

PATIENT PACKAGE LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

This medicine is dispensed with a physician's prescription only

Amandin 100

Film Coated Tablets

Active ingredient:

Amantadine – hemisulphate 100 mg

For the complete list of ingredients, please 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, refer to your physician or pharmacist.

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

1. WHAT IS THE MEDICINE INTENDED FOR?

For the treatment of Parkinson's Disease symptoms such as: muscle rigidity, tremors, reduced movement or immobility.

Therapeutic group: Anti-Parkinson drugs.

2. BEFORE USING THE MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient amantadine hemisulphate and its compounds, lactose, Orange Lake S (E 110) or to any of the additional ingredients that the medicine contains (please see section 6 'Additional Information').
- You suffer from severe heart failure (that is not compensated).
- You suffer from problems with the heart muscle, such as *cardiomyopathy*, *myocarditis*.
- You suffer from problems with nerve conduction of the heart muscle (atrioventricular block, severity grade 2 or 3).
- You suffer from a low heart rate (less than 55 beats per minute).
- You suffer from abnormal findings in the ECG test (prolonged QT interval, identifiable U waves).
- You have a first grade family relatives with congenital heart disease (QT syndrome).
- You have suffered in the past from severe cardiac arrhythmia problems (ventricular arrhythmias including a disorder called *torsade de pointes*).
- You suffer from low blood levels of potassium or magnesium.
- You are taking a medicine called *Budipine* or other medicines that can prolong the QT interval (see section on 'Drug Interactions').

Special warnings regarding the use of the medicine

Before and during treatment with Amandin 100 tablets, tell your physician if:

- You suffer from prostate gland enlargement.
- You suffer from increased intraocular pressure, such as closed-angle glaucoma.
- You suffer from kidney failure (in one of varying degrees of severity, please see details in section 3 'How should you use the medicine?').
- You suffer from states of agitation and confusion.
- You suffer from delirium syndromes or from psychosis (severe mental disorders).
- You are being treated with medicines containing memantine as the active ingredient; extra caution is required with these patients (see section on 'Drug Interactions').

Important Additional Information

In patients who have a heart pacemaker and whose QT interval cannot be accurately established, the attending physician (cardiologist) will use his judgment to decide whether treatment with **Amandin 100** tablets is possible.

In patients suffering from impaired kidney function, there might be elevated levels of the active ingredient in the body due to impaired clearance from the kidneys. This could cause symptoms identical to those caused by an overdose. Therefore, your physician will have to monitor and check the dose and the glomerular filtration rate during treatment with **Amandin 100** tablets (see section 3 'How should you use the medicine?').

For patients taking **Amandin 100** tablets who suffer from organic brain disease or convulsions special caution must be taken, as their condition could deteriorate.

If you experience strong heart palpitations, dizziness or momentary lapses of consciousness, stop using **Amandin 100** tablets immediately and consult with your physician so he can check your heart rhythm. If there is no arrhythmia, resumption of treatment with **Amandin 100** tablets may be possible, depending on the contraindications and drug interactions (see section 4 on 'Side Effects').

Do not stop taking **Amandin 100** tablets abruptly because in Parkinson's disease patients this can cause deterioration in their motor function or, in the worst case, complete loss of motor function.

Patients taking **Amandin 100** tablets along with neuroleptic medicines, used for treatment of mental disorders, can develop a life-threatening condition called malignant neuroleptic syndrome, if treatment with **Amandin 100** tablets is stopped abruptly. This condition is characterized by a sudden rise in body temperature, muscle rigidity and disorders of the autonomic nervous system.

Commonly seen in patients with Parkinson's disease are symptoms such as low blood pressure, drooling, sweating, rise in body temperature, feeling feverish, fluid retention and depression. They should be treated while taking into consideration side effects and possible drug interactions with **Amandin 100** tablets (see section 4 on 'Side Effects').

Consult with your physician in case you experience urinating problems.

Inform your physician if you, your family or your care givers notice that you are developing urges or an impulse to behave in an uncustomary manner, or that you are unable to resist an urge, impulse or temptation to perform certain actions that could be harmful to yourself or others. These side effects are called impulse Control Disorders, and may include such effects as addiction to gambling, excessive eating, wasting money, an abnormally powerful sex drive or an increased frequency of sexual thoughts and feelings. In this case, your physician may change the dose of your medicine, or stop its use completely.

In the event that you experience vision disturbances (such as blurred vision), refer to an ophthalmologist immediately.

Children

There is insufficient information about the use of **Amandin 100** tablets in children.

Elderly

Extra caution should be taken while using this medicine, especially by in patients suffering from agitation, confusion or delirium syndromes.

Tests and follow-up

Your physician will perform an ECG test for you (50 mm/s):

- Before treatment, and in the first and third week after starting the treatment.
- Before an increase in the dose and two weeks afterwards.
- Routinely, at least once per year.

Patients with a tendency to suffer from seizures (spasms and convulsions) or who have suffered from them in the past, as well as patients with cardiovascular disorders, must undergo periodic examinations by their physician during the course of treatment with **Amandin 100** tablets.

Drug interactions:

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell your physician or pharmacist. In particular, you should inform the physician or pharmacist if you are taking:

- Do not take **Amandin 100** tablets along with other medications that are known to be QT interval prolongation, such as:
 - Medicines for treatment of cardiac arrhythmias; Class IA medicines: quinidine, disopyramide, procainamide. **Class III medicines:** amiodarone and sotalol.
 - Antipsychotic medicines for the treatment of hallucinations, such as: thioridazine, chlorpromazine, haloperidol and pimozide.
- Certain medicines for the treatment of depression, tricyclic and tetracyclic antidepressants, such as: amitriptyline.
- Certain medicines for treatment of hay fever, antihistamine medications, such as: astemizole, terfenadine.
- Certain medicines for treatment of bacterial and fungal infections, antibiotics of the macrolide family, such as: erythromycin and clarithromycin.
- Certain medicines for treatment of bacterial infections, inhibitors of the gyrase enzyme, such as sparfloxacin.
- Certain medicines for treatment of fungal infections, such as drugs in the azole antimycotics group.
- Additional medicines such as: budipine, halofantrine, cotrimoxazole, pentamidine, cisapride or bepridil.

This list does not cover all possible interactions. Before using **Amandin 100** tablets in parallel with the use of additional medications, your physician will ensure that there are no additional interactions regarding QT interval prolongation.

- **Amandin 100** tablets can be taken along with additional medicines for the treatment of Parkinson's disease (there are no specific studies on the interactions between them), such as: levodopa, bromocriptine, trihexyphenidyl or medicines for the treatment of Alzheimer's disease such as memantine. In order to avoid side effects (such as mental reactions), the dosage of the medicines may need to be adjusted (see section 4, 'Side Effects').
- Treatment with the following medicines along with **Amandin 100** tablets may cause the following interactions:
 - Anticholinergic medicines: Intensification of the side effects of anticholinergic medicines (such as confusion or hallucinations) when used with additional medicines, such as: trihexyphenidyl, benzatropine, scopolamine, biperiden, orphenadrine and others.
 - Medicines that indirectly stimulate the sympathetic nervous system will cause intensification of the effect of **Amandin 100** tablets on the central nervous system.
 - Levodopa (a medicine for the treatment of Parkinson's disease) - the medicines have a synergistic therapeutic effect.
 - Memantine (a medicine for the treatment of Alzheimer's disease) - can intensify the therapeutic effect and the side effects of **Amandin 100** tablets.
 - Treatment in parallel with diuretic medicines such as hydrochlorothiazide or triamterene is liable to inhibit the release of the active ingredient amantadine hemisulphate and cause toxic blood levels, resulting in motor disorder, convulsions and confusion. Therefore, the use of **Amandin 100** tablets with medicines of this kind should be avoided. Note that this information may also be relevant for medicines that you have recently used.

Taking the medicine and food

There is no information available.

Use of the medicine and alcohol consumption

Do not consume alcohol while being treated with **Amandin 100** tablets, since it reduces alcohol tolerance.

Pregnancy and breastfeeding

Pregnancy

There is insufficient information about the use of Amandin 100 tablets during pregnancy. There have been reported cases of healthy children born to mothers who took the medicine, but there have also been reported cases of birth complications and defects. In animal studies the active ingredient of Amandin 100 tablets, amantadine hemisulphate, caused damage to the offspring of animals. The potential danger to humans is unknown.

The use of this medicine during pregnancy will be allowed only after your physician has determined that it is essential.

If you are taking this medicine during the first three months of pregnancy your physician will recommend an ultrasound examination.

If you are planning to become pregnant or suspect that you are pregnant, inform your physician immediately so that he can determine whether to continue treatment, stop treatment or switch to a different medicine.

Breastfeeding

The active ingredient, amantadine hemisulphate, passes into breast milk. If your physician decides that the treatment is necessary while you are breastfeeding, the baby must undergo monitoring examinations due to the risk of side effects such as skin rash, urinary retention, vomiting. Your physician may possibly instruct you to stop breastfeeding.

Driving and operating machines

Effects on concentration, alertness and the eye's ability to focus with respect to distances cannot be ruled out, in addition to other side effects in the treatment of Parkinson's syndrome. At the beginning of treatment (in addition to the limitations characteristic of the disease), there may be an impaired ability to drive and operate machines.

You might not be able to react sufficiently quickly and efficiently to unexpected or sudden events.

Consequently, you should not drive a car or any other vehicle, nor should you operate machines without consulting with a physician in advance.

Note that alcohol consumption can further decrease the ability to drive.

Important information on some of the ingredients of the medicine

This medicine contains **Orange Lake S (E110)**, which may cause allergic reactions.

This medicine contains lactose. If you have been told by your physician that you have an intolerance to some sugars, contact your physician before taking **Amandin 100** tablets.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to your physician's instructions. If you are not sure about the dosage or treatment regimen, consult your physician or pharmacist.

Do not switch between amantadine hemisulphate tablets and amantadine hydrochloride tablets.

Method of administration: Take **Amandin 100** tablets with a small amount of fluid, preferably during the morning or afternoon. Do not take the last dose of the day after 4 p.m. The duration of treatment will be determined by your physician according to the status of your illness and your response to the treatment. Do not stop the treatment without first consulting with your physician. The tablet can be split in two.

The dosage and treatment regimen will be determined by the physician only. The usual dosage is generally: During the first 4-7 days of treatment: one 100 mg tablet per day, after which the dosage will be increased by 100 mg (one tablet) once a week, up to the maintenance dosage. The effective dosage usually varies between 1-3 tablets twice per day (a dosage that varies between 200-600 mg of amantadine hemisulphate per day).

Adults: Specifically for those suffering from agitation, confusion or hallucinations, treatment should be started at a lower dosage.

If **Amandin 100** tablets are being taken along with additional medicines for the treatment of Parkinson's disease, your physician will adjust your dosage accordingly.

If you have been treated in the past with a PK-Merz infusion, your physician may begin treatment with **Amandin 100** tablets at a higher dosage.

Patients with renal impairment:

Your physician will adjust your dosage of **Amandin 100** tablets in accordance with your GFR values. (GFR is a measure of the body's filtration rate of blood plasma through your kidneys)

Do not exceed the recommended dose.

If you experience symptoms of severe poisoning, such as: nausea, vomiting, excitation, tremors, **lack of balance and lack of coordination of spatial movements (ataxia)**, blurred vision, sleepiness, depression, speech difficulties and seizures, refer to a physician or to the emergency room.

One case has been reported of a heart rhythm problem called malignant cardiac arrhythmia.

There have been observations of muscle spasms and cases ranging from confusion with hallucinations up to a state of coma in patients who took **Amandin 100** tablets with additional medicines for the treatment of Parkinson's disease.

There is no antidote for **Amandin 100** tablets. Therefore, in case of poisoning it is possible that gastric lavage or induction of vomiting will be performed in the emergency room. Blood filtering (hemodialysis) is not recommended in such cases.

Cases of life-threatening poisoning require intensive means of medical monitoring. The following procedures may be performed: provision of fluids, urinary acidification for the purpose of more rapid elimination of the medicine from the body, administration of sedatives, anti-convulsive measures and anti-arrhythmic (Lidocaine I.V.) can be also considered for treatment. For the treatment of neurotoxic symptoms - use of I.V. administration of Phosostigmine.

If necessary, the physician will perform an ECG test for you and will monitor conditions that might encourage arrhythmias, such as blood electrolyte imbalance (potassium or magnesium) or a slow heart rate.

If you have taken an overdose or if a child has accidentally swallowed the medicine, immediately refer to a physician or proceed to a hospital emergency room and bring the package of the medicine with you.

If you have forgotten to take the medicine at the required time, do not take a double dose. Take the next dose at the regular time and consult a physician.

Adhere to the treatment as recommended by your physician.

If you display intolerance to the medicine **do not stop the treatment with the medicine** or change the dosage even if your health status has improved without first consulting with your physician, as this could cause withdrawal symptoms and a deterioration in your condition.

Do not take medicines in the dark! Check the label and the dose each time 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, use of **Amandin 100** tablets may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Refer to a physician if you experience any of the following side effects:

Common side effects (effects that occur in more than one in ten users)

- Sleep disorders.
- Motor or mental agitation.
- Urinary retention in patients suffering from enlargement of the prostate gland.
- Hallucinations and paranoid delusions (cognitive and behavioral disorders), especially in adult patients with a tendency to hallucinate.

The frequency of these side effects may increase in patients taking **Amandin 100** tablets, who also take additional medicines for the treatment of Parkinson's disease (such as levodopa, bromocriptine) or for the treatment of Alzheimer's disease (memantine).

Additional common side effects (effects that occur in more than one in ten users)

- A skin reaction characteristic of **Amandin 100** called **LIVEDO RETICULARIS**, sometimes associated with accumulation of water in the ankle and lower leg area.
- Nausea.
- Dizziness.
- Dry mouth.
- Deregulations of blood circulation while standing up.

Uncommon side effects (effects that occur in 1-10 in 1,000 users)

- Blurred vision.

Rare side effects (effects that occur in 1-10 in 10,000 users)

- Blurred vision and temporary loss of visual acuity due to corneal edema - in such a case treatment with **Amandin 100** must be stopped and you should refer to an ophthalmologist immediately upon appearance of symptoms.
- Corneal lesions.
- Corneal swelling (corneal edema).
- Decrease in visual acuity.

Very rare side effects (effects that occur in less than one in 10,000 users)

- Changes in the blood (hematologic changes) such as leukopenia (very low white blood cell count) and thrombocytopenia (reduced blood platelet count).
- Heart rhythm disturbances such as ventricular tachycardia, ventricular fibrillation, **torsade de pointes** and QT prolongation. In most of these cases one of the following factors was in the background: overdose, administration in combination with other medicines or risk factors for arrhythmias (see section on 'Special warnings regarding use of the medicine').
- Increased photosensitivity, arrhythmias with increased heart rate.
- Epileptic fits (usually in patients who took a dose higher than that recommended by their physician).
- Muscle spasms and impaired sensory ability in the limbs.
- Suicide attempts have been reported in patients who were treated with **Amandin 100** tablets for other indications.
- Allergic reaction from the medicine's inactive ingredient Orange Lake S (E 110).

Side effects of unknown frequency

- Desire to behave unusually - a strong urge to behave in an exaggerated manner, unusual or increased sex drive, an uncontrollable drive to waste money and shop excessively, gorging food or eating compulsively (eating excessively even after satiation).

If one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, you should consult with your physician.

Reporting side effects:

Side effects can be reported to the Ministry of Health by clicking on the link "Report on Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

<https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants in order to prevent poisoning. Do not induce vomiting without explicitly instructed to do so by your physician.
- Do not use the medicine after the expiry date (exp. date) that appears on the external packaging. The expiry date refers to the last day of that month.
- Store at a temperature below 25°C.

6. ADDITIONAL INFORMATION

- In addition to the active ingredient amantadine - hemisulphate, the medicine also contains: Lactose monohydrate, microcrystalline cellulose, povidone (K 28/32), croscarmellose sodium, maize starch, talc, magnesium stearate (Ph. Eur.), polyacrylate dispersion 30%, titanium dioxide (E 171), orange lake S (E 110), macrogol 6000, hypromellose.
- What does the medicine look like and what are the contents of the package? Film coated tablets are round, orange and biconvex with a score on one side. Packaged in aluminum blister packs in packages containing 20, 30, 60, 100 tablets.
- Registration holder and address: Megapharm Ltd., P.O.B. 519, Hod Hasharon 4510501, Israel.
- Manufacturer and address: Neuraxpharm Arzneimittel GmbH, Elisabeth-Selbert-Straße 23, 40764 Langenfeld, Germany.
- This leaflet was checked and approved by the Ministry of Health in May 2019.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 162-30-35338