

Alzheimer's medications, milestones and disease management

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Alzheimer's disease and the urgent need for more effective treatments

have been making headlines this year, with the FDA approving limited use of a new drug for the first time in nearly two decades. We recently sat down with Lon Schneider, MD, Della Martin chair in psychiatry and neuroscience at the Keck School of Medicine of USC and the director of the California Alzheimer's Disease Center at USC, to discuss the role of medication in Alzheimer's treatment.

Q: What are currently the best ways to medically manage the disease?

A: It's a complicated question. There's a saying you hear in the field: "If you've seen one person with Alzheimer's...you've seen one person with Alzheimer's." What it means is the disease is multidetermined and complex, so therapeutic approaches should be personalized and multi-domained—involving not just medications, but also cognitive training, social interventions and attention to diet and exercise. A combination of these approaches has been shown to stabilize Alzheimer's patients and delay disease progression for those experiencing its early stages.

Q: Can medications be effective in mitigating behavioral symptoms of Alzheimer's?

A: Many people with dementia have behavioral symptoms such as anxiety, agitation and apathy—a lack of motivation to initiate or sustain activities. Some may develop actual delusions, where they misperceive what is happening around them and can become accusatory or particularly resistant.

For those symptoms, antidepressants, and occasionally anti-anxiety medications, have been used. Many people have also likely heard of another class of medication, known as antipsychotics, used in this context; a most common example is risperidone. It has been getting

considerable attention in light of concerns that it may be misused.

Q: Is it being misused?

A: Unfortunately, antipsychotics are often used—especially in nursing homes—to try to control a resident's agitation, anxiety, hostility or negativistic or uncooperative behaviors when non-drug interventions are called for but the staff don't have the skill or the time. This type of medication inhibits behavior, can cause body stiffness, drooling and difficulty walking and swallowing, and patients often become bed bound or sit all day. They used to be called "chemical restraints." There has been ongoing research to find better and safer non-drug and drug approaches to agitation in people with dementia.

Q: Are the drugs specifically approved for treating Alzheimer's—including the newest one greenlit by the FDA—considered to be effective?

A: Until this past June, there were two classes of drugs approved by the FDA and frequently used. Cholinesterase inhibitors, like Aricept and Exelon, are the most common. Then there's Namenda, which is a glutamate regulator. These medications may help a substantial number of people stabilize or improve cognition and function for a period of time.

In June, the FDA granted accelerated approval for a new medicine, called aducanumab (brand name Aduhelm). It's a monoclonal antibody and has demonstrated an ability to reduce amyloid plaques, which are one of the key pathological features we see in the brains of Alzheimer's patients. The antibody, which needs to be given monthly by intravenous infusion, didn't actually show evidence of improving or lessening decline in cognition or overall function, but the FDA felt the reduction in plaques alone might be a predictor of future benefit.

Q: How has the medical community responded to the FDA's decision?

A: It has generated significant discussion and controversy. In addition to aducanumab's uncertain effectiveness, the drug may cause swelling of the brain, known as edema, and very small hemorrhages in some patients, due to the disruption of the blood-brain barrier near the amyloid plaques. This is usually reversible and often is without symptoms. And the cost of treatment—approximately \$56,000 per year—is out of many people's reach. Even if Medicare agrees to cover it, the 20% copay still will be a serious burden for most people. Yet, some physician-specialists are more positive about the drug's prospects, feeling that reducing plaques may be central to defeating this disease.

Q: Are there other potential Alzheimer's drugs in the pipeline?

A: Yes—there are a number in late-stage development right now. Three of them, donanemab, lecanemab and gantenerumab, are in Phase III trials and will be finishing their studies at the end of 2022. Like aducanumab, these [monoclonal antibodies](#) also reduce amyloid plaques. The question is whether they'll show clinical benefit, and we won't know the answers until the clinical trials are completed.

Q: Where is the field moving in terms of research?

A: Right here at USC, scientists are investigating a number of small molecules, including those focused on reducing abnormal tau proteins, a second defining feature of Alzheimer's. We're also looking at molecules, like omega-3 fatty acids, that can affect other metabolic processes and can alter the metabolism of neurons of people with Alzheimer's. And we're finding ways to target the blood brain barrier, inflammation

around neurons, and to support cells in the brain called microglia, housekeeping cells that serve as an important, active immune defense. Another exciting area of research is prevention studies. We're working to identify people who may have the pathology of Alzheimer's but don't have symptoms and might never get them. This may give us a window into stopping the disease before it starts.

Provided by University of Southern California

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