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Desperate Families Embrace Unapproved Alzheimer Drug

By GINA KOLATA

Charles Baron watched for eight years as his wife, Betty, once lively and vibrant, a leader in her St. Louis community, slipped away, lost to the ravages of Alzheimer's disease. He tried everything to slow her decline — prescription drugs, nutritional supplements, diet, exercise.

"We tried everything that the doctors have been kind enough to say is not going to harm us," Mr. Baron said. But his efforts were of little avail. At 79, Mrs. Baron was on a steady downhill course. She still lived at home, but Mr. Baron relied on full-time help to care for her.

Then, in early April, Mr. Baron was listening to the radio and heard a news report about an Alzheimer's drug, memantine. The drug blocks a brain chemical, glutamate, which has been implicated in nerve cell death. A new study found that it seemed to have a modest effect in alleviating the symptoms of advanced Alzheimer's disease.

It is not a cure; it does not reverse the disease. And, for now, it is not sold in this country. Forest Laboratories, which has licensed it, has applied to the Food and Drug Administration to market it and does not expect to hear anything until fall. But that, Mr. Baron soon learned, was not an obstacle. The drug is sold in Europe, and the F.D.A. generally allows patients to import unapproved drugs for their personal use if there is no approved treatment for their condition and if they can supply the name and address of a doctor who will supervise the treatment. And there are plenty of Internet companies ready to fill the demand.

When Mr. Baron telephoned Forest, the company gave him three places to call, two in Europe and one in the United States. He chose the one in this country, GlobalRx, persuaded his wife's doctor to write a prescription, and sent in his order. Soon, the drug arrived in the mail and Betty Baron began taking it.

Over the past few months, Internet companies said, demand for the drug has surged. GlobalRx, which has just four full-time employees, says it had 150 memantine clients a few months ago. Now, with about 600, it says it cannot handle any more orders.

A British company, International Antiaging Systems, which will ship the drug even without a doctor's order, says that until recently it was supplying 50 patients a month. Now it is supplying about 500, most of whom are in the United States. The families pay for memantine out of pocket, typically $150 to $175 a month, plus about $60 for express delivery.

The phenomenon has taken Alzheimer experts by surprise. Family members of Alzheimer patients are often elderly, deferential to doctors, cautious and respectful of the Food and Drug Administration. But they say they have little choice — they feel that memantine offers hope, however small, in improving

symptoms of patients in the later stages of the disease, possibly helping those who are on the cusp of going to a nursing home, losing their ability to walk or talk, to bathe or even to watch television.

"This really has our heads spinning," said Dr. Steven DeKosky, who directs the University of Pittsburgh's Alzheimer's Disease Research Center.

He and others agonize over what to do. As researchers, they respect the F.D.A.'s strict demands that drugs be shown to be both safe and efficacious before they are approved. They also know too well that some drugs that seemed promising emerged as useless, or even dangerous, when subjected to the agency's scrutiny. Yet they see the anguish of family members who are desperate for something to slow the progress of the degenerative brain disease.

"We are all conflicted about this," said Dr. Ronald Petersen, director of the Mayo Clinic's Alzheimer's Disease Research Center in Rochester, Minn. "We want to help our patients and not endanger them, and at the same time we have a moral and ethical obligation to follow the F.D.A.'s guideline."

Some experts, like Dr. Lennart Mucke, a neurologist at the University of California at San Francisco, are uncomfortable with the imports of memantine and turn down patients' requests for help getting the drug.

"I totally understand how one would grasp for anything that looks promising," Dr. Mucke said. "But when it comes to drugs, we really have to make sure we do no harm and that we follow the guidelines that have been established."

He worries in particular about the precedent that is being established. "Everyone who believes that something should be on the market will be importing it," he said. "We can't allow that to happen."

Others, like Dr. John Morris, director of the Alzheimer's Disease Research Center at Washington University in St. Louis, have told families how to get the drug.

"Alzheimer's families are desperate for anything," Dr. Morris said. "I think it is justified to seek it out. It may not help, but I am willing to gamble that it may not hurt. Despite that, I don't prescribe it. I am pretty conservative and I am still holding out until the drug is approved by the F.D.A."

Yet while many drugs are sold over the Internet, the sale of memantine has a poignant twist — because of their disease, the people taking it often cannot say whether they want to risk it or not. "It's one thing to say `I'll take my chances on this drug that hasn't been approved,' and it's another thing to say `I'll give it to my mother,' " Dr. DeKosky said.

Family members of Alzheimer patients say they hear about memantine in support groups or from their doctors, their friends or the Alzheimer's Association's Web page. Many noticed the study, published in The New England Journal of Medicine on April 3, concluding that memantine might help slow the declining functions in patients with moderate to severe disease and reporting no significant side effects. And many discover that memantine has been used in Germany for years and that many doctors there consider it safe.

The study was led by Dr. Barry Reisberg of the New York University School of Medicine. He said he had urged Merz Pharmaceuticals, a German company that

owns the rights to the drug, to study the effects of memantine in patients with more advanced cases of the disease.

The company, Dr. Reisberg said, hesitated at first, saying it had limited money. "They kept saying, `We're Merz, not Merck,' " he recalled, but eventually Merz supported a study involving 252 patients who took memantine or a placebo for 28 weeks. The disease progressed at a slightly slower rate in those taking the drug, researchers concluded.

Still, Alzheimer experts in the United States remain cautious.

"It's going to be useful because it's a different drug, it has a different mechanism of action" than the three drugs on the market for mild to moderate disease, Dr. Petersen said. "I don't think it's a home run. I think its effects are pretty modest."

Some family members say they do not have the luxury of waiting.

A St. Louis woman, who asked not to be identified because her husband, who has Alzheimer's disease, is a private person and would be mortified if he knew his condition was being publicly discussed, clings to the sweet moments when she sees glimpses of the man he once was. These days, he cannot carry on a conversation, he cannot take a shower by himself, he cannot always stand up, and he spends most of the day dozing. But, she said, the other day he removed a piece of the chocolate coating on an ice cream bar and put it aside for her, as he used to do before he became ill. "This is for you," he told his wife.

She got a prescription from her husband's doctor and has ordered memantine, hoping that it will give her more of those moments, and maybe even reverse the disease. "If we would just get back to where we were a year ago," she said.

David Giere and his wife, Linda, got the dreadful news that she had Alzheimer's disease during Christmas week of 2001. They had gone to the Mayo Clinic to find out what was wrong with Mrs. Giere. At age 46, she seemed much too young to have Alzheimer's but had been losing her memory, was getting lost driving on familiar routes, and was finding herself unable to prepare her favorite recipes. "Meals got simpler and simpler," Mr. Giere said. "The Thanksgiving meal was a turkey; there were no side dishes."

The Gieres wept as they drove home from the Mayo Clinic to their home in Morrison, Colo., and their 7-year-old twin daughters. Mrs. Giere's disease, her husband said, has progressed since then. He asked Dr. Petersen about memantine. The doctor said that he would not write him a prescription but that in Mrs. Giere's situation, given that she was young and healthy, and that the drug seemed safe, it might be reasonable to try it. But he cautioned that its long-term safety was still unknown.

After an intensive effort to persuade Mrs. Giere's local doctor to go ahead, Mr. Giere got a prescription.

In February, Mr. Giere obtained memantine from a Canadian pharmacy that gets it from Europe. He is not sure whether it is helping, but Mrs. Giere is optimistic. "She keeps saying, `Look, I'm coming back,' " Mr. Giere said. It was difficult, he

added, to do an end run around the F.D.A.'s rigorous scrutiny of the drug's safety and efficacy.

Mr. Giere says he believes that for society, it is important to have regulatory agencies and it is destructive to ignore them. But he said he had to think of his family. "For Linda, the alternative is just to let the disease progress," Mr. Giere said.

As for Betty Baron, her husband is not sure what to think. At first, he said, she seemed much better with memantine and he saw glimpses of her old sparkle. But in a recent telephone interview, he said: "I have had a bit of concern in the last several days. There seems to be an increased drowsiness, a lengthening of her periods of sleep. There is a withdrawal from this engaged person she had become."

"But this is an up and down process," he noted. "I decided we should back off a bit, so I backed down to half a pill twice a day rather than a whole pill. And I will call the doctor."