TuSalud

Why the Next Big Hope for Alzheimer's Might Not Help Most Black Patients

While patient advocates are celebrating, critics predict the rollout of Leqembi will aggravate racial disparities in elder care.

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The FDA on [July 6] gave full approval to what many scientists and doctors believe is the first drug to show promise of slowing the progression of Alzheimer's disease.

But while patient advocates are celebrating, critics see it as the unfortunate triumph of a flawed theory of the disease's cause and predict the rollout of the drug will aggravate racial disparities in elder care.

An FDA advisory panel last month voted 6-0 to support FDA approval of lecanemab, from the Japanese pharmaceutical company Eisai. In a clinical trial involving nearly 1,800 early-stage Alzheimer's patients, the drug slowed progression of the disease somewhat in those who got biweekly infusions, compared with those given a placebo.

But the drug didn't reverse Alzheimer's symptoms, and it will require careful monitoring of patients for months or years, including many brain scans. Those receiving lecanemab, which carries the brand name Leqembi, were twice as likely as placebo recipients in the major trial to suffer hemorrhaging or swelling in the brain. These incidents, related to the drug's stripping away of amyloid proteins, were generally minor, but three deaths appear to have been caused by the drug.

With the FDA's approval of lecanemab, Eisai is set to promote it to the primary care physicians who treat most dementia patients and critics are speaking out. Some say the drug, which Eisai plans to market for $26,500 a year, offers false hope. Others say any positive impact it has won't benefit lower-income patients, who tend to be diagnosed too late for the drug to be effective, and usually receive care in settings ill-equipped to handle the drug's stringent requirements.

"The most likely consequence of this medication is to take resources and attention away from addressing basic supports for older adults with cognitive impairment," said Maria Glymour, chair of the Department of Epidemiology at the Boston University School of Public Health. The money spent on expensive drugs like lecanemab would be better invested in fighting diseases like high

blood pressure and diabetes, which hasten dementia, and on community-based services for older adults, she said.

The critique of lecanemab builds on another complexity of the drug's approval: Few African Americans were involved in testing it.

Of the 859 people infused with lecanemab during the trial, only 20 were Black. Minorities are often underrepresented in research, but this study had an additional barrier, said Carey Gleason, a clinical neuropsychologist at the University of Wisconsin School of Medicine and Public Health. Many Black volunteers in the trial "screened out," she said, because PET scans showed relatively low levels of amyloid in their brains. Lecanemab works by removing amyloid, so the trial organizers excluded patients — regardless of their Alzheimer's symptoms — if their PET scans were negative.

Eisai spokesperson Libby Holman said the company worked to enroll a diverse population but that amyloid levels "differed among racial and ethnic groups." She added, "If individuals do not have elevated amyloid, they do not have Alzheimer's disease."

Indeed, lecanemab's approval marks the culmination of the idea, formalized 32 years ago, that Alzheimer's disease can be understood as cognitive decline caused by amyloid buildup, the "trigger," in combination with the "bullet," a protein called tau.

For example, Blacks are up to twice as likely as whites to have Alzheimer's, yet they show equivalent levels of amyloid in most major studies. No one is sure why, but the hypothesis is that having multiple simultaneous health conditions and being exposed to environmental stressors put Blacks as a group at higher risk.

Furthermore, Blacks and other minorities tend to be diagnosed at later stages, which automatically excludes them from use of lecanemab, which was designed and approved to treat early-stage Alzheimer's.

"The drug has to be used in the very early window of the disease," Gleason said. "It's well documented that marginalized communities and people don't get access to diagnostic services as do more privileged populations, because our medical care is two-tiered."

"Lecanemab should still come to market," she said. "But we need to be investing in other pathways."

In its review of the costs and benefits of lecanemab, a 15-member panel appointed by the Institute for Clinical and Economic Review gave the drug low marks. Its rollout would aggravate elder care disparities, the panel said, by favoring wealthier patients who have more resources, better insurance, and an easier time getting to multiple appointments.

Advocates for minority health care are well aware of these risks. But many feel the only response is to push harder for access to the drug. There is no research to suggest the drug would not work

in Black people, said Carl Hill, chief diversity, equity and inclusion officer for the Alzheimer's Association, which is raising awareness of the drug through churches and grassroots groups.

Manly is not so sure. "There are reasons to question whether it would be safe in Black people," she said, noting that older Black people diagnosed with dementia have higher rates of vascular conditions like hardening of the arteries compared with white patients. That could pose potentially higher risks of brain hemorrhaging if they took the drug. In general, the trial's lack of representativeness across racial and ethnic groups means the drug may not perform as well against Alzheimer's disease across these groups, Manly said.

"In terms of equity I feel conflicted," she said. "I'd love for all families like mine to have equitable access to an Alzheimer's drug, but only if it's safe and effective."

Even the most optimistic Alzheimer's experts believe the drug's risks require careful selection of patients by highly trained clinicians with sufficient resources to detect and monitor any problems.

Jason Karlawish, a neurologist at the Perelman School of Medicine at the University of Pennsylvania, said the FDA should set up a Risk Evaluation and Mitigation Strategy, or REMS, which would require doctors administering the drug to follow a series of steps to reduce and monitor its dangers. A REMS, currently in place on about 60 drugs, generally limits access to a drug. While FDA's approval of lecanemab warned of risks, especially for people who are on blood thinners, it did not require a REMS.

The conflict between safety and access is only one paradox of lecanemab's arrival.

The FDA approved an earlier anti-amyloid treatment, Aduhelm, in 2021. but most doctors rejected it as ineffective and unsafe. Some Alzheimer's scientists who have long argued that amyloid isn't the whole answer feel that lecanemab's middling performance only confirms their thesis.

One skeptic is George Perry, a neurobiology professor at the University of Texas at San Antonio. He has hypothesized that amyloid and tau buildup are a reaction to the aging process that play a role in preserving, rather than wrecking, the brain. The accumulation of amyloid in older people's brains, in Perry's view, reflects the body's effort to fight aging disease.

Dementia clearly has many causes, said S. Ahmad Sajjadi, a clinician and neuroscientist at the University of California-Irvine. Ideally, patients will someday receive treatments as specific and targeted as those increasingly available to treat cancers, he said.

For now, for a select group of patients, lecanemab offers a whisper of hope that some will want to pursue, despite the risks, Karlawish said — perhaps a 10% chance of freezing the progression of the disease for months or even longer.

Patient groups such as the Alzheimer's Association, which funds much of the research in the field, are demanding broad access to lecanemab and oppose the Biden administration's plan to have Medicare initially pay for the drug only if patients are enrolled in a registry, a kind of post-

marketing clinical trial.

At a public hearing during the FDA advisory panel meeting on the drug, Alzheimer's Association CEO Joanne Pike noted that patients on lecanemab declined five months more slowly in their first 18 months on the drug, on average. That "deserves celebration," she said.

Perry, who has received research funding from the Alzheimer's Association, questions its strong support for the drug but isn't surprised, given the group's promise to its members and supporters to help find a cure for the disease.

"They've pushed amyloid so hard for 30 years," he said, "and they can't turn back."

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