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EPAR summary for the public

Circadin

melatonin

This document is a summary of the European Public Assessment Report (EPAR) for Circadin. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Circadin.

What is Circadin?

Circadin is a medicine that contains the active substance melatonin. It is available as white prolonged-release tablets (2 mg). 'Prolonged-release' means that melatonin is released slowly from the tablet over a few hours.

What is Circadin used for?

Circadin is used on its own for the short-term treatment of primary insomnia (poor quality of sleep) in patients aged 55 years or over. 'Primary' means that the insomnia does not have any identified cause, including any medical, mental or environmental cause.

The medicine can only be obtained with a prescription.

How is Circadin used?

The recommended dose of Circadin is one tablet a day, taken one to two hours before bedtime and after food. This dose can be continued for up to 13 weeks.

How does Circadin work?

The active substance in Circadin, melatonin, is a naturally occurring hormone, which is normally produced by a gland in the brain called the pineal gland. Melatonin is involved in co-ordinating the body's sleep cycle by acting on cells in specific areas of the brain and helping to bring about sleep. Its



levels in the blood normally increase after the onset of darkness and peak in the middle of the night. Older people may produce less melatonin, leading to the development of insomnia. By replacing the hormone, Circadin increases blood levels of melatonin, helping them to sleep. Because Circadin tablets release melatonin slowly over a few hours, they mimic the natural production of melatonin in the body.

How has Circadin been studied?

Circadin has been compared with placebo (a dummy treatment) in three main studies involving a total of 681 patients aged over 55 years with primary insomnia. The main measure of effectiveness was the number of patients who reported a significant improvement in their quality of sleep and ability to function normally on the following day, after three weeks of treatment. The patients assessed the severity of their symptoms using a standard questionnaire.

An additional study compared the effects of Circadin and placebo for up to six months.

What benefit has Circadin shown during the studies?

Circadin was more effective than placebo at improving quality of sleep and the patients' ability to function normally on the following day. When the results of all three studies were looked at together, 32% of the patients taking Circadin (86 out of 265) reported a significant improvement in symptoms after three weeks, compared with 19% of those taking placebo (51 out of 272).

The additional study showed that Circadin was more effective than placebo for at least 13 weeks.

What is the risk associated with Circadin?

Side effects with Circadin are not common. However, the following side effects are seen in between 1 and 10 patients in 1,000: irritability, nervousness, restlessness, insomnia, abnormal dreams, anxiety, migraine, lethargy (lack of energy), psychomotor hyperactivity (restlessness with increased activity), dizziness, somnolence (sleepiness), hypertension (high blood pressure), abdominal pain (stomach ache), dyspepsia (heartburn), mouth ulcers, dry mouth, hyperbilirubinaemia (high blood levels of bilirubin, a breakdown product of red blood cells, which can cause yellowing of the skin and eyes), dermatitis (skin inflammation), night sweats, pruritus (itching), rash, dry skin, pain in the extremities (arms and legs), symptoms of the menopause, asthenia (weakness), chest pain, glycosuria (sugar in the urine), proteinuria (protein in the urine), abnormal liver function tests and increased weight. For the full list of all side effects reported with Circadin, see the Package Leaflet.

Circadin can cause drowsiness, so it should be used with caution if this could pose a risk to safety, including in people who need to drive or use machines. Patients should avoid alcohol before, during and after taking Circadin.

Circadin should not be used in people who may be hypersensitive (allergic) to melatonin or any of the other ingredients.

Why has Circadin been approved?

The CHMP decided that, although Circadin has only been shown to have a small effect in a relatively small number of patients, its benefits are greater than its risks. The Committee recommended that Circadin be given marketing authorisation.

Other information about Circadin:

The European Commission granted a marketing authorisation valid throughout the European Union for Circadin to Rad Neurim Pharmaceuticals EEC Limited on 29 June 2007. The marketing authorisation is valid for five years, after which it can be renewed.

The full EPAR for Circadin can be found [here](#). For more information about treatment with Circadin, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 05-2010.