 15/01/2015.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ATROPINE SULPHATE Osel 0.5 mg/1 mL I.V./I.M./S.C. Ampoule Containing Solution for Injection

Sterile

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL ampoule contains;
Active substance: 0.5 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 is used;

– 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 (1 - 2 mL) intravenously (i.v.).

In less severe cases, the total dose may be repeated up to 0.03 mg/kg (about 2 mg) (4 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) (6 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 (0.6 - 1.2 mL) (approximately 0.5 mg) (1 mL). Alternatively, the same dose can be given intravenously just before the induction of anesthesia.
- Gastrointestinal radiography: 1 mg (2 mL) is administered by i.m. route.
- As an antidote: Doses up to 1 - 2 mg (2 - 4 mL) via s.c. or i.m. route or up to 4 mg (8 mL) by i.v. route is 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:

i.v. administration 0.01 - 0.03 mg/kg (0.02 - 0.06 mL/kg).

- Pre-anesthetic medication:

s.c. administration infants up to 3 kg 0.1 mg (0.2 mL),
children between 7-9 kg 0.2 mg (0.4 mL),
children between 12-16 kg, 0.3 mg (0.6 mL),
children between 20-27 kg, 0.4 mg (0.8 mL),
children weighing 32 kg, 0.5 mg (1 mL),
children weighing 41 kg, 0.6 mg (1.2 mL).

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

Geriatric population:

The recommended dose for adults is administered.

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, heart palpitations 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 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). Its impact on both autonomic ganglia and the nicotinic acetylcholine receptors in skeletal muscle is very small. 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

36 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

Amber coloured, 1 mL, type I glass ampoules, in carton 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

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First registration date: 30.06.1999

Date of revision of the registration: 04.05.2005

10. DATE OF REVISION OF THE TEXT
