Information on lecanemab treatment for patients and families:

The FDA has granted **full approval of lecanemab (Legembi™)**, an anti-amyloid antibody for the treatment of Alzheimer's disease in patients with mild cognitive impairment or mild dementia. This decision came after the FDA review of positive results from a Phase 3 randomized, controlled clinical trial that confirmed lecanemab's clinical benefit. These findings were **reported in the New England Journal of Medicine**.

Is lecanemab for everyone?

The FDA has set guidelines on who will be eligible to receive this treatment, summarized in the **FDA label**. Only individuals who meet these guidelines will be evaluated to receive it, for safety reasons some individuals will be ineligible to receive this treatment. Experts in the field have also published an **article documenting appropriate use recommendations.**

Some patients and families may decide they do not want to receive this medication. We will support you by answering your questions, providing medical expertise and guidance as you weigh this new medication option.

How does lecanemab work? Will it improve my cognitive and functional abilities?

Lecanemab works by lowering the level of beta-amyloid protein in the brain. This approach neither stops the disease process nor leads to improvement in symptoms or functional abilities. Rather, it slows the rate of cognitive and functional decline. In the Phase 3 research study, the group treated with lecanemab had a reliable slower decline on cognitive tests and questionnaires assessing functioning in activities of daily living than the group that received placebo (an approximately 5 month saving over the 18 months of the trial, on average). Not all experts agree on whether this represents a clinically significant difference.

The magnitude of the effect is likely different from person to person.

Will insurance cover lecanemab? If so, what will be the cost to beneficiaries?

The **Centers for Medicare and Medicaid Services (CMS) has indicated that coverage will be provided to Medicare beneficiaries** if enrolled in an approved **Alzheimer Patient Registry**. The medication costs approximately $26,500 a year. The exact cost to beneficiaries is not yet known and will vary by different insurance coverage plans. For example, individuals with Original Medicare will pay the standard 20% coinsurance of the Medicare-approved amount for lecanemab once they meet their Part B deductible, whereas patients with supplemental Medicare plans may have much of this deductible covered. Patients may also be responsible for some costs associated with infusions, MRI scans, health care provider appointments, and other aspects of treatment. Some private health insurance plans have announced plans to cover lecanemab with prior authorization, whereas other plans have not yet provided details.

Why are patient registries needed?

Patient registries will collect information from providers to help ensure appropriate patient selection and use of anti-amyloid antibody treatments for AD. Data about patient outcomes and safety will be of critical importance and will help us make decisions about future treatment options.

When and how can I receive lecanemab?

On August 22, 2023 the MGB Pharmacy & Therapeutics Committee approved lecanemab for addition to the MGB formulary. With this approval, the **MGB Alzheimer Therapeutic Program (ATP)** is working to complete the remaining steps required to deliver lecanemab to established patients within the MGB system. We expect to be able initiate treatments this fall. MGB physicians will be instructed on how to refer appropriate patients to the ATP to determine their eligibility and, if appropriate, to proceed with treatment. The ATP will be responsible for monitoring MGB patients on lecanemab.

Please check back on our websites for updates on when lecanemab will be available.
Memory Disorders Unit at MGH
Center for Brain/Mind Medicine at BWH

What evaluation is needed to determine whether I am eligible to receive lecanemab?

To be considered for treatment, you must be evaluated for cognitive changes and receive a diagnosis of mild cognitive impairment due to AD or mild AD dementia The following elements must be completed by your primary care doctor, neurologist, psychiatrist, or other referring provider prior to referral:

- Brief cognitive evaluation within 6 months of referral.
- MRI of brain within 12 months of referral
- Basic lab tests within 6 months of referral.
- Confirmation that you do not take a full-strength anticoagulation (blood-thinner) medication and/or any medication that suppresses the immune system on a chronic basis.
- Confirmation that you do not have a poorly controlled medical, neurological, or psychiatric condition in addition to AD.
- In addition, the following testing will be necessary to determine eligibility; these can be done either before referral or within the ATP:
    1. A test confirming that you have elevated brain amyloid, to be completed either prior to referral or after referral. Tests of cerebrospinal fluid (CSF; obtained by lumbar puncture) or amyloid positron emission tomography (PET) imaging may be used for this purpose. CMS currently does not cover amyloid PET, but this policy could change.

2. A test to determine what versions of the *APOE* gene you carry. This information is needed for understanding what your risk of side effects would be if you were to receive lecanemab.

Where, how, and for how long will this new treatment be given?

Lecanemab is given every 2 weeks by a healthcare provider through a needle placed in your vein (intravenous (IV) infusion) in your arm. Each infusion will last about 1 hour. The MGB ATP will be responsible for providing your schedule of infusions. Infusions will be given at Mass General Brigham hospitals and satellite facilities. This infrastructure is currently being developed. Arrangements have not yet been made to accommodate patients who reside part time in a different state, which will require coordination with other facilities providing treatment with lecanemab.

Lecanemab is currently given every two weeks, for a minimum of 18 months. Additional information is being collected on the treatment period to guide decision making once these 18 months are completed. In addition to infusion visits and regularly scheduled visits with their referring providers, patients receiving lecanemab in the ATP will be seen in the ATP clinic every 6 months (or more often, as indicated) and will have safety MRIs completed 2 months, 3 months, and 6.5 months into treatment (plus additional MRIs as indicated).

What are possible side effects of lecanemab?

Lecanemab can cause small areas of swelling or bleeding in the brain called amyloid related imaging abnormalities (ARIA). ARIA is usually asymptomatic and detected only by monitoring MRI scans. In the phase III study investigating lecanemab, only 2.8% of subjects receiving lecanemab had symptoms due to ARIA. Most symptoms were mild, involving temporary symptoms including headache, confusion, dizziness, changes in vision, nausea, or difficulty walking, and were temporary. However, ARIA-related swelling occurred in 12.6% of subjects receiving lecanemab, and 8.4% of subjects had both swelling and bleeding, often without producing symptoms. Patients will therefore need to be monitored with serial MRIs (usually monthly) until it resolves (usually within 6 months).

Rarely, ARIA can cause seizures or larger areas of inflammation and/or bleeding in the brain. The risks of ARIA, symptomatic ARIA, and serious symptomatic ARIA leading to hospitalization are highest in people carrying 2 copies of the *APOE* ε4 gene. In the phase 3 study, the rates of symptomatic ARIA with lecanemab treatment were 9.2% in participants with 2 *APOE4* genes, 1.7% in participants with 1 *APOE4* gene, and 1.4% in participants who did not carry an *APOE4* gene. The rates of serious symptomatic ARIA were 2.1% in participants with 2 *APOE4* genes, 0.4% in participants with 1 APOE4 gene, and 0.7% in participants who did not carry an *APOE4* gene.

Has anyone died from lecanemab?

In the first part of the lecanemab phase 3 trial where 1795 participants received either active drug (lecanemab, 898 participants) or placebo (salt water, 897 participants) over 18 months, there was no difference in the number of participants who died (6 receiving lecanamb and 7 receiving placebo). Following this part, participants were offered to continue in an extension (open label portion) of the study where everybody received active drug (lecanemab) and nobody received placebo (salt water). During this extension, 3 participants (out of about 900) died from side effects thought to be due to lecanemab Two of the deaths were related to brain hemorrhages (bleeding), one occurring in a participant on anticoagulation (a blood thinner), the other in a patient who received tissue plasminogen activator, a medication used to break down blood clots in patients with acute stroke. The third death occurred in a patient homozygous for *APOE4* (with 2 copies of the *APOE4* gene) who developed swelling and bleeding in the brain similar to a condition involving excessive amyloid protein in blood vessels in the brain with associated inflammation. Under the ATP protocol, patients on anticoagulation will not be eligible to receive lecanemab. A key purpose of the screening MRI prior to treatment is to identify findings such as small areas of bleeding (microhemorrhages) and other features suggesting amyloid protein in blood vessels that would lead to a higher risk of serious ARIA. Also, all patients will have *APOE* genotyping prior to deciding about treatment with lecanemab. This will allow us to identify patients with 2 copies of the *APOE4* gene, who are at higher risk for developing side-effects.

How is lecanemab different from donanemab? From aducanumab?

Donanemab is another anti-amyloid antibody recently investigated in a phase 3 clinical trial, with results suggesting it slows cognitive and functional decline in MCI due to AD and mild AD dementia. The results were recently **published in the Journal of the American Medical Association**. Because this study was completed more recently, the submission for full FDA approval of donanemab has yet to be reviewed by the FDA.

Aducanumab was studied in two phase 3 studies, that, for various reasons did not provide sufficient data to definitively determine its effectiveness for slowing symptoms of AD. It was granted accelerated approval from the FDA (rather than full approval) and is NOT covered by Medicare. Aducanumab is currently being investigated in a **Phase 3b/4 study** conducted at numerous sites including the **BWH Center for Alzheimer Research and Treatment**.

Do we know if lecanemab is effective for patients with early-onset AD? How about racial and ethnic minorities?

While the phase 3 study provided a preliminary analysis of selected subgroups of subjects with AD, it was not designed or powered to provide conclusive results about the effectiveness or side effects of lecanemab in these subgroups. Additional data from more subjects will be helpful to answer these important questions. This is one purpose of the registry noted above.

What will happen if I decide not to receive this treatment at this time?

Deciding to start treatment is a decision you should make with your family, and your physician. We will continue to be a resource for you if you decide not to receive treatment. We will review options with you and your physician, such as research, and supportive care.
Watch: Hope & Empowerment Through Research

Will I be eligible for lecanemab if I participated in a clinical trial investigating a different treatment for AD?

Prior participation in clinical therapeutic research studies will not make you ineligible to receive lecanemab, provided the other eligibility criteria are satisfied.

How would treatment with lecanemab impact my eligibility to enroll or continue in clinical research studies for AD?

At present, most if not all clinical therapeutic studies investigating potential new treatments for AD do not allow concomitant treatment with lecanemab. This could change in the future. We recommend speaking with your current provider and/or contacting us at the **Center for Alzheimer Research and Treatment** if you have questions about whether pursuing treatment with lecanemab or enrolling in a clinical therapeutic research study is the best option for you.

If you are currently enrolled in a clinical therapeutic study or an observational study, please contact your research site about the potential impact of pursuing treatment with lecanemab on your ongoing participation in the study.

Additional resources:

Memory Disorders Unit (MDU) at Mass General Hospital

Massachusetts Alzheimer's Disease Research Center (MADRC)
Tips for navigating the MADRC site

Center for Brain/Mind Medicine (CBMM) at Brigham & Women's Hospital

For those concerned about memory and thinking but do not have a diagnosis:
How to get a diagnosis
Road Map to Dementia Diagnosis

For those not eligible for this treatment and looking for other options. Learn about research opportunities that may be available to you:
Join a Study
Road Map to Research Participation

Alzheimer's Association

National Institutes of Health

References:

- FDA Approval- www.fda.gov/news-events/press-announcements/fda-converts-novel-alzheimers-disease-treatment-traditional-approval
- Lecanamab (Leqembi) phase 3 study results- www.nejm.org/doi/full/10.1056/NEJMoa2212948
- Appropriate use article- https://link.springer.com/article/10.14283/jpad.2023.30
- Medicare statement coverage of Leqembi - https://www.cms.gov/newsroom/press-releases/statement-broader-medicare-coverage-leqembi-available-following-fda-traditional-approval
- Alzheimer's Patient registry - https://qualitynet.cms.gov/alzheimers-ced-registry
- Clinical meaningfulness article
- Leqembi medication guide- sponsor