PROACTIVE STEPS TO ENSURE APPROPRIATE UTILIZATION OF THE FIRST DISEASE-MODIFYING THERAPY FOR ALZHEIMER DISEASE

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Widespread hope exists that aducanumab will soon gain Food and Drug Administration approval as the first disease-modifying therapy for patients with mild cognitive impairment associated with Alzheimer disease (AD), which could significantly impact the management of AD. If approved, challenges need to be addressed to properly identify patients who will benefit from treatment and ensure access. Guidance is necessary to ensure that all aspects of the Quadruple Aim—individual patient experience, population health, cost of care, and caregiver support— are addressed. Attainment of each of these aims is only possible through guidance, such as clinical pathways, that helps to achieve favorable clinical and financial outcomes across stakeholders.

The National Institute of Aging describes Alzheimer disease (AD) as an "irreversible, progressive brain disorder that slowly destroys cognitive and functional skills and, eventually, the ability to carry out the simplest tasks."[1] In most people with AD, symptoms first appear in their mid-60s.[2] Estimates vary, but experts suggest that more than 5.5 million Americans, most of them aged 65 years or older, may have dementia caused by AD.[1] The estimated increase in prevalence to 14 million by 2050 is anticipated to create a tremendous clinical and economic burden on the healthcare system,[3] particularly given the likelihood that most patients will require long-term care.

Recent estimates indicate that AD may rank third, just behind heart disease and cancer, as a cause of death in older people.[4,5] In addition to the high rate of patient mortality, the impact of AD on quality of life and caregiver burden make a cure for AD a top priority. Despite recent results from the Dominantly Inherited Alzheimer Network-Trials Unit international study,[6] showing the failure of both gantenerumab and solanezumab to slow memory loss and cognitive decline, widespread hope exists[7] that aducanumab will soon gain Food and Drug Administration approval as the first disease-modifying therapy (DMT) for patients with mild cognitive impairment (MCI) associated with AD, an intermediate state between normal cognition and dementia.[8]

Aducanumab's approval as a DMT could significantly impact the management of AD. In particular, challenges need to be addressed to ensure that appropriate patients (those who will reap the most benefits) are targeted. These challenges are the result of not only aducanumab's novel mechanism of action but also unique diagnostic requirements and the administrational challenges of an intravenous (IV) infusion; therefore, it requires the development of efficient and effective processes to enable the appropriate use of aducanumab. The following are recommendations for proactive steps related to each stakeholder group to ensure access and timely administration.

Patients

Patients first need to self-identify or be identified by their loved ones for screening, and then overcome the stigma associated with a diagnosis of MCI, an early stage of AD where DMTs may demonstrate maximum therapeutic impact. Addressing this stigma, especially for working adults, and educating patients on the diagnostic process are critical first steps.

Obtaining a diagnosis is just the beginning of a long journey for patients, who are then faced with assessing the benefits and costs of treatment. This requires patients to have a clear appreciation of treatment benefits and potential treatment-related reduction in downstream costs. Not only do patient out-of-pocket (OOP) costs—due to this therapy being a Medicare Part B benefit—need to be taken into consideration, but most patients will also be faced with a 20% copayment. Although a number of patients have Medigap insurance, resulting in OOPs of $0, dual-eligible (Medicare/Medicaid) individuals will also receive this benefit. Other costs beyond the direct costs include costs associated with perceived adverse side effects and administrative burden of distance and travel to an IV infusion site.

Clear articulation of treatment benefits and the potential reduction in associated costs must be communicated to patients, otherwise they will not be diagnosed or be in a position to receive treatment.

Providers

Providers also need to appreciate the value of treatment to be engaged in the diagnostic process, and they need to be provided with an efficient process for diagnosis and treatment. However, some additional challenges exist. For example, on the diagnosis side, many current diagnostic tools, such as the Montreal Cognitive Assessment and Mini-Mental State Exam, have copyright restrictions. Removing these restrictions and securing an efficient and effective process for timely diagnosis is critical.

Additional diagnostic restrictions include the fact that positron emission tomography (PET) scans currently have a National Coverage Determination (NCD) restricting their use. Even when this Centers for Medicare & Medicaid Services (CMS) block is removed, a new CMS requirement, the Clinical Decision Support Mechanism (CDSM), will decrease diagnosis by increasing the burden for getting these studies completed.[9] A CDSM is an interactive, electronic tool for use by clinicians that communicates appropriate use criteria information to users and assists them in making the most appropriate treatment decision for a patient's specific clinical condition—think of it as a prior authorization (PA) for radiologic studies.[10] The CDSM process will likely be a PA module within or available through certified electronic health record technology. Many primary care physicians (PCPs) may find the CDSM process time consuming, so referring patients to specialists may be their preferred route rather than diagnosing on their own. Some will use traditional specialist referrals, while others will follow the increasing trend of using eConsults. These eConsults can improve the efficiency in diagnoses for both patients and PCPs.[11] Additionally, new ways to diagnose patients using portable PET scanners may need to be adopted by PCPs and specialists to increase treatment rates.

Finally, providers will need to manage the challenges of buy-and-bill for an infused treatment. Providers like PCPs and others who manage AD are typically not used to managing buy-and-bill and, as such, may be reluctant to manage the associated financial risks due to waste and failure to collect patients' OOP costs. In addition, the physical management of dealing with an infusible product—from site of care to handling the medication correctly—is an obstacle that needs to be addressed. Many PCPs will not have the ability to infuse an IV product, nor the interest; thus, many patients will be referred to infusion centers or be administered novel biologics at home.

Health Systems

A growing number of PCPs are employed by health systems that house Centers of Excellence[12] for AD treatment. Therefore, it is important to address the concerns and the opportunities of this stakeholder group. Although the issues of health systems often mirror those of providers, there is one unique aspect that affects health systems: because most health systems participate in value-based contracts, such as the Medicare Shared Saving Program (MSSP), they are much more interested in the financial impact of treatment. The MSSP provides a set amount for which the health system is responsible when managing costs, similar to a diagnosis-related group (DRG). This set amount is based on historical treatment costs, so new and innovative treatments are not included in these benchmarks. Without inclusion of these costs, health systems will have a difficult time covering the cost of innovative treatments, since it may result in the health system paying CMS for costs in excess of their benchmark. Although the MSSP does not currently have a process allowing for innovative new treatments, the DRG system uses the New Technology Add-on Payment (NTAP). NTAP provides coverage for new treatments that are not included in the DRG set payment.

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Initial reimbursement for health systems may be a challenge for novel AD products because a MSSP will not cover the full costs of treatment without an adjustment. New policies from CMS will be needed to address this issue.

CMS Services

CMS is the natural leader for optimizing the processes and standards around new AD treatments. Their policies should reflect the long-term value of an AD therapy to ensure appropriate access to diagnosis and treatment, the benefits of which, again, extend to the caregiver, long-term care costs, and patient quality of life and productivity. As such, this would mean the removal of the above-mentioned NCD PET Scan Medicare Coverage restrictions, which could negatively impact long-term access to innovative treatments like those needed to finally cure AD. Additionally, data published in April 2019 from the CMS-funded IDEAS trial have shown that real-world evidence supports the reimbursement of PET scans for Medicare patients who have MCI or dementia.[13] Core elements of the patient management plan changed after review of the results from beta-amyloid PET scans in a majority of patients with MCI. The most common change in management involved AD drug use, which changed in 43.6% of patients with MCI and 44.9% of patients with dementia.[13] These data should result in fewer restrictions by CMS for PET scans.

Payers

Although AD is considered one of the most expensive disease areas from a total cost perspective, the exposure that many payers currently face is limited. Most of the cost burden results from lost wages, caretakers, and long-term care facilities—none of which directly impact commercial health plans. This dynamic undermines typical cost offset arguments, especially as the launch of a disease-modifying biologic stands to significantly increase the budget impact shouldered by payers.

Adding to these concerns is the perception that aducanumab might initiate a landslide of patients seeking chronic treatment as well as a surge of physicians trialing the first DMT to come to market in AD. While payers acknowledge that they can enforce the trial inclusion/exclusion criteria to mitigate budget impact, two additional complications arise. First, the criteria for use should consider the most appropriate patients, which may be broader than the inclusion/exclusion criteria used in the clinical studies. This is often the case, as clinical study design tends to be more restrictive than real-world applications. Second, to determine which patients are most appropriate for treatment, patients will need to undergo beta-amyloid testing. In aducanumab clinical trials, patients underwent betaamyloid.

PET scans, although cerebral spinal fluid testing may also be an option, assuming the results are concordant. The challenge is that PET scans are expensive, and, while most plans do not cover them for the diagnosis of AD (in accordance with the CMS NCD), payers acknowledge that screening is ultimately a cost-saving mechanism. In short, payers are caught between the expense of treatment and the expense of a sudden spike in pricey PET scans—they are looking to CMS for their next move.

Where Pathways Can Help

Given that the process for diagnosis and treatment of AD via an infused DMT is completely different, identification of the critical steps in this journey is vital. As described above, from patient self-identification to final treatment and follow-up, steps in this pathway must be carefully defined. What is needed are either pathways that call out the individual stakeholders or pathways that are unique to each, because the steps in the journey of AD treatment with an infused DMT is very different for patients, providers, health systems, CMS, and payers.

Guidance is necessary to ensure that all aspects of the Quadruple Aim—individual patient experience, population health, cost of care, and caregiver support—are addressed. Attainment of each of these aims is only possible through guidance that helps to achieve clinical and financial outcomes in this uncharted territory. Comprehensive pathways can lead the way.

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“Guidance is necessary to ensure that all aspects of the Quadruple Aim... are addressed.”

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