Opportunities and strategies for accelerating patient access to treatments for Alzheimer's disease

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This article is part of a series about challenges and opportunities in developing treatments for dementia.

The year 2023 may be remembered as a turning point in the treatment of Alzheimer's disease. The announcement from the U.S. Federal Drug Administration (FDA) confirming the clinical benefit of Leqembi (lecanemab) to treat the disease is a landmark in the history of drug development for this long-term, progressively debilitating condition.[1] In May 2023, Eli Lilly and Company reported positive results of a Phase III study showing that donanemab significantly slowed cognitive and functional decline in people experiencing early disease symptoms.[2] (FDA approval is pending.) In October 2023, the Centers for Medicare & Medicaid Services (CMS) expanded coverage of brain amyloid positron emission tomography (PET) imaging for diagnosis and treatment of Alzheimer's after many years of evaluation by the FDA. The CMS program typically leads the way for commercial payers.[3] Note that the prior stance of CMS was to cover one scan when a patient was in a study under Coverage with Evidence Development (CED) requirements.

These are exciting developments in the urgent quest to address neurodegenerative conditions that are notoriously difficult to diagnose and treat.[4] Until very recently, treatments for Alzheimer's disease were targeted largely to purportedly "symptomatic" therapies (mitigating memory problems, cognitive function, and behavioral symptoms) offering no prospect of slowing progression or recovery. An accurate diagnosis via imaging was not necessarily considered essential because the treatments targeted symptoms rather than the etiology of the disease.

1 FDA Converts Novel Alzheimer's Disease Treatment to Traditional Approval
2 Lilly's Donanemab Significantly Slowed Cognitive and Functional Decline in Phase 3 Study of Early Alzheimer's Disease
3 Alzheimer's Association Applauds CMS Decision to Cover PET Imaging for Alzheimer's Disease Diagnosis
4 Revisiting FDA Approval of Aducanumab

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For healthcare payers, Alzheimer's disease is a highly prevalent, high-cost condition that, like obesity, has a devastating cumulative impact on healthcare resources. The global prevalence of Alzheimer's disease is expected to rise to 152 million cases by 2050, nearly tripling the number of people living with the disease.[5] According to a 2022 Congressional report, more than 6 million Americans suffer from Alzheimer's disease, costing the U.S. economy an estimated $321 billion in 2022, not including billions of dollars in unpaid caregiving.[6] Unique to Alzheimer's patients compared to other diseases is the frequent loss of self-care and the resultant burden on family caregivers and/or costly institutional care.

Breakthroughs in disease modification

These breakthrough therapies seek to address physiological features and disease modification for those with early-onset disease. Leqembi, developed by Eisai Inc., has been proven to reduce amyloid plaques that form in the brain, a defining disease characteristic. Likewise, donanemab is an investigational amyloid plaque-targeting therapy that aims to slow the advance of the disease.

The difficulty of accurate diagnosis persists, which, of course, has a significant impact on costs for the payers given the costs of scans in contrast to "paper and pen" cognitive function tests. A drug can feasibly arrest the progress of the disease for early onset when it can be diagnosed, and in late stages, the treatments can be somewhat helpful, but the costs are not sustainable. From a societal vantage point, it may be unrealistic (and perhaps unnecessary) to treat every person showing early signs of memory loss and possible accumulation of myeloid bodies with these costly drugs. From a payer's standpoint, the imaging data does not necessarily show how the accumulation of myeloid bodies in the brain is impacting the patient on a day-to-day basis. As for measuring survival data, which is the typical benchmark for oncology, trials for Alzheimer's disease would have to be run for decades.

Payer acceptance of surrogate endpoints

There has been a growing body of examples of regulatory approvals based on surrogate endpoints – which historically were controversial when viewed by payers who look to clinical outcomes (usually success in classical primary endpoints in trial designs). However, we are seeing that payers are beginning to accept surrogate endpoints and shorter-term data in making reimbursement decisions, especially with a bridge from the surrogate endpoint or biomarker to a true clinical outcome. In the Leqembi example, the FDA confirmed that clinical data demonstrated the drug's effect on a surrogate endpoint – reducing amyloid plaques in the brain – that is reasonably likely to predict a clinical benefit to the patient. Similarly, donanemab met the primary endpoints

5 World Health Organization (WHO) Global Status Report 2021
6 The Economic Costs of Alzheimer's Disease, Joint Economic Committee Democrats, 2022

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measuring cognition and activities of daily life, with a secondary endpoint of CDR-SOB in Phase III studies. In this case, if the drug can slow the disease trajectory, there is immense economic and clinical value, especially since the patient can stay at home longer and avoid institutional care.

That raises yet another challenge: the burden on the caregiver. At Parexel, a clinical research organization working with drug developers, our primary focus is supporting appropriate clinical development and patient access activities. But in a disease like Alzheimer's, we need to consider the caregiver's voice, not just the perspective of the healthcare system and the patient. Are the economic costs of in-home care a factor in reimbursement decisions? Is the pricing of the treatment influenced by these realities?

Strategies and best practices

Successfully realizing opportunities to develop treatments for Alzheimer's will require careful consideration of all these challenges and points of view. In our experience at Parexel, we have identified several best practices summarized here.

- Design clinical trials encompassing careful selection of patient populations with a strategy for creating a bridge from surrogate endpoints to demonstrable and measurable outcomes.
- Think well in advance about potential product value. Partner with payers early in the process to get their reaction to the clinical data, patient population, price points, and so on to understand their expectations. Explore the indirect costs and burdens of your indication.
- Maintain as much transparency as possible throughout the development lifecycle.
- Prepare for success after regulatory approval. Ensure that development operations have a strong policy connection to commercial teams and create product positioning that sets the right expectations for efficacy, duration of treatment, and pricing.
- Work with the growing body of real-world evidence and data to show post-approval and post-study benefits in study and real-world populations.
- Plan for value- and outcomes-based agreements and monitor for efficacy in the commercial, post-approval context.

Parexel delivers product market access strategy, so clinical and development plans merge with regulatory and health economic strategies to drive business success and patient outcomes.

With a real-world point of view relevant to regulatory approval and reimbursement, health technology assessment, and value measurement and communication, Parexel Access Consulting brings insights and analyses to payer stakeholders to demonstrate value, drive successful commercialization, and deliver novel therapies to patients to address unmet needs.

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