Sleep Drugs Found Only Mildly Effective, but Wildly Popular

By STEPHANIE SAUL

Your dreams miss you.

Or so says a television commercial for Rozerem, the sleeping pill. In the commercial, the dreams involve Abraham Lincoln, a beaver and a deep-sea diver.

Not the stuff most dreams are made of. But if the unusual pitch makes you want to try Rozerem, consider that it costs about $3.50 a pill; gets you to sleep 7 to 16 minutes faster than a placebo, or fake pill; and increases total sleep time 11 to 19 minutes, according to an analysis last year.

If those numbers send you out to buy another brand, consider this, as well: Sleeping pills in general do not greatly improve sleep for the average person.

American consumers spend $4.5 billion a year for sleep medications. Their popularity may lie in a mystery that confounds researchers. Many people who take them think they work far better than laboratory measurements show they do.

An analysis of sleeping pill studies found that when people were monitored in the lab, newer drugs like Ambien, Lunesta and Sonata worked better than fake pills. But the results were not overwhelming, said the analysis, which was published this year and financed by the National Institutes of Health. The analysis said that viewed as a group, the pills reduced the average time to go to sleep 12.8 minutes compared with fake pills, and increased total sleep time 11.4 minutes. The drug makers point to individual studies with better results.

Subjects who took older drugs like Halcion and Restoril fell asleep 10 minutes faster and slept 32 minutes longer than the placebo group. Paradoxically, when subjects were asked how well they slept, they reported better results, 52 extra minutes of sleep with the older drugs and 32 minutes with the newer drugs.

“People seem to be getting a lot of relief from sleeping pills, but does getting 25 minutes of sleep really give you all that relief?” asked Dr. Wallace B. Mendelson, the former director of a sleep disorders unit at the University of Chicago. “A bigger aspect of this is that they change a person’s perception of their state of consciousness.”

Dr. Mendelson is semiretired and is a consultant for pharmaceutical companies.

Dr. Karl Doghramji, a sleep expert at Thomas Jefferson University in Philadelphia, agreed. “Sleeping pills do not increase sleep time dramatically, nor do they decrease wake time dramatically,” he said. “Despite those facts, we do find patients who, when they take them, have a high level of satisfaction.” Dr. Doghramji has disclosed in the past that he is a consultant to pharmaceutical companies.
Most sleeping pills work on the same brain receptors as drugs to treat anxiety. By reducing anxiety, the pills may make people worry less about not going to sleep. So they feel better.

Another theory about the discrepancy between measured sleep and perceived sleep involves a condition called anterograde amnesia. While under the influence of most sleep medications, people have trouble forming memories. When they wake up, they may simply forget they had trouble sleeping.

“If you forget how long you lay in bed tossing and turning, in some ways that’s just as good as sleeping,” said Dr. Gary S. Richardson, a sleep disorders specialist at Henry Ford Hospital in Detroit who is a consultant and speaker for pharmaceutical companies and has conducted industry-sponsored research.

Sleep, after all, causes a natural state similar to amnesia, one reason toddlers often forget their violent nightmares by the next morning. If you stay in bed, as most people taking sleeping pills do, amnesia is not a bad thing.

Even some people who sleepwalked while taking Ambien, which was implicated in cases of odd, sometimes dangerous behavior while sleeping, believed they were having a good night’s sleep. Rosemary Eckley, a graphic artist in New London, Wis., said she thought she was sleeping well on Ambien but woke to find her wrist broken, apparently in a fall while sleepwalking, she wrote in an e-mail exchange.

Reports of sleep-eating and sleep-driving on Ambien are reminiscent of problems nearly 20 years ago with Halcion. Some people who took that drug to sleep on airplanes developed a condition known as traveler’s amnesia. They landed at their destinations, then got lost or forgot where they were, prompting the authorities in several countries to withdraw Halcion from the market.

Reports show that Ambien and similar drugs, advertised as safer than benzodiazepines like Halcion, can cause similar problems. The reports prompted the Food and Drug Administration to ask manufacturers to develop warning guides for distribution with virtually all sleep drugs. Despite such problems, most specialists say sleeping pills are generally safe. Dr. Mark W. Mahowald, director of the Minnesota Regional Sleep Disorders Center, which is involved in documenting cases of sleep-eating under the influence of Ambien, said serious side effects were rare and should not discourage the use of the pills.

The class of drugs known as nonbenzodiazepines, sometimes called “Z” drugs, includes Ambien, Lunesta and Sonata. Ambien and its generic equivalent, zolpidem, are the most widely used, together accounting for 40 percent of the market.

Newer drugs like Lunesta and Ambien CR, a controlled-release formula, cost about $4 a pill. Zolpidem recently sold for $2 a pill on walgreens.com.

Of the three drugs in the class, Sonata, which also retails for about $3.50 a pill, remains in the body the shortest time and, therefore, is normally used by people who have trouble falling asleep but no problem staying asleep. The advocacy organization Public Citizen’s Health Research Group says its benefits are so minimal it should not be used.

King Pharmaceuticals, the maker of Sonata, did not respond to several messages seeking comment.

A study by an Oregon State University group that reviews the safety and effectiveness of drugs found that
Lunesta offered little benefit over generic Ambien or older benzodiazepines, but cost more. Jonae Barnes, a spokeswoman for Lunesta’s maker, Sepracor, said the company strongly disagreed and added that the Oregon group did not adequately consider waking time after falling asleep, an area in which Lunesta performed better.

Users also sometimes report that Lunesta leaves a bad taste in their mouths, according to studies of the drug.

Dr. Mahowald said the older drugs, including Halcion, also known as triazolam, offered better value than the newer ones.

“We tend to use the old benzodiazepines,” he said of his practice. “They appear to be as effective as some of the newer ones, and they’re infinitely less expensive.” Dr. Mahowald said that his center participated in industry-sponsored clinical research, but that he did not personally work as a consultant or adviser to pharmaceutical companies.

Such drugs, which include flurazepam, brand name Dalmane, and temazepam, Restoril, sell in generic versions for 30 to 50 cents each.

Another inexpensive alternative, and one of the most widely used sleep medications in this country, is the antidepressant trazodone. It works well in many patients, but some people say it leaves them groggy the next day, according to Dr. Daniel Carlat, a psychiatrist in Newburyport, Mass., who publishes The Carlat Psychiatry Report and declines industry financing. In men, trazodone has been linked to rare cases of priapism, prolonged and painful erections.

Some patients who fear using sleeping pills turn to over-the-counter remedies like Tylenol PM and Advil PM. Those contain the painkillers acetaminophen and ibuprofen combined with an antihistamine, diphenhydramine, the ingredient in the allergy medication Benadryl.

Antihistamines are known to make people sleepy, but there is little evidence that they improve sleep. They can also cause next-day sedation that impairs driving, as well as racing heartbeat and constipation. The Medical Letter, which reviews drugs, recommends against using antihistamines for sleep. Some doctors say users of Tylenol PM may be taking acetaminophen they do not need. Acetaminophen overdoses can cause liver failure.

Rozerem, with its unusual advertising campaign, has at least one benefit over other medications. Because it works by a different mechanism from the others, it is not a controlled substance and apparently does not affect the ability to form memories. It may be the sleeping pill of choice for elderly people who have trouble falling asleep, but suffer memory problems.

Still, researchers and drug companies have yet to find a holy grail. “The problem is, there is no ideal hypnotic,” said Dr. Manisha Witmans, a sleep medicine specialist at the University of Alberta’s Evidence-Based Practice Center. “The magic pill for sleep has not been invented yet.”