FDA advisory panelist outlines issues with aducanumab's approval for Alzheimer's disease

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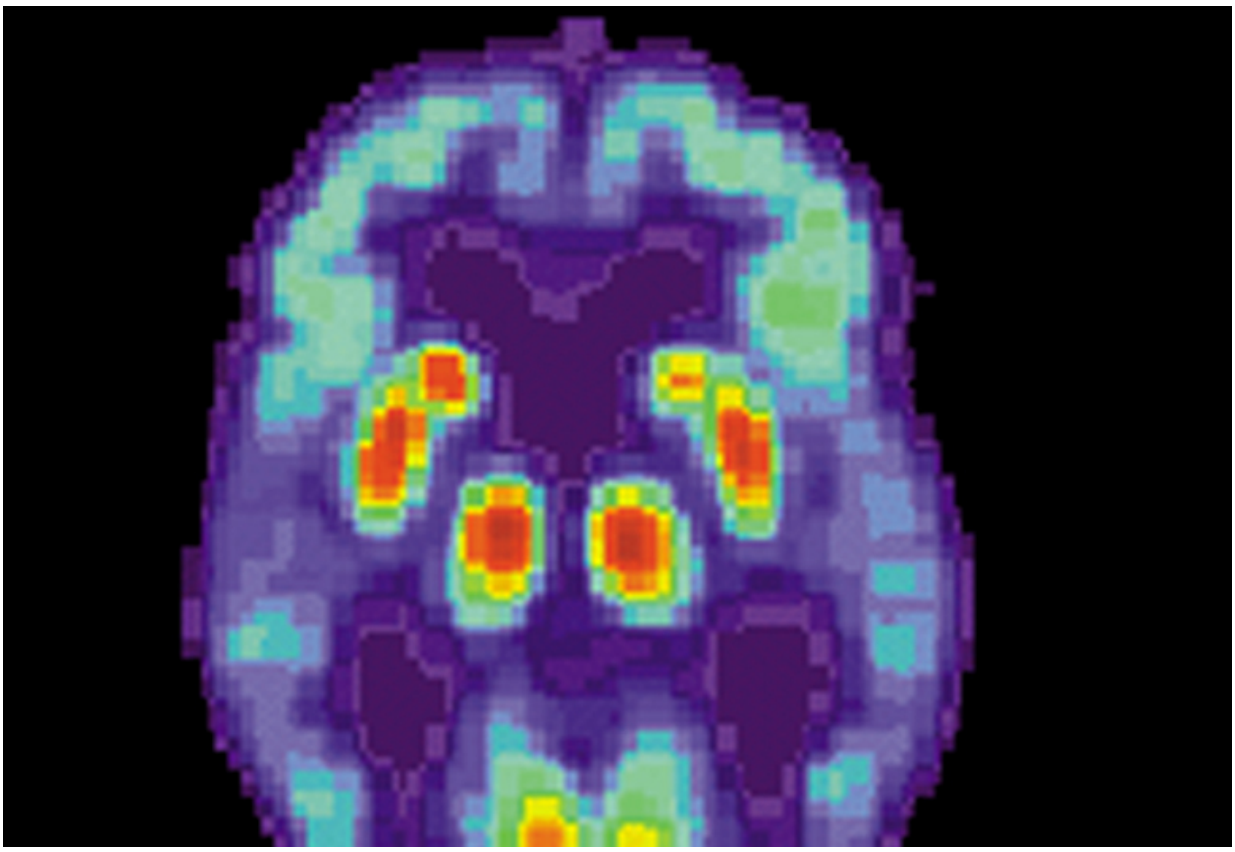

PET scan of a human brain with Alzheimer's disease. Credit: public domain

Despite near unanimous objection from its advisory panel, the U.S. Food

and Drug Administration (FDA) granted aducanumab approval to treat Alzheimer's disease on June 7, 2021. In a commentary published in *Annals of Internal Medicine*, a member and former Chair of the advisory panel and an aducanumab site investigator explain why this unprecedented "accelerated approval" is problematic for clinical research and patient care.

Under accelerated approval, a drug is approved based on its effect on a surrogate marker of a disease rather than clinical outcomes. The product is expected to provide a meaningful advantage over other available therapies for a serious disease. Aducanumab's phase 1 study indicates the drug reduces beta-amyloid (the surrogate marker of disease), but whether beta-amyloid alone is a valid surrogate for the treatment of Alzheimer's is notably unclear and still a topic of ongoing important study. With the surprising approval, treating an amyloid level becomes clinical practice.

The authors express grave concern that aducanumab's approval will have important consequences for drug development, regulation, and patient care. While the world waits for the results of randomized and controlled clinical trials required to confirm aducanumab's clinical benefits (or not), insurers and payers will have to use the scant information available to determine which patients should take it and how to cover it. The copays for aducanumab, which may be as much as 20% of the total cost, will be added to the already substantial financial burden many American families face due to Alzheimer's disease. Also, clinicians will have to address with patients, uncertainty regarding whether the drug is even beneficial or safe.

According to the authors, the effect of aducanumab's approval will reverberate for years. Patients, caregivers, providers, and scientists must navigate treatment of Alzheimer's disease with an uncertain treatment. Time will tell whether or not it is safe and effective.

More information: *Annals of Internal Medicine* (2021). https://www.acpjournals.org/doi/10.7326/M21-2603