Insomnia is the most common sleep disorder, occurring in 30 – 45% of adults. It is 1.5 times more likely to occur in women than in men.1

MELATONIN – MARKER FOR CIRCADIAN RHYTHMS
Melatonin is a naturally occurring hormone that is key to sleep and the sleep-wake cycle in humans and animals.6 In the body, melatonin is produced by the pineal gland in the brain when night falls. The retina detects failing light, and the level of melatonin gradually increases, reaching its peak in the middle of the night in natural circumstances.2

In the morning when plasma levels of melatonin decrease, sleep ends and wakefulness begins.6 Melatonin is not a sedative, but a sign of darkness or night-time, and is a cue for innate night-time behaviour. For example, in nocturnal animals, melatonin stimulates wakefulness.10

Studies have shown that when administered during the day, melatonin causes feelings of fatigue and drowsiness like those experienced when naturally preparing for sleep.5,6 These difficulties are of prime concern in older adults, who may already experience some decline in cognitive function due to natural ageing.7

Our circadian rhythm (or ‘body clock’) is influenced by melatonin, as it acts as a ‘cue’, anticipating sleep. It is also an important physiological regulator of the sleep-wake cycle.8

The rise in prevalence of sleep disorders associated with age is reflected by the decrease in melatonin levels that occur with age.12

In humans, melatonin induces heat loss, reduces arousal and related brain activity and delays production of cortisol, which increases blood pressure and blood sugar, in preparation for sleep.3 Studies have shown that when administered during the day, melatonin causes feelings of fatigue and drowsiness like those experienced when naturally preparing for sleep.

Melatonin excretion is much less for elderly than for young.8

Fig. 1: Position of the pineal gland in the brain

Fig. 2: Circadian rhythm

Fig. 3: Melatonin excretion is much lower for the elderly than for the young
Circadin® and the role of melatonin in sleep

ABOUT CIRCADIN®

Circadin® is a novel, first in class sustained-release melatonin tablet formulation, which releases melatonin and mimics the physiological pattern of melatonin secretion. This is one of the features that distinguish Circadin® from ordinary preparations of melatonin.13

MODE OF ACTION

Because of its novel formulation, Circadin® releases melatonin gradually over 8–10 hours thereby mimicking the body’s natural release of melatonin and resulting in the re-setting of natural circadian rhythms and the encouragement of natural, restorative sleep.14

Circadin® has been demonstrated to preserve the natural sleep architecture. In Fig 4, the dark line (baseline) represents natural deep sleep which is maintained by Circadin®, in contrast to the hypnotic, zolpidem.14

MOOD OF ACTION

Because of its novel formulation, Circadin® releases melatonin gradually over 8–10 hours thereby mimicking the body's natural release of melatonin and resulting in the re-setting of natural circadian rhythms and the encouragement of natural, restorative sleep.14

Circadin® is different from ordinary preparations of melatonin and is the first melatonin-containing prescription drug approved in the EU. Without the sustained-release matrix formulation, melatonin levels would peak and then rapidly fall due to short half-life (40–50 minutes) of melatonin, and this would not provide levels of melatonin throughout the sleeping period that mimic the natural profile and therefore would not reset the natural rhythms.14

Fig 5 compares the melatonin concentration in blood plasma over time seen with Circadin® and immediate-release melatonin.

Circadin® shortens sleep latency (time to get to sleep) but more importantly Circadin® has been shown to significantly improve sleep quality (see Fig 6) and morning alertness (the behaviour following awakening). These are the pre-conditions for normal daily performance and productivity, leading to better quality of life.15, 16, 17

These features distinguish Circadin® from other available treatments. Circadin® is indeed the first sleep agent to demonstrate improvements in quality of life.15, 16, 17

SAFETY AND TOLERABILITY

Unlike other sleep medications, Circadin® does not impair memory, daytime vigilance, or driving performance. Because Circadin® works via the natural sleep pathway, there are no rebound and withdrawal effects – the side effect profile is benign and there is no evidence of dependency.16

WHO CAN USE CIRCADIN®?

Circadin® is indicated as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients who are aged 55 or over.14

REFERENCES

14. Neurim, data on file
15. Neurim, data on file

Fig 4: In contrast to zolpidem, Circadin maintains natural deep sleep quality of life.15, 16, 17

Fig 5: Melatonin levels following administration of Circadin® versus IR melatonin

Circadin (n=168)
Placebo (n=165)

P=0.014
LSEQ= Leeds Sleep Evaluation Questionnaire

Mean change from baseline in QoS (LSEQ, mm)

Circadin (n=169)
Placebo

Fig 6: Significant improvement in quality of sleep, compared to placebo

Fig 2: Chemical structure of Circadin®