PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS - 1986
This medicine is dispensed with a physician's prescription only

Mestinon Dragees 60 mg

Each dragee contains:
Pyridostigmine bromide 60 mg

For a list of inactive and allergenic ingredients, see section 6 - "Additional information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, consult your physician or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. What is this medicine intended for?

Treatment of myasthenia gravis.

Therapeutic group:
Cholinesterase inhibitors.

Mestinon Dragees 60 mg contain the active ingredient Pyridostigmine bromide which acts as an inhibitor of the cholinesterase enzyme. This in turn blocks excessive breakdown of acetylcholine, a substance that transmits nerve impulses to the muscles.

Patients who have myasthenia gravis feel that their muscles are weak and tire easily. In severe cases, they may even decline to muscle paralysis.

2. Before using the medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient Pyridostigmine bromide, **to other bromides** or to any of the additional ingredients that the medicine contains (please see section 6, "Additional information").
- You suffer from mechanical obstruction of the digestive or urinary tract.

Special warnings regarding use of the medicine
Before starting treatment with Mestinon Dragees 60 mg, tell your physician if:

- You suffer from diseases of the respiratory tract such as asthma, bronchospasm or chronic obstructive pulmonary disease (COPD)
- You suffer from heart diseases such as: worsening of heart failure (symptoms at rest), cardiac conduction disorders (AV block) or heart rhythm disorders such as slow heart rhythm, or you have recently had a heart attack (arrhythmia is more common in the older population)
- You suffer from low blood pressure
- You suffer from a stomach ulcer
- You have had gastrointestinal surgery
- You suffer from epilepsy
- You suffer from Parkinson's disease

- You suffer from kidney problems
- You suffer from vagotonia, a condition in which the vagus nerve is overactive, causing symptoms such as a slower heart rate, low blood pressure, constricted pupils
- You suffer from an overactive thyroid gland
- You have had surgery to remove your thymus gland

If you are taking very high doses of **Mestinon Dragees 60 mg**, you may need atropine or other anticholinergic substances to specifically counteract the muscarinic effect without impairing the nicotinergic effect.

Drug interactions:
If you are taking or have recently taken any other medicines, including non-prescription medicines or nutritional supplements, tell your physician or pharmacist.
Particularly if you are taking:

- Steroids or any other medicine that suppresses the immune system
- Anticholinergic medicines. Atropine and scopolamine inhibit the muscarinic effect of Pyridostigmine bromide, the active ingredient of **Mestinon Dragees 60 mg**. These medicines reduce intestinal motility, which can affect the absorption of Pyridostigmine bromide by the body.
- Medicines that contain methylcellulose. These medicines may interfere with the absorption of **Mestinon Dragees 60 mg.** Avoid using medicines containing methylcellulose while taking **Mestinon Dragees 60 mg.**
- Antibiotics of the aminoglycoside group, such as neomycin and kanamycin
- Local anesthetics or preparations used as general anesthetics
- Medicines to treat arrhythmias
- Muscle relaxants used during surgery such as pancuronium or vecuronium. If you are having surgery, inform your physician that you are taking **Mestinon Dragees 60 mg**. **Mestinon Dragees 60 mg** may also prolong the effect of other muscle relaxants such as suxamethonium.
- Preparations containing ***N,N-diethyl-m-toluamide (DEET).*** Avoid applying them to large areas of skin while taking **Mestinon Dragees 60 mg**.

Pregnancy, breastfeeding and fertility:
Consult with your physician of you are pregnant, breastfeeding, think you are pregnant or are planning a pregnancy.

Pregnancy
The active ingredient in **Mestinon Dragees 60 mg** crosses the placental barrier. Only use this medicine during pregnancy if your physician has decided that the treatment is necessary. In particular, avoid taking high doses of this medicine.
Intravenous administration of cholinesterase inhibitors – the group to which **Mestinon Dragees 60 mg** belongs – can cause premature contractions in pregnancy. The risk for premature contractions increases towards the end of pregnancy. It is not known whether oral use of the medicine may induce premature contractions.

Breastfeeding
The active ingredient in **Mestinon Dragees 60 mg** passes into breast milk in small amounts. In a very limited number of cases studied, no effects on breast-fed infants/children were observed. If treatment with **Mestinon Dragees 60 mg** is required, the infant/child should be monitored for possible side effects, or weaned.

Fertility:
Mestinon Dragees 60 mg have not been found to have any effect on male or female fertility in animal studies.

Driving and using machines:
Using **Mestinon Dragees 60 mg** may cause reduced visual acuity and constricted pupils, thus impairing your ability to drive or operate machines.
Do not drive or operate machines if you feel that this medicine is affecting your vision.
Children should be warned against activities such as riding bicycles or playing close to the road, etc.

Important information about some of the medicine's ingredients:
Mestinon Dragees 60 mg contain sucrose. If your physician has told you that you are intolerant to certain sugars, consult your physician before starting treatment with **Mestinon Dragees 60 mg.**
Patients suffering from hereditary fructose/galactose intolerance, glucose-galactose malabsorption or sucrase-isomaltase deficiency should not use **Mestinon Dragees 60 mg**.

3. How should you use the medicine?

Always use this preparation according to your physician's instructions. You should check with your physician or pharmacist if you are unsure about the dosage or treatment regimen of this medicine.
The dosage and treatment regimen will be determined by your physician only. The usual dosage is generally:

Adults:
Multiple doses of 30 to 120 mg are given at intervals throughout the day. **Mestinon Dragees 60 mg** must not be divided. For a 30 mg dosage, use a tablet containing 30 mg of Pyridostigmine bromide.

The total daily dose is usually in the range of 120-1200 mg, but higher doses than these may be needed by some patients in accordance with dose titration.

Children:
Children under 6 years old should receive an initial dose of 30 mg of Pyridostigmine bromide. **Mestinon Dragees 60 mg** must not be divided. For a 30 mg dosage, use a tablet containing 30 mg of Pyridostigmine bromide.
The dosage for 6-12 years old children is 60 mg. Dosage should be increased gradually, in increments of 30 mg daily, until maximum improvement is obtained.
The total daily dosage usually ranges from 30 to 360 mg.

Special populations
Elderly
There are no specific dosage recommendations for **Mestinon Dragees 60 mg** in elderly patients.

Patients with impaired kidney function
Mestinon Dragees 60 mg are mainly excreted unchanged by the kidneys. Lower doses, and adjustment of the dosage in accordance with the patient's individual response, may therefore be required in patients suffering from kidney problems.

Patients with impaired liver function
There are no specific dosage recommendations for **Mestinon Dragees 60 mg** in patients with liver failure.

Do not exceed the recommended dose.

Mestinon dragees 60 mg must not be divided.

Swallow the dragees with water or any other non-alcoholic beverage.

If you have accidentally taken an overdose or if a child has accidentally swallowed the medicine, immediately consult a physician or proceed to a hospital emergency room and bring the package of the medicine with you. Taking an overdose of this medicine may cause a cholinergic crisis, which can lead to pronounced muscle weakness or even muscle weakness to the extent of paralysis, among others.
The following additional symptoms can manifest: extreme slowing of the heart rate or even cardiac arrest; periodic acceleration of the heart rate, a drop in blood pressure to the extent of circulatory collapse; dizziness, nausea and vomiting, involuntary discharge of urine, defecation accompanied by cramps, diarrhea, increased bronchial secretions, contraction of the bronchial muscles combined with possible constriction of the airways, pulmonary edema, increased secretion of tears and saliva, increased nasal secretion, light to heavy sweating, reddened skin, constricted pupils and impaired visual acuity, incidental muscle cramps, involuntary muscle twitching, and general weakness.
Symptoms involving the central nervous system can occur, including restlessness, confusion, slurred speech, nervousness, irritability, hallucinations, as well as seizures and coma (see section 4 - "Side effects").

If you forgot to take this medicine at the scheduled time, do not take a double dose to make up for the forgotten dose. Take the next dose at the usual time and consult your physician.
If you forget to take more than one dose, consult your physician.
Adhere to the treatment regimen as recommended by your physician. Even if there is an improvement in your health condition, do not stop treatment with this medicine without consulting with your physician.

Do not take medicines in the dark! Check the label and the dose <u>every time</u> you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult your physician or pharmacist.

4. Side effects

As with any medicine, the use of **Mestinon Dragees 60 mg** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

The following side effects may occur during treatment with **Mestinon Dragees 60 mg:**

Rare side effects (effects that may affect up to 1-10 in 10,000 users):

- Skin rash (usually disappears after stopping use of the medicine. Medicines containing bromide should not be used).

Side effects of unknown frequency (frequency has not yet been determined):

<u>Immune system disorders</u>

- Hypersensitivity to the medicine (allergy)

<u>Psychiatric disorders</u>

- In the presence of organic brain changes, psychopathological symptoms may occur during treatment with **Mestinon Dragees 60 mg**, even to the extent of psychosis, and existing symptoms may intensify.

<u>Nervous system disorders</u>

- Circulatory collapse (syncope)

<u>Eyes</u>

- Constricted pupils
- Increased secretion of tears
- Impaired ability of the eye to adapt to near/far vision (e.g., blurred vision)

Cardiovascular system

- Arrhythmias (e.g., palpitations), accelerated heart rate, slowed heart rate, cardiac conduction disorders (**atrioventricular block**), spasms of the coronary arteries (**Prinzmetal angina**)

Vascular disorders

- Flushing
- Low blood pressure

Respiratory tract

- Increased bronchial secretion combined with constriction of the airways; asthmatic patients may experience respiratory symptoms.

Digestive tract

- Nausea, vomiting, diarrhea
- Increased gastrointestinal activity, abdominal discomfort (e.g., weakness, pain, cramps)
- Increased salivation

Skin

- Increased sweating
- Urticaria (hives)

Muscles

- Muscle weakness
- Reduced muscle tone
- Involuntary muscle twitching
- Muscle tremors
- Muscle cramps

Kidneys and urinary tract

- Sudden and strong urge to urinate

Side effects are generally dose-related.
During treatment with **Mestinon Dragees 60 mg** (mainly with oral doses exceeding 150-200 mg Pyridostigmine bromide/day), the following side effects may occur: episodes of sweating, increased salivation, increased tear secretion, increased bronchial secretions, nausea, vomiting, diarrhea, abdominal cramps (due to increased gastrointestinal activity), increased urge to urinate, muscle tremors, muscle cramps, muscle weakness, and impaired ability of the eye to adapt to near/far vision.
After taking higher doses (500-600 mg Pyridostigmine bromide/day orally), the heart rate may slow, cardiovascular reactions may occur and blood pressure may become excessively low (see section 3 – "How should you use the medicine?").
The side effects listed may also be signs of an overdose or a cholinergic crisis. It is important to check the cause of the side effects with your physician.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, ask your physician for advice.

Side effects can be reported to the Ministry of Health by clicking the link "Report Side Effects of Drug Treatment" on the homepage of the Ministry of Health website (*www.health.gov.il***), which will direct you to the online form for reporting side effects, or by entering the link:** *https://sideeffects.health.gov.il*

5. How should the medicine be stored?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by your physician.

- Do not use this medicine after the expiry date (exp. date) which appears on the package exterior. The expiry date refers to the last day of that month**.**
- Do not store at a temperature higher than 25°C.
- Store in the original package.
- The preparation may be used for 3 months after first opening.
- Do not throw away medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. Additional information

- In addition to the active ingredient Pyridostigmine bromide, the medicine also contains:
  Colloidal anhydrous silica, maize starch, povidone K 30, pregelatinised starch, talc, magnesium stearate
  Dragee coating:
  Sucrose crystalline, rice starch, talc, acacia spray-dried gum, hard paraffin, iron oxide red (E 172), light liquid paraffin, iron oxide yellow (E 172)

- What the medicine looks like and what the package contains:

  Light orange to orange colored round, convex, sugar-coated tablets,

  packaged in a glass bottle containing 20 or 150 dragees

- Registration holder and address: MegaPharm Ltd., P.O.B. 519, Hod Hasharon 4510501, Israel

- Manufacturer and address: ICN Polfa, Rzeszów, Poland

- **Reviewed in February 2022 in accordance with the guidelines of the Ministry of Health.**

- **Registration number of the medicine in the National Drug Registry of the Ministry of Health:** 130-84-21200