

FDA Approves a New, Nonnarcotic Sleep Aid

BY ALICIA AULT
Contributing Writer

The Food and Drug Administration has approved a new, nonnarcotic therapy for insomnia, eszopiclone. Most sleep aids are approved for only short-term use of a week to 10 days, but eszopiclone can be safely prescribed for longer, according to the FDA.

Formerly known as Estorra and now called Lunesta, eszopiclone is a nonbenzodiazepine hypnotic that is a pyrrolopyrazine derivative of the cyclopyrrolone class. It is manufactured and sold by Sepracor Inc. of Marlborough, Mass. The drug will be available in mid-January.

In early spring, the company plans to start a \$60 million print and broadcast direct-to-consumer advertising campaign, according to Jonae Barnes, a Sepracor spokeswoman.

Sepracor also plans to use its 1,250-person sales force to call on psychiatrists, primary care physicians, and hospitals, Ms. Barnes said.

The company sees huge market potential for the drug, noting that \$2.1 billion of prescription sleep aids are sold each year in the United States and that 100 million Americans have chronic or occasional insomnia.

The National Sleep Foundation found in its most recent annual poll in 2002 that al-

most 60% of adults have insomnia several nights a week or more.

Eszopiclone was studied in six phase III randomized, double-blind placebo trials, three of which were included in Sepracor's FDA approval package. The drug was superior to placebo in sleep latency and sleep maintenance for transient insomnia and superior in sleep latency and total sleep time in five 6-month studies in chronic insomnia. In two 2-week studies of patients aged 65-86, eszopiclone was also superior to placebo.

There was no major impact on memory or cognitive function in any of the studies, and only about 1% of patients on the highest dose—3 mg—experienced

withdrawal signs. In addition, there was very little rebound insomnia.

Patients who do not respond after 7-10 days of treatment may have an underlying psychiatric disorder, warns the label, which adds that the lowest possible effective dose should be used.

Eszopiclone will be available in 1-mg, 2-mg, and 3-mg tablets, and it will likely sell for \$3.70 a pill, according to Sepracor. The recommended dose is 2-3 mg for adults up to 65 years old and 2 mg for adults over age 65.

Eszopiclone is also in trials as an insomnia therapy for patients with depression, rheumatoid arthritis, perimenopause, and chronic insomnia. ■

Sleep and Attention Problems Often Coexist in Adults

BY DOUG BRUNK
San Diego Bureau

SEATTLE — Many adults who have obstructive sleep apnea or insomnia also have attention-deficit disorder as well as neuromuscular and psychiatric conditions, results from a detailed analysis suggest, according to Clifford G. Risk, M.D.

"The sleep specialist isn't done when he says, 'It's sleep apnea. Use continuous positive airway pressure,' or 'It's insomnia; take a sleeping pill,'" Dr. Risk remarked at a press briefing that was held during the annual meeting of the American College of Chest Physicians.

"He has to work out what the concurrent conditions are at the same time he's trying to improve the insomnia or sleep apnea," Dr. Risk explained during the briefing. "The assessment of patients with a sleep disorder and impaired daytime cognition may represent a complex interplay between the sleep disorder and comorbid dual diagnoses."

Dr. Risk and his associates at a sleep disorder center in Marlborough, Mass., evaluated 58 patients who had presented with sleep apnea or insomnia. The investigators administered a wide battery of standardized tests to assess the severity of obstructive sleep apnea, attention-deficit problems, depression, and insomnia.

All of the patients received treatment for their respective conditions, including continuous positive airway pressure (CPAP) treatment for obstructive sleep apnea, cognitive behavior therapy and/or hypnotic medication for insomnia, and psychiatric evaluation and possible medication for primary attention deficit disorder.

Of the 34 patients who were found to have sleep apnea, 16 had baseline Adult

Self-Report Scale (ASRS) symptom checklist scores that suggested moderate or severe impairment of attention. After CPAP treatment, 60% of these patients had substantially improved their attention scores.

"However, 40% continued to report serious attention deficits following treatment, and required further neuropsychiatric evaluation and specific interventions," reported Dr. Risk, who serves as director of the sleep disorder center.

Of the 24 patients who had insomnia, 54% had baseline ASRS scores that suggested moderate or severe impairment of attention.

Nine of these patients suffered from a primary muscular disorder, including fibromyalgia, chronic fatigue, multiple sclerosis, peripheral neuropathy, and postpolio syndrome.

In addition, 15 suffered from a primary psychological disorder, including depression, bipolar disorder, and anxiety, Dr. Risk said.

There were serious rheumatologic and neurologic diseases causing sleep disturbances in the patients who had insomnia, Dr. Risk said.

"If they slept through the night, we found that they were mostly in stage 1 or 2 sleep. They never got to restorative sleep stage 3 or 4. So they had a lack of restorative sleep due to a light or fragmented sleep," he added.

He and his associates have begun trying to identify reversible risk factors in each patient with insomnia to design specific interventions that may be of benefit.

Dr. Risk concluded that a multidisciplinary approach to treating patients with sleep difficulties "may be necessary in order to isolate additional comorbidities that are causing persistent impairment." ■

Behavioral Therapy Can Help To Put Sleep Problems to Rest

BY NANCY A. MELVILLE
Contributing Writer

LAS VEGAS — Behavioral therapies can break the habits and misconceptions that cause chronic insomnia, provided that psychiatric or medical problems are not at play, Dr. Bashir Chaudhary said at a meeting on primary care sponsored by the Southern Medical Association.

Among patients with chronic insomnia (lasting longer than 6 months), the cause is psychiatric in about 35% of cases, psychophysiological in 15%, related to use of drugs or alcohol in 12%, restless legs syndrome in 12%, and sleep apnea in 6%, said Dr. Chaudhary, emeritus professor of medicine at the Medical College of Georgia, Augusta, and director of the Georgia Sleep Center at the college.

In the absence of medical and psychiatric problems, chronic insomnia may be caused by psychophysiological factors, in which the patients' anxiety about lack of sleep becomes a big part of the problem.

"These are people who are stressed about sleep all day long," Dr. Chaudhary said. "They become obsessively worried about it." Such patients often have conditioned themselves to experience insomnia in their own sleeping environment; if they sleep elsewhere—in another room or at another place—they often have no problem falling or staying asleep.

Other forms of insomnia can typically be swiftly corrected by addressing direct causes, but psychophysiological cases can often take more effort on the part of the pa-

tient and the physician. "Most of the time I spend in cognitive therapy is with these patients," he said, adding that behavioral techniques and lifestyle guidelines can be effective.

One behavioral therapy approach is stimulus control, which aims to decrease cues for nighttime arousals and focus on cues that help induce sleep. Some key recommendations include:

- ▶ Go to bed only when sleepy.
- ▶ Get out of bed if not asleep within 20 minutes.
- ▶ Wake up at the same time every day. "This is the most important," he said.
- ▶ Do not take naps.

Sleep restriction therapy is another effective technique. Dr. Chaudhary advised asking patients how much sleep they get during a typical night, adding about 2 hours to that, and having them restrict themselves to that length of time in bed. Patients should be instructed to wake up at their regular time, but to go to bed at the time that would provide the allocated amount of sleep. If, after several weeks, patients report getting good quality sleep at least 85% of the night, then add increments of about 15 minutes. But if they are not getting the 85%, then further restrict the sleep time.

A metaanalysis of studies shows that nonpharmacologic therapies are highly successful in insomnia, with techniques improving sleep onset in 81% of cases, reducing sleep latency by 35 minutes, and resulting in 74% extension of sleep maintenance (*Am. J. Psychiatry* 1994;151:1172-80). ■

Ten Commandments of Good Sleep

As part of his cognitive therapy, Dr. Chaudhary offers patients his "Ten Commandments of Good Sleep":

1. Thou shalt not stay in bed too long.
2. Thou shalt avoid daytime naps.
3. Thou shalt maintain the circadian cycle.
4. Thou shalt avoid stimulants after lunch.

5. Thou shalt not take a "toddy" before bedtime.

6. Thou shalt not go to bed hungry.

7. Thou shalt not smoke.

8. Thou shalt exercise regularly.

9. Thou shalt keep the bedroom at a comfortable temperature.

10. Thou shalt keep the noise down.