

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

The medicine is dispensed with a doctor's prescription only

Slenyto 1 mg Slenyto 5 mg Prolonged-release tablets

Active ingredient and its quantity per dosage unit:

Slenyto 1 mg, each prolonged-release tablet contains 1 mg melatonin.

Slenyto 5 mg, each prolonged-release tablet contains 5 mg melatonin.

Inactive and allergenic ingredients in the preparation: see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Further information".

- Read the leaflet carefully in its entirety before you/your child start using the medicine.

- This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

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

- The medicine is intended for children and adolescents aged 2 to 18 years of age.

1. WHAT IS THE MEDICINE INTENDED FOR?

Slenyto is intended for the treatment of insomnia (sleeplessness) in children and adolescents, aged 2 to 18 years old, with autism spectrum disorder (ASD) and/or Smith-Magenis syndrome, when a healthy sleeping routine is not helpful.

Therapeutic group: Medicines that affect the brain (psycholeptics), melatonin receptor agonist.

Slenyto is a medicine that contains the active ingredient melatonin. Melatonin is a hormone naturally produced by the body. Slenyto shortens the time it takes to fall asleep and lengthens the duration of sleep.

2. BEFORE USING THE MEDICINE

Do not use the medicine if you/your child is sensitive (allergic) to the active ingredient (melatonin), or to any of the additional ingredients contained in the medicine, which appear in section 6.

Special warnings regarding use of the medicine Before treatment with Slenyto, tell the doctor or the pharmacist if you/your child:

- has liver or kidney problems. Talk to your doctor before taking/giving Slenyto as its use is not recommended in such cases.
- suffers from an autoimmune disease [where the body is attacked by its own immune (defense) system]. Use of Slenyto in such cases is not recommended, since no studies have been conducted on Slenyto in people with autoimmune diseases. Talk to your doctor before taking/giving Slenyto as its use is not recommended in such cases.
- feels drowsy (see section below on "Driving and using machines").

Smoking

Smoking can increase the breakdown of melatonin by the liver, which may make this medicine less effective. Please tell your doctor if you/your child starts or stops smoking during treatment.

Children and adolescents

Do not give this medicine to children below in age of 2 years, as it has not been tested at these ages, and its effects are unknown.

Drug interactions

If you/your child is taking, or has recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist.

Particularly if you/your child is taking:

Taking Slenyto with the following medicines can increase the risk of side effects, or may affect the way that Slenyto or the other medicine works:

- fluvoxamine (used for the treatment of depression and obsessive compulsive disorder).
- methoxypsoralens (used to treat skin disorders, e.g., psoriasis).
- cimetidine (used to treat stomach problems, e.g., ulcers).
- quinolones, e.g., ciprofloxacin and norfloxacin and rifampicin (used to treat bacterial infections).
- estrogens (used as contraceptives or in hormone replacement therapy).
- carbamazepine (used to treat epilepsy).
- non-steroidal anti-inflammatory medicines, e.g., aspirin and ibuprofen (used to treat pain and inflammation). Avoid using these medicines, especially in the evening.
- beta-blockers (used to control blood pressure). Take these medicines in the morning.
- benzodiazepines and non-benzodiazepine hypnotic drugs such as zaleplon, zolpidem and zopiclone (used to induce sleep).
- thioridazine (used to treat schizophrenia).
- imipramine (used to treat depression).

Use of the medicine and food

Take the tablets after dinner, i.e., on a full stomach.

Use of the medicine and alcohol consumption

Do not drink alcohol before, during or after taking Slenyto, because alcohol weakens the effectiveness of the medicine.

Pregnancy, breastfeeding and fertility

If you/your daughter is pregnant, breastfeeding, think you/your daughter may be pregnant or is planning to become pregnant, ask your doctor for advice before taking this medicine.

Tell your doctor or pharmacist before using Slenyto if you or your daughter:

- is planning a pregnancy. In animal studies, melatonin was not found to have an effect on male and female fertility.
- is pregnant or might be pregnant. As a precautionary measure, it is preferable to avoid the use of melatonin during pregnancy.
- is breastfeeding or planning to breastfeed. It is possible that melatonin passes into breast milk, therefore, your doctor will decide whether you or your daughter should avoid breastfeeding while taking melatonin.

Driving and using machines

Do not drive or operate dangerous machines while using the medicine, as Slenyto may cause sleepiness. After taking this medicine, you/your child should not drive a vehicle, ride a bicycle, or use machines until the sleepiness has completely passed. If you/your child suffers from prolonged sleepiness, consult the doctor. Children should be warned against riding a bicycle or playing near the street, and the like.

Important information about some of the ingredients of the medicine

Slenyto contains lactose monohydrate, which may cause an allergic reaction in patients who are sensitive to lactose.

Slenyto 1 mg contains lactose monohydrate in each tablet that is equivalent to 8.32 mg lactose.

Slenyto 5 mg contains lactose monohydrate in each tablet that is equivalent to 8.86 mg lactose.

If you/your child has been told by the doctor that you have an intolerance to certain sugars, consult the doctor before starting treatment.

3. HOW TO USE THE MEDICINE?

• Always use the preparation according to the doctor's instructions.

• Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

• The dosage and treatment regimen will be determined by the doctor only.

The recommended dosage is generally:

The recommended starting dosage is 2 mg (two 1 mg tablets), once daily. If there is no improvement in your/your child's symptoms, your doctor may increase the dosage of Slenyto in order to find the most suitable dosage for you/your child. The maximum daily dosage that

you/your child will receive is 10 mg (two 5 mg tablets).

Do not exceed the recommended dosage.

Take Slenyto in the evening, 30 to 60 minutes before bedtime. Take the tablets after dinner, i.e., on a full stomach.

Method of administration – Slenyto is intended for oral use. **Do not halve, crush or chew! Swallow the tablets whole.** Halving, crushing and chewing damages the unique properties of the tablets, which means that they will not work properly.

The whole tablets can be put into food like yoghurt, orange juice or ice cream to help with swallowing them. If the tablets are mixed with these foods, they should be taken immediately and not left or stored, as this may affect the way the medicine works. If the tablets are mixed with any other type of food, the tablets may not work properly.

Duration of treatment – You/your child should be monitored by your/his doctor at regular intervals (recommended every 6 months) to check that Slenyto is still the right treatment for you/him.

If you/your child accidentally took a higher dosage, you/your child should refer to a doctor or pharmacist as soon as possible. Taking a higher dosage than recommended may cause you/your child to feel drowsy.

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

If you/your child forgot to take the medicine, it can be taken at bedtime that same night, but after this time, no other tablet should be taken before the next evening.

If you forgot to take this medicine at the required time, do not take a double dose to compensate for a forgotten dose.

If you/your child stops taking the medicine, talk to your/his doctor before stopping treatment with Slenyto.

Adhere to the treatment regimen as recommended by the doctor.

Do not take medicines in the dark! Check the label and the dose each time you/your child takes medicine. Wear glasses if you/your child needs them.

If you/your child has further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Slenyto 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.

Refer to a doctor in case of unexpected behavioral changes, such as aggressiveness, which may frequently occur (affect between 1 and 100 to 1 in 10 people). The doctor may want you/your child to stop taking this medicine.

Common side effects (effects that occur in 1-10 users in 100)

- Changes in mood
- Aggression
- Irritability
- Drowsiness
- Headache
- Sudden onset of sleep
- Swelling and inflammation of the sinuses accompanied by pain and blocked nose (sinusitis)
- Tiredness
- Hangover feeling

Uncommon side effects (effects that occur in 1-10 users in 1000)

- Depression
- Nightmares
- Agitation
- Stomach ache

Side effects of unknown frequency (reported following use in adults)

- Epileptic fits
- Visual impairment
- Breathlessness (dyspnea)
- Nose bleeds (epistaxis)
- Constipation
- Decreased appetite
- Swelling of the face
- Skin lesion
- Feeling abnormal
- Abnormal behavior
- Low levels of white blood cells (neutropenia)

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report 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://sideeffects.health.gov.il/>

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine, and all other medicines, should be stored in a safe place out of the reach and sight of children and/or infants, to avoid poisoning.

Do not induce vomiting unless explicitly instructed to do so by a doctor!

Do not use the medicine after the expiry date (exp. date) that appears on the package.

The expiry date refers to the last day of that month.

Storage conditions:

Do not store at a temperature above 30°C.

Do not dispose of medicines in the toilet or household waste bin.

Ask the pharmacist how to dispose of a medicine that is no longer needed, in order to protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Slenyto 1 mg

Lactose monohydrate, calcium hydrogen phosphate dihydrate, ammonio methacrylate copolymer type B (Eudragit RSPO®), talcum, sodium carboxymethylcellulose, silica colloidal anhydrous (Aerosil®), magnesium stearate, maltodextrin, dextrose monohydrate, lecithin, titanium dioxide, iron oxide red, iron oxide yellow. The tablet contains lactose monohydrate (see "Important information about some of the ingredients of the medicine" section).

Slenyto 5 mg

Lactose monohydrate, ammonio methacrylate copolymer type A (Eudragit RLPO®), calcium hydrogen phosphate dihydrate, sodium carboxymethylcellulose, silica colloidal anhydrous (Aerosil®), magnesium stearate, maltodextrin, dextrose monohydrate, lecithin, titanium dioxide, iron oxide yellow. The tablet contains lactose monohydrate (see "Important information about some of the ingredients of the medicine" section).

What the medicine looks like and the contents of the pack:

Slenyto 1 mg – Slenyto prolonged-release tablets 1 mg dosage are pink, film-coated, non-imprinted, round, biconvex, 3 mm-diameter tablets. Available in blister packs in a carton package containing 60 tablets.

Slenyto 5 mg – Slenyto prolonged-release tablets 5 mg dosage are yellow, film-coated, non-imprinted, round, biconvex, 3 mm-diameter tablets. Available in blister packs in a carton package containing 30 tablets.

Manufacturer and License holder and address: Neurim Pharmaceutical (1991) Ltd., Hanechoset 8, Tel Aviv, 6971000

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Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Slenyto 1 mg – 165-84-36331-00

Slenyto 5 mg – 165-85-36332-00