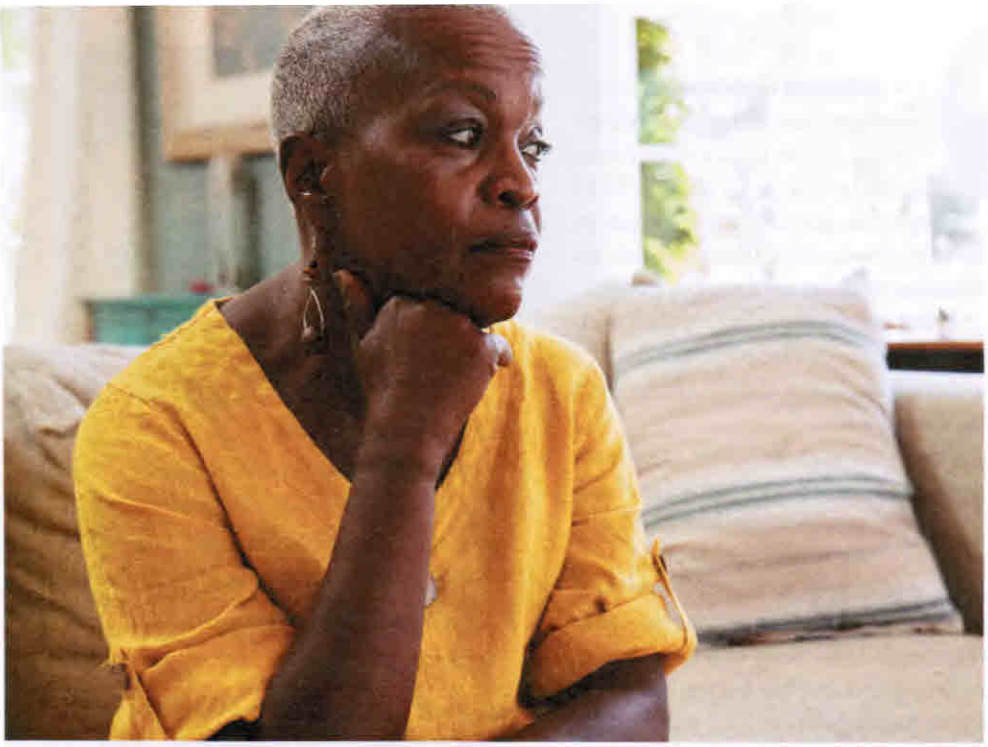

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The New Alzheimer's Drug

Here's what we know so far about the most recently approved medication: Leqembi.

Sarah Kremen, MD
Cedars-Sinai

Just two years after the aducanumab (Aduhelm) controversy, the U.S. Food and Drug Administration has approved another drug for Alzheimer's disease. This medication, lecanemab (Leqembi), certainly fared better in clinical trials, though it's still a far cry from the kind of miracle drug the world is hoping for. Let's take a look at what we know so far.

What does it do?

In phase III clinical trials, Leqembi significantly cleared amyloid-a protein, which forms plaques and disrupts brain function, and decreased the accumulation of tau protein, which forms tangles inside neurons in the memory centers of the brain.

In practical terms, it slowed the rate of memory loss and functional ability decline in people with early-stage Alzheimer's disease.

"It's important to recognize that this medication does not reverse cognitive decline, it only slows it down," explains Sarah Kremen, MD, director of the Neurobehavior Program in the Jona Goldrich Center for Alzheimer's and Memory Disorders, and leader of the Alzheimer's Disease Clinical Trial Program at Cedars-Sinai.

It's not yet clear how beneficial that slowing will be in real life. "We see benefits in the data, but we don't yet know how people will be impacted day to day. We're hopeful that it's going to prolong our patients' ability to function, but that might be a difference of as little as three months," she says.

"From the perspective of a scientist, it is exciting that an experimental treatment targeting brain amyloid in Alzheimer's disease appears to slow cognitive decline," Madhav Thambisetty, MD, a neurologist and a senior investigator at the National Institute on Aging, told the *New York Times*. But "from the perspective of a physician caring for Alzheimer's patients, the difference between lecanemab and placebo is well below what is considered to be a clinically meaningful treatment effect."

How is Leqembi different from other Alzheimer's medications?

"Medications that we have been giving to patients for dementia due to Alzheimer's disease are different from Leqembi because they are not disease modifying," Dr. Kremen says. "This means that they may help memory for some amount of time, but they do not have an effect on the underlying disease process, such as the buildup of amyloid and tau proteins in the brain."

Who can be treated with Leqembi?

Leqembi is designed for people who have either mild cognitive impairment or mild dementia due to Alzheimer's disease. It's not for people with moderate or severe dementia, where their memory and other cognitive functions are so impacted that they need to rely on other people for help with daily living.

What types of pre-treatment testing will patients need?

Before taking Leqembi, patients will need a diagnostic evaluation to confirm that their dementia or cognitive impairment is due to Alzheimer's disease, and they will need testing to confirm the presence of amyloid, which is what the medication is designed to treat. This can be done through specialized brain imaging, which is not widely available or covered by insurance, or through spinal fluid tests, Dr. Kremen says.

What are the safety concerns?

In the phase III clinical trial, about 17 percent of the participants who were taking Leqembi experienced brain bleeding and 13 percent experienced brain swelling. As such, Leqembi isn't recommended for anyone taking blood thinners, or who has significant brain bleeds, brain swelling, aneurysms, vascular malformation, brain tumors, or an uncontrolled bleeding disorder.

"The side effect we're most concerned about is large brain bleeds,

which are fairly rare but can happen," Dr. Kremen says. "So people need to go into this with eyes open, because we're not going to be able to completely mitigate this risk."

People with one or two copies of the APOE4 gene are at increased risk of brain bleeds and swelling and will need to take this into account when deciding whether to be treated.

What is the treatment process like?

The medication is given by intravenous infusion over one hour every two weeks. Patients will need to have an MRI before the fifth, seventh, and 14th infusions to check for brain swelling and brain bleeds. The physicians will also monitor for infusion reactions, such as low blood pressure or difficulty breathing.

How much will it cost?

In January, Eisai, the Japanese pharmaceutical company that developed and tested, the drug said the list price would be $26,500 per year.

Medicare hasn't announced whether it will cover Leqembi or the tests necessary to screen patients. Leqembi is currently approved under accelerated approval only. If the FDA grants full approval, then Medicare coverage is more likely.

When might this treatment be available for patients?

"Before making this treatment available to patients, we have to take steps to ensure that we're giving the drug as safely as possible to patients who will face the least risk and receive the greatest benefit—a critical process that takes time," Dr. Kremen says. "These steps include reviews by our pharmaceutical team, creating new protocols for infusions and treatment monitoring, and training medical providers about this medication. She estimates that it could take up to a year for the drug to become available. ■

Bottom Line Health interviewed **Sarah Kremen, MD**, director of the Neurobehavior Program in the Jona Goldrich Center for Alzheimer's and Memory Disorders, Cedars-Sinai, Los Angeles.

[THE NATURAL WAY]

Jamison Starbuck, ND

Managing Grief Homeopathically

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Recently, my almost 19-year-old cat, Ishtar, died peacefully at home and in my lap. With her passing, I again experienced the deep pain and crystalline purity of grief. Defined by Merriam-Webster as *deep and poignant distress caused by or as if by bereavement*, grief will inevitably touch each of our lives more than once.

It profoundly affects our health, showing itself in family practice every day as patients relay their feelings about the death of a loved one, or the loss of a job, home, financial security, personal health, or a marriage. Yet as recently as November 2019, researchers wrote in *PLoS One* that "there is a curious lack of training for physicians about what grief is and how it might impact patient care and their own well-being."

I chose naturopathic medicine, in part, because acknowledging and supporting emotions, including the pain of loss, is integral to effective treatment. I know there is no single remedy for the challenge of grief. Therapy, support groups, nervous system and sleep medications, nutritional changes, body work and re-evaluating one's life are among the treatments I've recommended. But homeopathic remedies remain my preferred medicine because they are gentle, effective, safe, and work not to drug the pain of grief, but simply to restore balance and calm. For grief I most often use:

Natrum muriaticum. This remedy helps people who cope silently with grief. People who benefit from Natrum muriaticum are likely to contain their emotions, remaining quiet, rarely crying, and often isolating alone with their sadness. Instead of sorrow, they may talk about a headache, fatigue, or indifference.

Ignatia amara. This treatment is helpful for people in whom grief creates a sense of panic, an inability to focus, and strong outward expressions such as weeping, sighing, or speaking. I recently used Ignatia with a patient whose daughter had just been killed in a terrible accident. For 15 minutes, she wandered around my treatment room, wringing her hands, pacing, and weeping. She was unable to do anything but stammer a few details and repeat her daughter's name. I gave her a dose of Ignatia and within five minutes, she was sitting on my couch making concrete, thoughtful plans for travel and the care of her two grandchildren.

Aconitum napellus (Aconite). This is used for people who have great fear or worry after a loss. I've used Aconite with patients with grief-induced high anxiety after a death, divorce, infidelity, or job loss. People who need Aconite usually are restless, shaky, and express fear of the future rather than talking about their current grief.

Pulsatilla. When grief leaves someone feeling abandoned, alone, and forsaken, Pulsatilla is the best remedy. People needing Pulsatilla will seek comfort from others and don't like being alone. They may want to be hugged, held, and taken care of, and will seek comfort foods like ice cream or grilled cheese sandwiches.

With homeopathic medicine, use the smallest dose possible to create a positive change. I recommend starting with two pellets of a 30C potency of one remedy, placed under the tongue, twice daily for three days. Don't take it too close to a meal. If needed, you may repeat one dose of two pellets once a week for up to six weeks.

Jamison Starbuck, ND, is a naturopathic physician in family practice in Missoula, Montana, and producer of Dr. Starbuck's Health Tips for Kids, a weekly program on Montana Public Radio, MTPR.org. She is a past president of the American Association of Naturopathic Physicians and a contributing editor to *The Alternative Advisor: The Complete Guide to Natural Therapies and Alternative Treatments.*