Patient Leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is sold only with a doctor's prescription

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved by the Ministry of Health in December 2014 and was updated in accordance with the Ministry of Health's directives on February 15, 2019

Circadin

Prolonged-release tablets

Composition:
Each tablet contains 2 mg melatonin
(Melatonin 2mg)

Inactive ingredients: See list in section 6 and also in the section "Important information about some of the medicine's ingredients".

- **Read the leaflet in its entirety before using the medicine**. This leaflet contains concise information about the medicine. If you have any further questions, please contact your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is similar to yours.
- The medicine is intended for adults over the age of 55.

1. What is the medicine intended for?

Melatonin, the active ingredient in Circadin, belongs to a group of natural hormones produced by the body.
Circadin is used for a short-term treatment of primary insomnia (sleeplessness, difficulty falling asleep or staying asleep or poor quality of sleep) in patients aged 55 or over.
Insomnia is defined as 'primary' when it is not the result of an identified cause, such as a medical, mental or environmental condition.
Therapeutic group: A hormone secreted by the body.

2. Before you use the medicine

Do not use this medicine if - you are sensitive (allergic) to the active ingredient or to any of the other ingredients of this medicine (a list of the inactive ingredients can be found in section 6).

Special warnings regarding the use of this medicine:
Before treatment with Circadin , tell your doctor if:

- You are pregnant or breastfeeding (see "Pregnancy and breastfeeding" section).
- You are suffering from liver or kidney disorders. Using Circadin is not recommended in these conditions since no studies on Circadin were conducted in people with liver or kidney diseases.
- You are suffering from intolerance to certain sugars.
- You are suffering from an autoimmune disease (a disease in which the body is attacked by its own immune system). Using Circadin is not recommended in these conditions since no studies on Circadin were conducted in people with autoimmune diseases.

Circadin may cause sleepiness and therefore may impair your ability to perform any activity requiring alertness, such as driving (see "Driving and using machinery" section).

Smoking may reduce Circadin's effect, since ingredients in the tobacco smoke may increase the breakdown of melatonin in the liver.

Do not administer the medicine to children 0 to 18 years old, since its effect on them has not been studied and is unknown.

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

- Fluvoxamine (for the treatment of depression and obsessive-compulsive disorder), psoralens (for the treatment of skin disorders such as psoriasis), Cimetidine (for the treatment of gastric ulcers), antibiotics from the Quinolone family and Rifampicin (for treating bacterial infections), estrogens (found in contraceptive pills or in medicines for hormone replacement therapy) and Carbamazepine (for the treatment of epilepsy).
- Drugs belonging to the family of adrenergic agonists or antagonists, such as certain medicines for controlling blood pressure by blood vessel contraction, medicines for reducing nasal congestion, antihypertensive medicines; medicines belonging to the family of opiate agonists or antagonists such as medicines for treating narcotic addiction, prostaglandin inhibitors (such as non-steroidal anti-inflammatory drugs), anti-depression medicines, Tryptophan and alcohol.
- Benzodiazepines and other sleep-inducing medicines that do not belong to the benzodiazepine group, such as Zaleplon, Zolpidem and Zopiclon.
- Thioridazine (for the treatment of schizophrenia) and Imipramine (for the treatment of depression).

Using the medicine and food
Circadin should be taken after a meal.

Using the medicine and alcohol consumption
Do not drink alcohol before, during or after taking Circadin, since alcohol reduces the medicine's efficacy.

Pregnancy and breastfeeding
Do not use Circadin if you are pregnant, if you think you are pregnant, if you are trying to become pregnant or if you are breastfeeding.

Consult a doctor or a pharmacist before using this drug.

Driving and use of machinery
Circadin might cause sleepiness. If this is how the medicine affects you, do not drive or operate dangerous machinery while using the medicine. If you suffer from persistent sleepiness, consult a doctor.

Important information about some of the medicine's ingredients
Circadin contains lactose monohydrate which may cause an allergic reaction in lactose-intolerant patients. Consult a doctor before starting treatment, if your doctor tells you that you are intolerant to certain sugars.

3. How to use this medicine?

Always use according to the doctor's instructions. If you are not sure, check with your doctor or pharmacist.
The dosage and manner of treatment will only be determined by the doctor. The standard dose is usually:
One tablet taken daily (2 mg), after food, 1-2 hours before bedtime. You may continue this dosage for a period of up to 13 weeks.
Do not exceed the recommended dose.

Instructions for use: Do not chew! The medicine should be swallowed whole after a meal. Do not cut in half or crush the tablet.

- **If you have accidentally taken a higher dosage** proceed to a doctor or a pharmacist as soon as possible. Exceeding the recommended dosage may make you feel drowsy**.** If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

- **If you forget to take the medicine,** take the tablet as soon as you remember, before going to sleep, or at the usual time of the next dose and then proceed as usual. Do not take a double dose.
- You should follow the treatment course as recommended by your doctor.
- **If you stop taking the medicine:** No harmful effect is known when treatment is discontinued suddenly or prematurely. There are no known withdrawal symptoms following end of treatment with Circadin.
- Do not take medicines in the dark! Check the label and the dose each time you take a medication. Wear glasses if you need them.

If you have further questions about using the medicine, consult a doctor or a pharmacist.

4. Side-effects

Like with any medicine, the use of Circadin may cause side effects in some patients. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.
Stop use and contact a doctor immediately if the following serious side effects appear:
Appear infrequently (frequency of up to 1:100 patients)

- Chest pain

Appear rarely (frequency of up to 1:1000 patients):

- Loss of consciousness or fainting
- Serious chest pain resulting from angina pectoris
- Palpitations
- Depression
- Vision disorders
- Blurred vision
- Disorientation
- Vertigo (dizziness)
- Presence of red blood cells in urine
- Reduced amount of white blood cells in the blood.
- Reduced amount of platelets in the blood, which increases the risk for bleeding or contusions
- Psoriasis

Contact a doctor if the following non-serious side effects appear:

Appear infrequently (frequency of up to 1:100 patients)

Irritability, nervousness, restlessness, insomnia, abnormal dreams, nightmares, anxiety, migraines, headaches, exhaustion, psychomotor hyperactivity (restlessness accompanied with increased activity), dizziness, fatigue, hypertension, upper abdominal pain, gastrointestinal disorders, mouth ulceration, dry mouth, nausea, hyperbilirubinaemia (a change in the composition of the blood which could cause yellowing of the skin or the eyes), dermatitis, night sweats, pruritus or rash, dry skin, limb pains, menopausal symptoms, weakness feeling, secretion of glucose or protein in urine, abnormal liver function tests and weight increase.

Appear rarely (frequency of up to 1:1000 patients):
Shingles (Herpes zoster, a viral disease), high levels of lipids in the blood, low levels of calcium in the blood, low levels of sodium in the blood, mood swings, aggression, nervousness, crying, stress symptoms, waking up early in the morning, increased libido, deteriorated mood, memory impairment, concentration disorders, dreaminess, restless legs syndrome, poor quality of sleep, pins and needles sensation, teary eyes, dizziness when standing up or sitting down, hot flashes, heartburn (reflux of acid from the stomach to the esophagus), gastrointestinal disorders, mouth blisters, tongue ulceration, abdominal pain, vomiting, abnormal sounds from the digestive system, gastric flatulence, increased saliva secretion, bad breath, abdominal discomfort, stomach disorders, gastritis, eczema, skin rash, inflammation on the skin of the hands, itchy rash, nail disorders, arthritis, muscle cramps, neck pain, muscle cramps at night, priapism that might be painful, prostate inflammation, fatigue, pain, thirst, larger than usual volume of urine, night urination, increased liver enzymes, abnormal results of blood electrolytes and laboratory tests.

Frequency not known (cannot be established from the available data):
Hypersensitivity reaction, swelling of mouth or tongue, swelling of the skin and abnormal milk secretion.
If one of the side effects aggravates, or when you suffer a side effect not mentioned in this leaflet, you should consult the doctor.
Side effects may be reported to the Ministry of Health by clicking the "Report Side Effects from Drug Treatment" found on the home page of the Ministry of Health's website (www.health. gov.il) which redirects to the online form for reporting side effects, or by accessing the link:
https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. How to store the medicine?

Avoid poisoning!
This medicine, and all other medicines, must be stored in a safe place out of the reach of children and/or infants, to avoid poisoning.
Do not induce vomiting unless explicitly instructed to do so by the doctor!

- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of the mentioned month.

Storage conditions:
Do not store above 25°C. Store in the original package in order to protect from light.
- Do not discard medications in the toilet or into residential waste cans. Ask the pharmacist how to discard unnecessary medications, in order to protect the environment.

6. Further information

- In addition to the active ingredient, this medicine also contains:
Ammonium methacrylate copolymer type B, calcium hydrogen phosphate dihydrate, lactose monohydrate, silica (colloidal anhydrous), talc and magnesium stearate.
Each tablet contains 80 mg lactose monohydrate (see "Important information about some of the medicine's ingredients" section).

How the medicine looks and what are the contents of the package: a tablet, round, double-concave, of a white to off-white color. The tablets come in a blister pack of 7, 20, 21 tablets or a box containing 2 blister packs of 15 tablets (30 tablets).
It is possible that not all package sizes are marketed.

The manufacturer and the registration owner and his address:
Neurim Pharmaceuticals (1991) Limited, HaBarzel St.27, Tel Aviv 6971039.
Marketed by Teva Pharmaceutical Industries Ltd., POB 3190 Petach Tikva

- Medicine registration number in the National Medicine Registry of the Ministry of Health: 139.92.31648
- For the sake of simplicity and ease of reading, this leaflet is worded in the masculine/feminine gender, but the medicine is intended for both genders.

References for leaflet escalations and modifications: EMA
approved patient leaflet, 14/08/2013