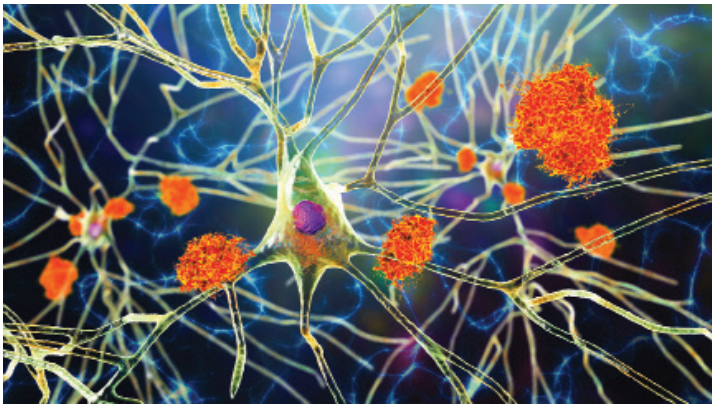
Lecanemab *(Leqembi)*

Information for patients and families about a new drug for Alzheimer's disease

Knowing whether to use the new Alzheimer's disease treatment ***lecanemab*** *(trade name:* ***Leqembi****) can be a complicated decision. Here is a summary of the most current, balanced evidence about its* ***benefits****,* ***side effects****, and other* ***burdens****.*

The effects of lecanemab on memory



Lecanemab (Leqembi) is an antibody designed to attack and destroy amyloid protein in the brain. Many scientists think that the build-up of amyloid is the cause of Alzheimer's disease. However, some patients with Alzheimer's disease may not have much amyloid buildup, and some patients with amyloid in their brain do not have major symptoms.

The drug does not improve memory; rather, it slightly slows the rate of memory loss. It was studied only in people with early Alzheimer's disease or a less severe condition, mild cognitive impairment (MCI); it isn't approved for use in those with moderate or severe memory loss.

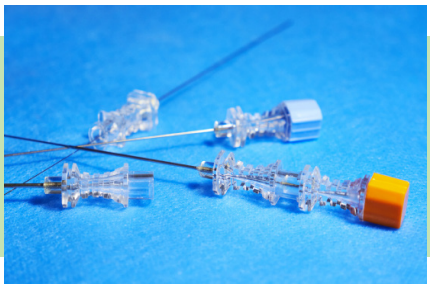
Leqembi is not a pill. It is an intravenous (I.V.) liquid that must be given every two weeks through a drip directly into a patient's vein. This must be done in a doctor's office, infusion center, or hospital. These every-other-week treatments may need to be continued for 18 months or longer.

Since lecanemab doesn't make people's mental functioning improve but just seems to slow the rate of decline, doctors differ on how much it will help patients. Some experts feel that the difference is so small it might not even be noticeable, while others feel that even a very minor effect may be better than nothing. In the main study of the drug, that effect occurred mostly in men. For women or those under 65 years old, this drug seemed to have no effect.

Measuring amyloid levels before starting the drug

Because lecanemab is designed to destroy amyloid in the brain, it should be given only to people who have high brain amyloid levels. Before treatment is begun, a patient should have one of two tests to measure amyloid:

Test 1 - PET scan (Positron Emission Tomography): *A special chemical is injected into the blood to measure amyloid levels in the brain. The patient is then put through a scanning machine like those used for MRI or CAT scans. PET scanning equipment may be hard to find outside of large medical centers.*



Test 2 - Lumbar puncture ('spinal tap'): *A needle is inserted into the spinal cord area in the back to take a sample of the fluid that surrounds the brain.*

In addition, before starting lecanemab patients should have an MRI brain scan. This test is repeated periodically throughout the treatment, and more often if drug side effects are seen. To undergo a brain MRI, the patient's head is put in a plastic cage, and their body is passed into a small tunnel where powerful magnets spin around to create an image of the brain tissue. The test takes about 20 minutes, during which the patient has to remain motionless. The procedure is quite noisy, and patients are given ear plugs and headphones to make it more bearable. Some patients, especially older people with dementia, may not be able to tolerate the noise or may become claustrophobic in the scanner tunnel and cannot complete the procedure. Sometimes sedation is required to enable people to finish the test.

After lecanemab is started, additional MRI brain scans are recommended during treatment. These scans are recommended about every three months for the first year or more often for patients who develop worrisome symptoms. These scans check for the development of brain swelling and/or bleeding that might occur, even without symptoms.

Genetic testing

Some patients' genes may make them less likely to benefit from lecanemab or may make them especially sensitive to the risks of brain bleeding or swelling. APOE is a gene whose presence raises the risk of developing Alzheimer's disease, and APOE ε4 is one variant of this gene. People with at least one copy of the APOE ε4 gene, and especially those with two copies of it, are at much higher risk of having brain swelling or bleeding when given lecanemab. Furthermore, people with two copies of the gene, who could be at greater risk of memory loss, actually showed no benefit from the drug. As a result, the FDA suggests that patients be tested for APOE ε4 before being given lecanemab.

Side effects of lecanemab

About a quarter of patients given the drug had some kind of reaction to the IV treatments during the infusion, including fever or other flu-like symptoms such as chills, aches, feeling shaky, or joint pain. Between a third and a fifth of patients also had their white blood cell count drop initially when starting treatment, which could increase risk of infection. These problems usually improved in most people. Severe allergic reactions (hypersensitivity) also occurred in a very small number of patients.

When the antibody in lecanemab attacks amyloid, it can sometimes cause new problems, including swelling of the brain and small areas of brain bleeding. This occurs in about one out of five patients given the drug, or about double the rate seen in comparison patients. This swelling or bleeding often causes no symptoms, or it can lead to headache, confusion, dizziness, vision changes, nausea, difficulty speaking, weakness, or seizures. In addition to the regular repeat MRI brain scans needed throughout treatment, additional brain MRIs are needed in patients who develop these symptoms to make sure these changes are not continuing or getting worse. Such side effects don't occur in all patients, and can often be relieved if the drug is stopped or the dose reduced. However, sometimes these areas of brain bleeding can become bigger. This problem appears to be rare, but it is not yet clear how often it occurs. A small number of patients taking lecanemab along with anticoagulants (blood thinners) have had serious strokes leading to death. More needs to be learned about whether and how much anticoagulant drugs may contribute to brain bleeding risks in people taking lecanemab.

Over time, patients in studies of amyloid-attacking drugs like lecanemab have been found on average to have shrinking of brain size compared to subjects given comparison treatments. It isn't known what problems, if any, this can cause.

Treatment with lecanemab requires many different healthcare professionals to administer the drug safely. Primary care doctors will need to refer patients to dementia specialists, who can do formal tests of mental functioning, help access PET scans, lumbar punctures, and MRI scans, and make the decision on whether lecanemab is needed. Medicare requires that all patients prescribed lecanemab must be enrolled in a nationwide registry to gather more information on its effects and risks.

How much does lecanemab cost?

The expense of lecanemab (Leqembi) may be an important factor for some patients and families. Its manufacturer has set a list price for the drug of $26,500 per patient for each year of treatment; that does not include the additional costs of doctor visits, tests, and infusion charges required, which have been estimated at about $7,300 more per year – making for a total of $33,800 per year. Medicare will pay for 80% of these tests and of the drug cost for people with "Part B coverage," with the rest of the bill potentially payable by the patient. Many patients in Medicare have supplemental ("Medigap") coverage that can help pay that amount, or they may be enrolled in a "Medicare Advantage" or retiree health insurance plan that may do so, but not all people will have such supplementary coverage. One estimate found that for some patients, their share of the total bill could be as high as $6,600 per year. The nation as a whole could pay between $2 billion and $5 billion annually for the drug.

Summary

More than anything, patients with memory loss need a thorough evaluation to search for potentially treatable causes other than Alzheimer's disease. These might be medication side effects, depression, or other medical conditions. These should be addressed before considering any new drug. Most patients with Alzheimer's disease and their families or caregivers will need help in dealing with the fact that the condition usually gets worse with time. It's important to plan ahead and help patients achieve the best quality of life possible.

The world has been waiting many decades for an effective, safe, and affordable medication to address the devastating condition of Alzheimer's disease. If lecanemab stopped or reversed memory loss, were very safe, and didn't impose important burdens on patients, families, and the health care system, it could have been the important step forward we all have hoped for. However, that is not clearly the case. In the end, it might still be a reasonable choice for some patients and families who are willing to deal with its problems in order to try and slow this cruel disease, even slightly. But other families, patients, and medical professionals will weigh its limited benefits, worrisome risks, and substantial toll on patients and the Medicare program as a whole and conclude that the tradeoff may not be worth making.

More information on Alzheimer's disease and caring for older patients with cognitive impairment is at: AlosaHealth.org/dementia/

These materials for families and patients are being disseminated with support from the Pennsylvania Department of Aging PACE program, the John A. Hartford Foundation, and Aetna. They will be updated as new information becomes available.

Alosa Health
Balanced information for better care

These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition.

Alosa Health is a non-profit educational organization that accepts no funding from any pharmaceutical company.