Ramelteon Benefits Shift Workers With Insomnia

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ORLANDO — Ramelteon is effective for a subset of patients with insomnia, according to a presentation at a psychopharmacology congress sponsored by the Neuroscience Education Institute. In addition, because the agent works on melatonin receptors, a potential off-label use is for patients with shift-work disorder.

Ramelteon (Rozerem, Takeda Pharmaceuticals) targets the melatonin receptors MT1 and MT2. The agent is approximately 10 times more potent than melatonin. Other approved drugs promote sleep by increasing γ-aminobutyric acid (GABA), which is normally released by the suprachiasmatic nucleus in the brain.

"Ramelteon is a very interesting drug. It is the first on the market for sleep that does not work on the GABA system," Dr. Wallace B. Mendelson said. The melatonin receptor agonist is a very short acting drug with a half-life of 1-2 hours. "It is very potent for helping people fall asleep but not as effective for those who wake up early. So it's for a subset of patients."

The Food and Drug Administration approved ramelteon for treatment of insomnia characterized by difficulty with sleep onset. "It is not a DEA-classified substance, only a hypnotic without potential for dependence," said Dr. Mendelson, psychopharmacology consultant for many pharmaceutical companies, including Takeda Pharmaceuticals North America Inc.

A delay to peak therapeutic effect is another distinction of ramelteon, compared with benzodiazepines and newer, nonbenzodiazepine GABA agonists such as zolpidem (Ambien, Sanofi-Aventis) or eszopiclone (Lunesta, Sepracor). Dr. Mendelson said, "It can take up to a week for full effect, so caution patients that they may not feel tired right away." Dr. Mendelson is also a consultant, an advisor, and on the speakers' bureau for Sanofi-Aventis and Sepracor Inc.

People with shift-work sleep disorder can experience excessive daytime sleepiness because their body rhythm stays the same but the world changes around them, Dr. Mendelson said. "No one knows why some people are more susceptible to this, except it is harder to adapt to nighttime shift work as you get older."

Pharmacotherapy with a sleep aid might be sufficient for a shift worker who complains only of sleepiness or trouble going off to sleep, Dr. Mendelson said. However, "if they are having trouble with both sleep and waking, it might make sense to try to help them shift to the new time. One way is to use melatonin."

Exogenous melatonin can shift circadian rhythms. Melatonin taken in the evening can shift a person's circadian rhythm earlier while melatonin in the morning can shift it later, he said.

"I have a real issue with the quality and standardization of melatonin. It's not consistent, which is why I prefer a drug like Rozerem," Dr. Mendelson said. "Rozerem is not indicated for this, but some research indicates it can shift circadian rhythm with off-label use similar to melatonin."

Another option for circadian rhythm adjustment is bright light therapy. "I like bright light therapy because it's more benign—but it works the opposite." In the morning, the therapy pushes circadian rhythm phase earlier, and at night, it pushes it later.

Insomnia rarely occurs alone, Dr. Mendelson said. "About 80% of insomnia patients you see have some other disorder. The old name was secondary insomnia. Us sleep guys are now calling this comorbid insomnia."

Ramelteon might be an appropriate choice for patients with sleep apnea, Dr. Mendelson said. A significant minority of sleep apnea will present with insomnia as the primary complaint. "We need to carefully diagnose because most of the agents we prescribe for insomnia can make sleep apnea worse, except ramelteon or the tricyclic antidepressants."

The probability of diagnosing a psychiatric disorder increases among patients who complain of insomnia (Sleep Med. 2005;6:549-53). In this study, a survey of 200 general hospital patients indicated 57% reported insomnia and 50% reported at least one psychiatric disorder.

Insomnia can play a major role in several psychiatric illnesses, especially depression, Dr. Mendelson said. "Targeting insomnia with sleep aids and behavioral therapy can improve outcomes." Insomnia may also signal depression onset. "On average, 41% of people will have insomnia preceding depression." ■