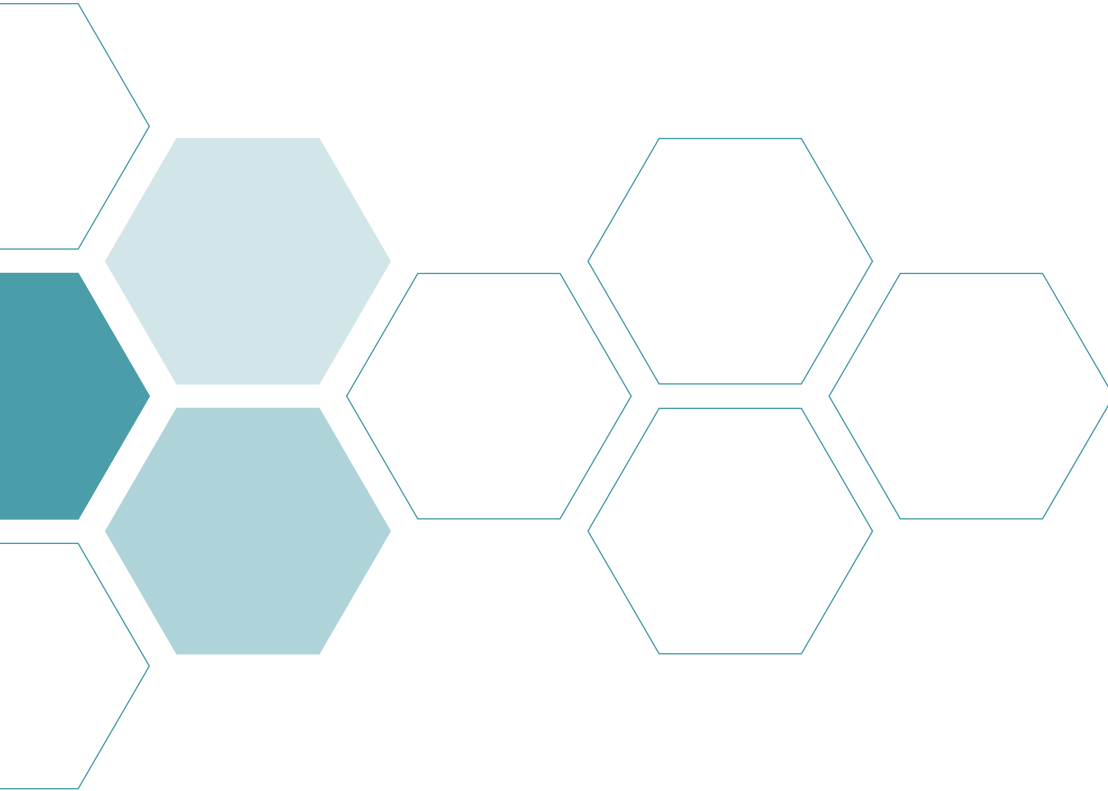


NAMCP Medical Directors Spotlight Guide: Alzheimer's Disease Patient Treatment Journey— Managed Care Considerations

The Journey for Patients with Alzheimer's Disease and Implications
for Policy and Coverage for Medical Directors of Purchasers,
Health Plans, and Providers



JOURNAL of MANAGED CARE MEDICINE

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Mission Statement

The mission of the National Association of Managed Care Physicians (NAMCP) Medical Directors Institute is to open the lines of communication between medical directors in managed care and treating physicians to help them jointly better navigate and understand what is happening in managed care and the daily management and practice of disease. The NAMCP Medical Directors Institute brings resources and updates, strategic reviews, and key information to medical directors for insurers, employers, providers, and integrated delivery networks. Unique Executive Councils focus on emerging technologies, oncology and value-based contracting for manufacturers and managed market leaders.

This guide discusses the journey for patients with Alzheimer's Disease and their care partners and implications of that journey for treatment and support. Awareness of a cohesive patient-centric care pathway/patient journey can lead to enhancements in dementia care tailored for the individual patient, at the right time (i.e., stage of disease), and the right treatment delivered in the most effective manner. Managed care treatment and policy for dementia and Alzheimer's Disease can be strengthened in the context of the emerging landscape, understanding of Alzheimer's Disease, and the role that early diagnosis, testing and treatment can have on both patients and their care partners. Early intervention can impact the total cost of care as well as patient access to needed care and well-being. This guide is part of a series of activities and initiatives within the NAMCP Institute to support medical directors from purchasers, plans, and provider systems, and to eventually achieve greater collaboration leading to improved patient outcomes.

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Alzheimer's Disease Patient Treatment Journey 2024

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TABLE OF CONTENTS

The Journey for Patients with Alzheimer's Disease and Implications for Policy and Coverage for Medical Directors of Purchasers, Health Plans, and Providers <i>Dawn Holcombe, MBA, FACMPE, ACHE</i>	4
Mission Statement.....	2
Introduction.....	4
Diagnosis of Early AD.....	6
Clinical and Managed Care Considerations for Cognitive Screening and Early Diagnosis of AD.....	8
Treatment Selection and Initiation for Early AD Intervention.....	9
Monitoring and Surveillance During Treatment with Anti-Amyloid Drug Class.....	11
Summary – Key Managed Care Implications to Support Early Management and Slowing Progression of AD.....	12
References.....	13

NAMCP Medical Directors Spotlight Guide: Alzheimer's Disease Patient Treatment Journey — Managed Care Considerations

The Journey for Patients with Alzheimer's Disease and Implications for Policy and Coverage for Medical Directors of Purchasers, Health Plans, and Providers

Dawn Holcombe, MBA, FACMPE, ACHE

INTRODUCTION

Alzheimer's Disease is a Progressive¹ and Relentless Disease and Represents a Crucial Unmet Need in Healthcare²

Alzheimer's Disease (AD) is a progressive², fatal² neurodegenerative disease that accounts for 60 to 80 percent of dementia² (a group of symptoms, including difficulties with memory, language and problem-solving, that affect a person's ability to perform daily activities) cases.² AD was the fifth leading cause of death in those aged 65 and older in 2019 and was the seventh leading cause of death in the United States (U.S.) in 2020 and 2021, after COVID entered the ranks of the top 10 leading causes of death.²

However, 4.6 million people in the U.S., [an estimate made by the Institute for Clinical and Economic Review (ICER) based on 2019 data] have mild cognitive impairment (MCI) due to AD or mild AD dementia, but only 2.28 million patients with MCI due to AD or mild AD dementia are diagnosed.⁶ About one-third of people with MCI due to AD develop AD dementia within five years.² MCI can be caused by many processes, including cerebrovascular disease and other causes, but more than 60 percent of cases are due to AD.¹

Understanding Alzheimer's Disease and Recognizing Signs of Early Alzheimer's Disease

"I look at her pictures and remember her years of volunteer service. She was so vibrant, so beautiful, so smart and the cruelty of depriving her of all she worked for seems like some invisible slap in the face that just doesn't stop. I can't do anything about it except keep her with me at home, keeping someone with her at all times, keeping her fed, the bills paid, and answering her questions over and over. I just get so sad about it sometimes...I'm sorry...I sound like I'm complaining... I'm just missing my mom."

Caregiver Post³

Clinical Aspects of AD, Awareness, Early Detection and Diagnosis

With a physically debilitating disease, a person is often aware of the decline, of time passing, and of the love and support of care partners, but with a debilitating mental or cognitive disease, the struggle is often more difficult on the support system and loved ones. Delaying that decline for patients can mean more time to enjoy social connections, work, and family relationships, as well as delaying the financial drain of advancing disease on individuals, insurers, care partners, and the healthcare infrastructure in general.

Millions of Americans are living with AD, with an estimated 16 million unpaid care partners helping to look after them.⁵ Part of the challenge for better management of AD is early identification and differentiation of growing cognitive issues versus normal aging.¹ Resources have been developed for people to consider when cognitive changes may suggest discussion of concerns about memory loss with a physician. See Exhibit 1 for changes that suggest AD or dementia that patients or their loved ones may use to start that conversation to support early diagnosis.

"When you ask, a large percentage of people say they forget things, but it's not particularly sensitive nor specific. I was always taught that if people come in and tell you they are having memory problems, the majority of the time it is not significant, compared to when relatives and friends come in and complain...If a family member says, 'Yes, I'm seeing things (with memory problems),' that to me is much more of a red flag."

Small primary care practice provider¹

Exhibit 1: Signs of Alzheimer’s Dementia Compared with Typical Age-Related Changes¹

Signs of Alzheimer’s Dementia	Typical Age-Related Changes
Memory loss that disrupts daily life: One of the most common signs of Alzheimer’s dementia, especially in the early stage, is forgetting recently learned information. Others include asking the same questions over and over, and increasingly needing to rely on memory aids (for example, reminder notes or electronic devices) or family members for things that used to be handled on one’s own.	Sometimes forgetting names or appointments but remembering them later.
Challenges in planning or solving problems: Some people experience changes in their ability to develop and follow a plan or work with numbers. They may have trouble following a familiar recipe or keeping track of monthly bills. They may have difficulty concentrating and take much longer to do things than they did before.	Making occasional errors when managing finances or household bills.
Difficulty completing familiar tasks: People with Alzheimer’s often find it hard to complete daily tasks. Sometimes, people have trouble driving to a familiar location, organizing a grocery list or remembering the rules of a favorite game.	Occasionally needing help to use microwave settings or record a television show.
Confusion with time or place: People living with Alzheimer’s can lose track of dates, seasons and the passage of time. They may have trouble understanding something if it is not happening immediately. Sometimes they forget where they are or how they got there.	Getting confused about the day of the week but figuring it out later.
Trouble understanding visual images and spatial relationships: For some people, having vision problems is a sign of Alzheimer’s. They may also have problems judging distance and determining color and contrast, causing issues with driving.	Vision changes related to cataracts.
New problems with words in speaking or writing: People living with Alzheimer’s may have trouble following or joining a conversation. They may stop in the middle of a conversation and have no idea how to continue or they may repeat themselves. They may struggle with vocabulary, have trouble naming a familiar object or use the wrong name (e.g., calling a watch a “hand clock”).	Sometimes having trouble finding the right word.
Misplacing things and losing the ability to retrace steps: People living with Alzheimer’s may put things in unusual places. They may lose things and be unable to go back over their steps to find them. They may accuse others of stealing, especially as the disease progresses.	Misplacing things from time to time and retracing steps to find them.
Decreased or poor judgment: Individuals may experience changes in judgment or decision-making. For example, they may use poor judgment when dealing with money or pay less attention to grooming or keeping themselves clean.	Making a bad decision or mistake once in a while, such as neglecting to schedule an oil change for a car.
Withdrawal from work or social activities: People living with Alzheimer’s disease may experience changes in the ability to hold or follow a conversation. As a result, they may withdraw from hobbies, social activities or other engagements. They may have trouble keeping up with a favorite sports team or activity.	Sometimes feeling uninterested in family and social obligations.
Changes in mood, personality and behavior: The mood and personalities of people living with Alzheimer’s can change. They can become confused, suspicious, depressed, fearful or anxious. They may be easily upset at home, at work, with friends or when out of their comfort zones.	Developing very specific ways of doing things and becoming irritable when a routine is disrupted.

Source: 2023 Alzheimer’s Facts and Figures, Page 9, <https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf>

*For more information about the symptoms of Alzheimer’s, visit [alz.org/alzheimers-dementia/10_signs](https://www.alz.org/alzheimers-dementia/10_signs).

The Center for Disease Control (CDC) notes that there is compelling data for initiatives toward early diagnosis. Nearly 90 percent of Americans say that if they were exhibiting confusion and memory loss,

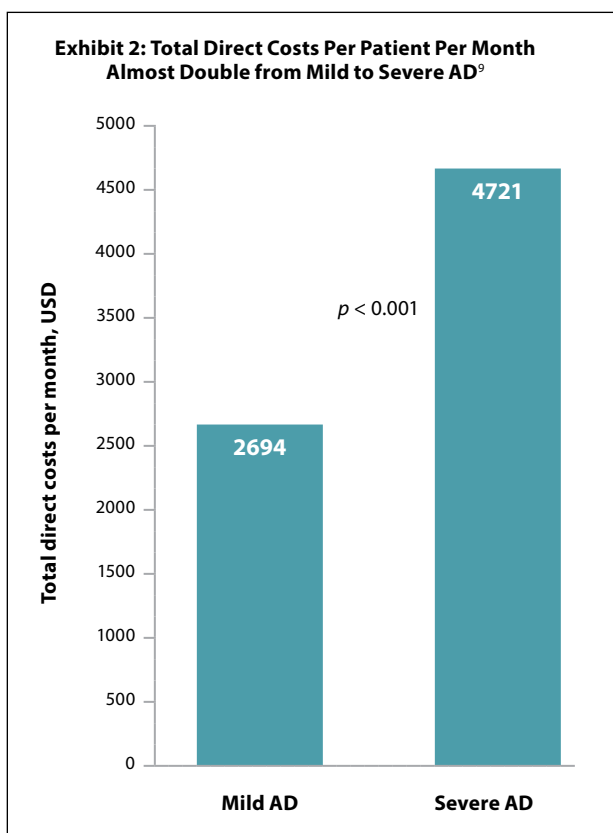
they would want to know if the cause of the symptoms was AD. Among those whose memory problems were creating functional difficulties, 42 percent had not shared these issues with a provider.³⁶

"At my doctor's office, they have a screening form that looks like it is for depression. If they had a screening form for forgetfulness, it might be easier to open the door for people if they have those issues."

Alzheimer's Association focus group member¹

Managed Care Considerations – The Economic Burden of Progressive AD

Per patient costs may almost double as disease progresses from mild to severe AD dementia, as shown in Exhibit 2. These costs include total direct medical (patient out-of-pocket and insurance costs for hospitalization, doctor visits, dentist visits, outpatient surgery, prescription drugs, home healthcare, etc.) and indirect household costs. Higher costs of care may not be indicative of increased disease burden. Such costs may be driven by a decline in ability to self-manage comorbid chronic conditions as well as a greater risk for accidents and injuries that increase with decreasing cognitive ability.⁹



*Fully adjusted for age, gender, race, education, mental status, residential region, hypertension, diabetes, cancer, lung disease, heart disease and stroke. p -values are from tests across all given cognitive states¹

AD = Alzheimer's disease

References: Ton TGN et al. *Alzheimers Dement.* 2017; 13(3):217-224

The financial, health, and societal burden of AD and mild dementia in patients affects all care partners as well. Eighty-three percent of the help provided to older adults in the United States comes from family members, friends, and other unpaid care partners.¹

In 2022, care partners of people with Alzheimer's or other dementias provided an estimated 19 billion hours of informal (unpaid) assistance, a contribution valued at \$339.5 billion.¹ The total lifetime cost of care for someone with dementia was estimated at \$392,874 in 2022 dollars. Seventy percent of the lifetime cost of care is borne by family care partners in the form of unpaid caregiving and out-of-pocket expenses for the person with dementia. Current estimates of the lifetime costs of care may underestimate the financial impact of a relative's dementia on a family care partner's health and workplace productivity, as other potential costs such as home modifications, respite service use and health/work productivity challenges are not considered in cost estimates.¹

Six in 10 care partners of people with Alzheimer's or another dementia were employed or had been employed in the prior year while providing care. These were people who worked an average of 35 hours per week while caregiving.¹

Managed care health plans and employer benefit design will find value in supporting early diagnosis for AD for both patients and their care partners. Besides direct patient costs of care, the effort, energy, and time that care partners place in providing support and care can impact their own insurers if they deprioritize their own healthcare or fall sick taking care of the patient. The CDC reports that economic modeling shows early diagnosis can greatly reduce healthcare costs across the nation, particularly through reduced hospitalizations and improved management of chronic conditions—potentially up to \$64,000 per person with dementia.³⁶

Diagnosis of Early AD

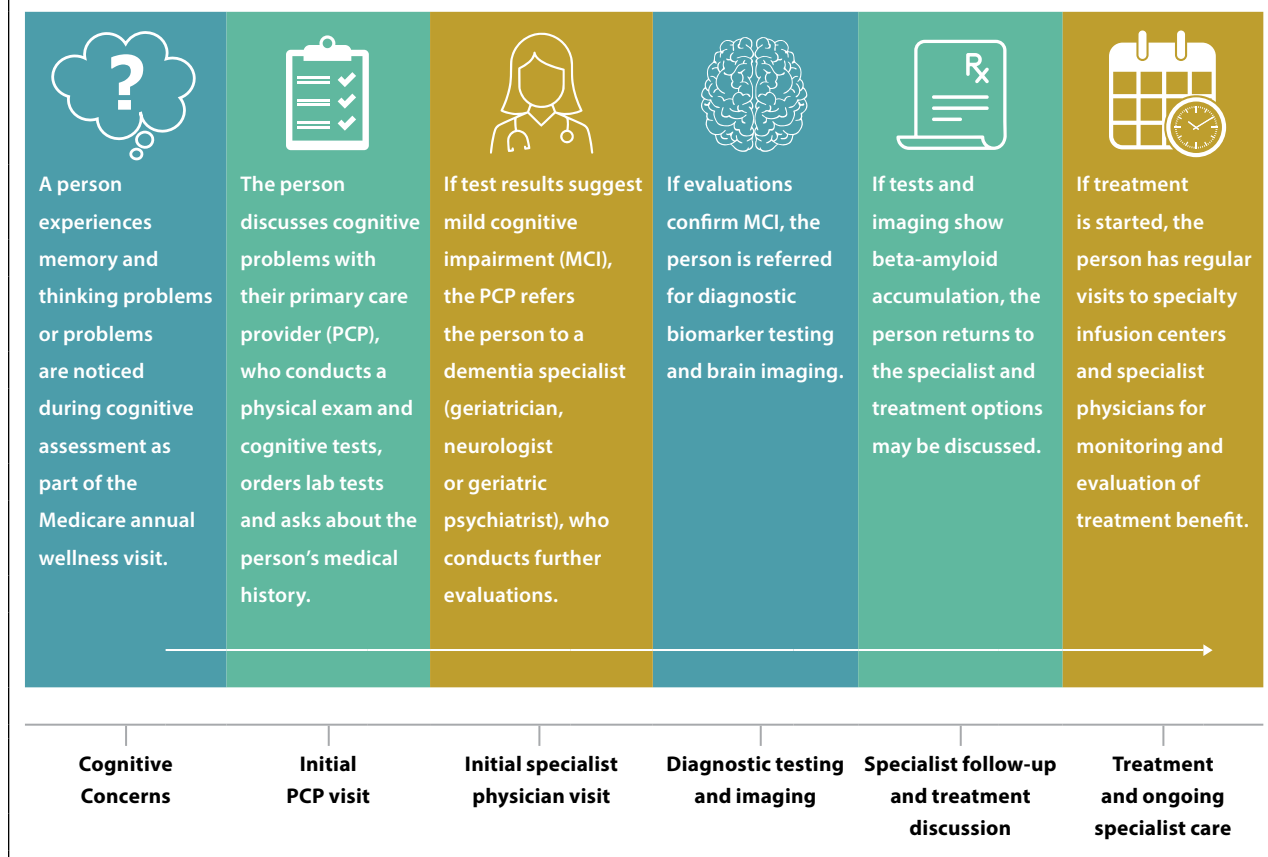
The Importance of Clinical Assessment and Early Diagnosis

The 2023 Alzheimer's Disease Facts and Figures Special Report found that only four in 10 Americans would talk to their doctor right away when experiencing symptoms of mild cognitive impairment. The rest indicated that they would live with their symptoms for a while, potentially until they become worse, or others expressed concern.¹

"I don't (speak to my doctor) because it doesn't seem like that big of a deal...not yet. It would have to be something dramatic. Losing my train of thought is not enough."

Alzheimer's Association focus group member¹

Figure 3: Patient Journey from Awareness of Cognitive Issues to Care from a Physician Specialist and Treatment¹








Source: 2023 Alzheimer's Facts and Figures Report, P. 87, <https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf>

The Earlier MCI Due to AD and Mild AD Dementia Are Diagnosed and Treated, The Greater the Opportunity for Benefit¹

About one-third of people with MCI due to AD develop AD dementia within five years.^{2,10,11} They begin to experience subtle deterioration in memory and judgement/problem-solving skills, although

symptoms may not yet interfere with daily activities.¹ Thus, MCI due to AD and mild AD are critical points for intervention, and intervening early can delay progression. Exhibit 4 illustrates the continuum of AD from preclinical, mild cognitive impairment (MCI), mild AD dementia, moderate AD dementia, to severe AD dementia.³⁷

Exhibit 4: Alzheimer's Disease Continuum ^{1,10,12,13,14,15,16,17,37}

AD continuum ¹						
	Preclinical AD 	MCI due to AD 	Mild AD dementia 	Moderate AD dementia 	Severe AD dementia 	
Duration in stage	2–15 years ²		3–7 years ²		2–6 years ²	1–7 years ²
Cognitive	• Appears normal ¹	• Subtle problems with memory, language, and thinking ¹	• Losing or misplacing a valuable object ⁵ • Forgetting material that was just read ⁵	• More problems with memory and language ¹ • More likely to become confused ¹ • Forgetful of events or personal history ⁴	• Ability to communicate verbally is greatly diminished ¹ • Loses awareness of recent experiences ⁵	
Neuropsychologic	• Appears normal ¹	• Subclinical changes: depression, anxiety, irritability, and aggression ³	• Anxiety ⁶ • Apathy ⁶ • Irritability ⁶ • Depressive symptoms ⁶	• Suspicious and agitated ¹ • Moody or withdrawn ⁵ • Delusions or compulsive, repetitive behavior ⁵	• Worsening hallucinations and agitation ⁷	
Functional	• Appears normal ¹	• Symptoms may not interfere with daily activities ¹ • Able to maintain hobbies ⁴	• Can function independently, but likely requires assistance ¹ • May still be able to drive ¹ • Difficulty performing tasks in social or work settings ⁵	• Difficulty bathing, dressing, and maintaining a home ¹⁴ • Trouble controlling bladder/bowels ⁵ • Changes in sleep pattern ⁵	• Difficulty eating, drinking, and walking ¹⁴ • Becoming bedbound and more susceptible to physical complications ¹ • Needs around-the-clock assistance ⁵	

AD = Alzheimer's disease; MCI= mild cognitive impairment.

Sources:

1. Alzheimer's Association. 2023 Alzheimer's disease facts and figures. *Alzheimer's Dement.* 2023 ;19(4) :1598-1695.
2. Vermont L et al. *Alzheimer's Dement.* 2019 ;15(7) :888-898.
3. Caselli RJ et al. *J Am Geriatr Soc.* 2018;66(4):671-678.
4. Cohen S et al. *J Prev Alzheimer's Dis.* 2022;9(3):507-522.
5. Alzheimer's Association. Stages of Alzheimer's. Accessed November 16, 2022. <https://www.alz.org/alzheimers-dementia/stages>.
6. Zvěřová M. *Clin Biochem.* 2019;72:3-6.
7. Jicha GA, Carr SA. *J Alzheimer's Dis.* 2010;19(1):253-272.
8. Alzheimer's Association. 2022 Alzheimer's disease facts and figures. *Alzheimer's Dement.* 2022;18(4):700-789.
9. Christensen DD. Prim Care Companion *J Clin Psychiatry.* 2002;4(2):63-69.

Clinical and Managed Care Considerations for Cognitive Screening and Early Diagnosis of AD

To identify AD early, cognitive screening and structural imaging are key first steps. Both treating physicians and managed care plans can support patients with flexibility to accommodate a variety of diagnostic tools.¹⁸

Treating physicians will be most familiar with the options for diagnosis and may express a preference for specific tools to inform individual patient diagnosis based on familiarity and/or preference of the health system or practice.¹⁸ Health plans will benefit from collaboration and close communication with treating providers regarding the physician's preferences and utilization of diagnostic tools. After a patient has presented with suspected cognitive changes, they may be assessed with calibrated diagnostic tools that are sensitive to MCI and mild AD dementia.¹⁸ While there are many cognitive assessment options for screening and testing to assess AD, it is not necessary to conduct all of them for assessment. Some commercial health plans are recognizing the value of allowing diagnosis with just one or two tests selected by the physician as appropriate for a given patient, thus potentially avoiding the time delays,

redundancy, and additional costs of requiring all the available tests.^{38,39}

Confirming Presence of Amyloid Beta Pathology

Biomarker-confirmed AD diagnoses enable the early identification of patients who may be appropriate for amyloid beta (Aβ) targeting therapies.¹ Aβ biomarkers are the first biomarkers to present abnormally in the course of AD and can be measured by CSF Aβ42 or amyloid PET.²¹ Elevated levels of Aβ can be determined 15 years before the onset of symptoms with a position emission tomography (PET) scan²⁰ and 20 years before the onset of MCI with a cerebrospinal fluid (CSF) assay.¹⁹

Physicians can now identify these biomarkers for AD in patients and begin a conversation with those patients and their families as to the most appropriate treatment options to fit the individual needs of each patient.

"Education is important. I need to know what I should do to delay the process. I want the doctor to provide strategies and education...what can I do to prevent it from (getting) worse."

Alzheimer's Association focus group member⁷

Managed Care Considerations – Diagnosis and the Medicare Cognitive Assessment and Care Plan Services

Testing and Diagnosis Barriers – Applying multiple coverage restrictions will delay timely patient AD diagnosis and restrict access to timely interventional treatment for a disease that will continue to progress unless it can be slowed down by the newer targeted therapies. If physicians are required to execute the battery of all possible cognitive tests for an AD diagnosis, they and the patient are likely to run into access challenges for testing sites and specialists. Patients and their care partners may be reluctant or unable to travel to distant urban centers for a battery of tests and delay addressing the indications of potential early AD symptoms. Some patients in rural areas may not have easy transportation or access to specialists capable of conducting the screening and imaging needed for diagnosis.

Medicare has established a billing code and instructions for timely patient AD diagnosis that may be of value to commercial health plans and employers. If a patient shows signs of cognitive impairment during a routine visit, as of January 1, 2024, Medicare covers a separate visit to thoroughly assess the patient's cognitive function and develop a care plan—under Medicare Cognitive Assessment and Care Plan Services (Current Procedural Terminology (CPT) code 99483. Among the expected cognitive assessment elements of the clinical visit would be to use standardized instruments for the staging of dementia.²²

Typically, a physician could spend 60 minutes face-to-face with the patient and independent historian to perform the following elements during the cognitive assessment:

- Examine the patient with a focus on observing cognition.
- Record and review the patient's history, reports, and records.
- Conduct a functional assessment of Basic and Instrumental Activities of Daily Living, including decision-making capacity.
- Use standardized instruments for staging dementia like the Functional Assessment Staging Test (FAST) or Clinical Dementia Rating (CDR).
- Reconcile and review for high-risk medications, if applicable.
- Use standardized screening instruments to evaluate neuropsychiatric and behavioral symptoms, including depression and anxiety.
- Conduct a safety evaluation for home and motor vehicle operation.
- Identify social supports including how much care partners know and are willing to provide care.

- Address Advance Care Planning and any palliative care needs.

Source: Cognitive Assessment & Care Plan Services, U.S. Department of Health & Human Services Guidance Portal²²

Patients with MCI Due to AD and Mild AD Dementia and Their Care Partners Need Support to Manage This Disease More Effectively

Improved Alzheimer's disease care requires conversations about memory at the earliest point of concern and a knowledgeable, accessible care team that includes primary care physicians and physician specialists to diagnose, monitor disease progression and treat when appropriate. This is especially true now, in an era when treatments that change the underlying biology of Alzheimer's are available.¹

With the availability of newer therapies, it is essential to educate and motivate healthcare professionals who are involved in all areas of AD care and care access to:

- 1) diagnose and treat MCI due to AD and mild AD dementia early and
- 2) ensure that access restrictions are not overly burdensome on the patient and provider.

Treatment Selection and Initiation for Early AD Intervention

Clinical Biomarkers and Anti-Amyloid Drug Class Treatment Initiation

Given the evident need as established by the CDC, recent advances are starting to open the possibility of early treatment. Biomarker-confirmed AD diagnoses create a path toward interventional treatment that may help to slow the progression of AD. These advances mark a significant change in the understanding about AD and offer improved treatment choices for patients and their families at the critical beginning of the disease.

"In a perfect world, we'd have treatments that completely stop decline and even restore function. We're not there, but this represents an important step toward that goal. So, there's hope. There's optimism. Our patients, particularly patients who are at earlier stages of the disease, have their lives to live and are really interested in living life fully. Anything that can help them do that for a longer period of time is welcome."

Dr. Scott McGinnis, Assistant Professor of Neurology at Harvard Medical School and Alzheimer's disease expert at Brigham and Women's Hospital²³

Anti-Amyloid Drug Class for Treating Early AD

Clinical research continues to identify potential anti-amyloid therapies that may help to slow the progression of disease in the appropriate patient. Anti-amyloid AD treatments are a newer emerging class of AD treatments, and ongoing research and clinical trials for AD treatments continue with the goal of providing more treatment options for patients with AD.^{24,25,26} Development of potential new treatment modalities continues for AD, including additional formulations.²⁷

Symptomatic Treatment for Patients With AD

Symptomatic Treatment – Before the advent of the anti-amyloid class of treatments, physicians had standard-of-care agents that were approved for the management of symptoms of AD. Several are also only recommended for moderate and/or severe stages of AD. Thus, only treating a patient with early AD using symptomatic treatments delays potential for slowing disease progression.²⁸

Managed Care Considerations – Treatment Selection and Initiation

Access for medications may be considered in terms of the patient’s ability to receive the treatment, to remain compliant and adherent, and be approved by their health plan for the treatment. CMS removed restrictions for patients with AD to give patients a better chance at treatments to slow the progression of AD by opening up access to needed PET beta amyloid imaging related to treatment. CMS updated their Beta Amyloid Positron Tomography in Dementia and Neurodegenerative Disease Version 1 National Coverage Determination on October 13, 2023, to remove the NCD and the limitations it had previously set that limited patients with AD to just one lifetime PET scan.²⁹

Alzheimer’s Disease Registries

Accompany Arrival of Anti-Amyloid Drug Class

Medicare announced on June 22, 2023, that drugs with traditional FDA approval to slow the progression of Alzheimer’s disease will be covered by Medicare, with collection of real-world utilization known as Coverage with Evidence Development (CED). The drugs must be prescribed in settings that also support the collection of real-world information to study their usefulness for people with Medicare. “Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer’s Disease Registry” was launched nationwide by CMS on July 6, 2023. The CMS data registry collects information from all providers across all states. The CMS registry is designed with a high ease of use and does not

restrict access based upon requirements for clinical information submitted.³⁰

Clinicians will provide the following information to the registry at <https://qualitynet.cms.gov/alzheimers-ced-registry>:⁴⁰

Clinician/Submitter Demographic Information

- Clinician’s National Provider Identifier (NPI)
- Address of the submitter (chosen from a drop-down menu based on the NPI)

Patient’s Demographic Information

- Medicare Beneficiary ID (MBI)

Patient’s Clinical Information

- Individual’s clinical diagnosis (mild cognitive impairment or mild Alzheimer’s disease dementia).
- Whether the individual is taking any anticoagulation or antiplatelet drugs.
- Results of the individual’s amyloid positron emission tomography (PET) scan, cerebrospinal fluid (CSF) test, or other amyloid test.
- Specific anti-amyloid monoclonal antibody being administered.
- Whether there is evidence of adverse events such as brain swelling or hemorrhage referred to as ARIA-E or ARIA-H.
- Results of at least one test each of cognition and overall function that were used to diagnose and treat the individual with mild cognitive impairment or mild Alzheimer’s disease dementia.

Source: “CMS Announces New Details of Plan to Cover New Alzheimer’s Drugs”, Department of Health & Human Services Centers for Medicare & Medicaid Services Press Release, June 22, 2023³⁰

The CMS National Patient Registry data collection portal direct link (found at <https://qualitynet.cms.gov/alzheimers-ced-registry>) requires at least one cognitive test result (the Montreal Cognitive Assessment (MoCA) score or other cognitive test) and at least one functional test results (the Functional Activities Questionnaire (FAQ) score or other functional test).³¹

On January 31, 2024, CMS published a list of studies that have been determined to meet the requirements for coverage under CED for AD. That list may be found at <https://www.cms.gov/medicare/coverage/coverage-evidence-development/monoclonal-antibodies-directed-against-amyloid-treatment-alzheimers-disease-ad>.³²

Coverage Evaluations and Complex Prior Authorization Criteria May Delay Timely Access to Early AD Treatment, Potentially Impacting Opportunity to Slow Disease Progression

When CMS issues a new National Coverage Determination (NCD) most commercial insurers tend to adjust their own coverage accordingly. Despite initiatives to educate on the importance of early AD identification and slowing progression, some U.S. health plans and Medicare Advantage Plans have been slower to recognize coverage for biomarker screening and anti-amyloid treatments—sometimes still labeling them as not medically necessary or investigational.

When determining commercial coverage parameters for anti-amyloid treatments, commercial insurers may inadvertently or mistakenly reference clinical trial criteria from earlier trials or from trials of earlier anti-amyloid treatments versus the trials upon which traditional FDA approval was based. Andy Liu, MD, associate professor of neurology at Duke University noted that “The biggest hurdle is probably just variability. There is a lag in terms of the policies, with many of them still based on the aducanumab criteria.”³³

Considerations for Managed Care Capture of AD Clinical Information and Patient Site of Treatment Concerns

General registries and policies should allow for the timely capture of important AD clinical information without burdening patients and physicians with required completion of multiple cognitive and/or functional tests. Variation in accessibility and timing for multiple tests is likely to restrict access for patients and physicians, and delay both treatment and the utility of the registry process. The ease of use and access of the CMS AD registry provides valuable information for managed care plans and payers in developing their own policies for AD coverage criteria.

Clinical Considerations – Site of Treatment Options

Given the research and development of different AD treatment modalities, providing provider and patient choice in Site of treatment (self-administered at home for an injection versus infusion center for infusion) will allow for flexibility based upon the individual patient’s needs. Patients and their care partners experience individual challenges of access, support needs, understanding and diagnosis—going to the doctor’s office for an infusion or being able to receive an injection in their home—can make a large difference in patient compliance and adherence for targeted treatment to slow disease progression.

Anti-amyloid therapies prescribed for patients with

MCI or mild dementia due to AD add complications to the expectations for patient compliance and adherence with targeted therapy treatment administration.²⁷

Managed Care Considerations – Site of Treatment Options

Having site of treatment choices is about far more than convenience; it can mean treatment versus non treatment, and appropriate treatment may help to slow the progression of AD, thus allowing patients and their care partners to enjoy family, work, and social connections longer, as well as their quality of life.

In most cases, the functional and cognitive issues will vary depending on each patient. This may mean that one patient is able to dress, leave the house, travel to a medical office for treatment, while another may not be able to function with the processes and decision-making for taking those steps, and would be better served receiving an injection at home. In other cases, the patient may be fairly functional at home, but reliant on a care partner for successful travel outside the home, adding significant demands upon the limited available time of such care partner to keep the patient compliant with medication schedules. These variations will require flexibility for treatment site of care that will be critical for the patient and their medical team to ensure successful patient compliance and adherence to the medication plan, an important consideration for managed care coverage and benefit design.

“We sometimes cannot get Mom to dress in clean clothes, brush her teeth, or leave the house to go to an appointment. Other times, she has gone to an appointment with her care partner and refused for over an hour to get back in the car for the drive home, because she decided that he was not the person who drove her to the appointment and not someone she knows. She threatened to walk away from the car but was an hour from home and did not know how to get home by walking. A home administered treatment could be an option to help simplify steps for the patient and care partner.”

Confidential - Daughter of AD patient, Feb. 20, 2024

Monitoring and Surveillance During Treatment with Anti-Amyloid Drug Class

Clinical Information for

Monitoring and Surveillance

Surveillance magnetic resonance imaging (MRI) examinations during clinical trials of the anti-amyloid drugs showed vasogenic edema and cerebral microhemorrhages in a subset of patients. In July 2010, an Alzheimer’s Association Research roundtable work group introduced the term Amyloid Related Imaging Abnormalities (ARIA) to describe such

MRI findings in patients undergoing monoclonal antibody therapy for AD. ARIA refers to imaging findings seen exclusively on MRI as no Positron Emission Tomography (PET) findings of ARIA have been described. Although PET has a central role in AD diagnosis, PET currently has no role in the diagnosis and evaluation of ARIA.³⁴

ARIA is a consequence of amyloid presence in blood vessel walls that can occur spontaneously in patients with AD or as a result of treatment with a monoclonal antibody that removes amyloid.^{41,42} ARIA can be broadly categorized into ARIA characterized by brain edema or sulcal effusions (ARIA-E) and ARIA characterized by microhemorrhages and superficial siderosis (ARIA-H).³⁴

Routine surveillance MRI should be supplemented with ad hoc MRI in patients with new-onset symptoms potentially associated with ARIA. This careful monitoring can help detect ARIA early. Patient counseling (preferably by the clinical team and/or neurologist) regarding ARIA is recommended to avoid unnecessary alarm related to imaging results. This can be described to patients as “temporary swelling” in the brain and as “spots of bleeding” in or on the surface of the brain. Patients should also be counseled at the same time that most of these imaging manifestations are clinically silent, and it is expected for the patient to be asymptomatic despite having positive MRI findings.³⁵

Managed Care Considerations for Monitoring and Surveillance

If multiple MRIs are required by the payers for approval for continuing infusion doses, care coordination may become a challenge. To add a cumbersome process that requires scheduling and executing the MRI test, requiring the HCP to submit results to the payer, allowing time for the payer to review and approve, and then scheduling the patient for an appointment in time for the next scheduled MRI is very likely to mean delays in treatment and possible impact on the slowing of AD. Managed care desires for monitoring and surveillance will require awareness of and allowances for timely care coordination so that patient treatment is not compromised.

Summary – Key Managed Care Implications to Support Early Management and Slowing Progression of AD

Early diagnosis and timely intervention to slow the progression of AD in early AD and mild dementia patients may reduce the burden on the patients, insurers, and care partners. Patients starting to face functional and cognitive decline now have more

clinical rationale to seek screening and assessment from their physicians. Advances in cognitive assessments and biomarker screening may improve the awareness and diagnosis rates for the estimated 4.6 million people in the U.S., who have MCI due to AD or mild AD dementia. Targeted therapies now have the potential for appropriate patients to slow the progression of AD and mild dementia due to AD. Slowing the disease may help to reduce the burden on patients and care partners, and potentially reduce the total cost of care.

- Delaying the progression of early onset AD not only improves the mental and health status of the AD patient, slowing the onset of the health and cost burden of advancing AD, but also positively improves the productivity and fiscal impact of the family and care partners.⁴
- MCI due to AD and mild AD are critical points for intervention, and intervening early can slow progression. Delaying progression in earlier stages of AD may allow patients to retain crucial cognitive, neuropsychological, and functional abilities for a longer period of time.
- Managed care coverage criteria should allow for the timely capture of important AD clinical information without burdening patients and physicians with required completion of multiple cognitive and/or functional tests. It is not necessary to conduct all available diagnostic tools. Variation in accessibility and timing for multiple tests is likely to restrict access for patients and physicians, and delay both treatment and the utility of the review process. Just one or two tests selected by the physician as appropriate for a given patient can avoid time delays, redundancy, and additional costs of requiring all the available tests. The ease of use and access of the CMS AD registry provides valuable information for managed care plans and payers in developing their own policies for AD coverage criteria.
- When considering inclusions and parameters for AD coverage, managed care plans will want to recognize the role of registries, symptomatic treatments, and early trials criteria that have evolved with expanded information.
 - General registries and policies should allow for the timely capture of important AD clinical information without burdening patients and physicians with required completion of multiple cognitive and/or functional tests. The ease of use and access of the CMS AD registry provides valuable information for managed care plans and payers in developing their own policies for AD coverage criteria.

- Symptomatic treatments are only recommended for moderate and/or severe stages of AD. Thus, coverage restrictions that might only allow treating a patient with early AD using symptomatic treatments delays potential for slowing disease progression.
- The rapid evolution of clinical knowledge and trial results regarding early intervention and slowing of AD progression will require managed care plans to exercise diligent understanding of evolving treatment parameters, and to avoid using outdated earlier clinical trial criteria for coverage that will restrict patient access and delay timely treatment.
- Managed care support of early diagnosis and biomarker testing for appropriate use of anti-amyloid treatments can greatly reduce^{36,37} direct healthcare costs for AD patients across their member base, as well as improve the indirect costs associated with time demands, and other health stressors for care partners.
- Unique individual manifestations of early AD will create challenges that will require benefit design and coverage flexibility in cognitive assessment, screening, and treatment sites of care.
- With coordinated coverage, early identification, diagnostics, and treatment to slow the progression of advanced AD, patients, providers, employers, and managed care organizations together can improve the journey of patients with Alzheimer's Disease, impact the total costs of care and improve patient outcomes.
- Dementia care and integration of AD is now more manageable as a targeted patient-centric pathway journey, with appropriate support.

For the first time, physicians have biomarkers to look for in diagnosing early AD and mild dementia due to AD, with treatments that can slow the progression of the disease. This new patient-centric pathway journey begins with recognition of cognitive concerns. The medical and health plan community have a new opportunity to educate and support Americans that have their own issues or see cognitive issues in loved ones. There is now value in turning to the medical community for intervention that can preserve dignity and quality of life in the face of AD by slowing the progression and impact of Alzheimer's Disease.

REFERENCES

1. 2023 Alzheimer's Disease Facts and Figures. Alzheimer's Association. 2023.
2. 2023 Alzheimer's Disease Facts and Figures: Alzheimer's Dementia, 2023. pp 1598-1695.
3. Caregiver Post, March 2015, Aging Care Caregiver Forum, Alzheimer's & Dementia Discussions, <https://www.agingcare.com/discussions/hard-watching-mom-slipping-away-alzheimers-178224.htm>
4. National Plan to Address Alzheimer's Disease: 2022 Update : Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health, and Human Services, 2022.
5. Caregiving for a Person with Alzheimer's Disease or a Related Dementia, Alzheimer's Disease and Health Aging, Centers for Disease Control and Prevention, June 30, 2023, <https://www.cdc.gov/aging/caregiving/alzheimer.htm>
6. ICER.AlzFinalEvidenceReport.2021., Grace A. Lin, Melanie D. Whittington, Patricia G. Synnott, et al., Institute for Clinical and Economic Review. 8/5/2021. pp 1-157.
7. Assessing the Preparedness of the U.S. Health Care System Infrastructure for an Alzheimer's Treatment. Liu JL, et al. s.l. : Rand Corp., 2017. pp 1-16.
8. Early Intervention in Alzheimer's Disease: A Health Economic Study of the Effects of Diagnostic Timing. Barnett, J., et al. May 7, 2014, *BMC Neurology*, Vol 101, pp 1471-2377.
9. The Financial Burden and Health Care Utilization Patterns Associated with Amnesic Mild Cognitive Impairment, Ton T., et al., *Alzheimer's & Dementia*, March 2017, Vol 13, pp 217-224
10. Alzheimer's Association. Alzheimer's Association-Alzheimer's Stages. Alzheimer's Association. [Online] 6 30, 2022. [Cited: 10 20, 2023.] <https://www.alz.org/alzheimers-dementia/stages>.
11. Alzheimer's Association. New Alzheimer's Association Report Finds Doctors and the Public Face Challenges in Understanding and Distinguishing Early Alzheimer's Development from "Normal Aging." Alzheimer's Association 2022. p 1.
12. Duration of Preclinical, Prodromal, and "Dementia Stages of Alzheimer's Disease in Relation to Age, Sex and APOE Genotype, Vermunt, L., et al., *Alzheimer's & Dementia*, 2019, Vol 15, Iss 7, pp 888-898.
13. Personality Changes During the Transition from Cognitive Health to Mild Cognitive Impairment, Caselli, R., et. al., *Journal American Geriatric Society*, 2018 Vol 66 pp. 1-8
14. Lecanemab Clarity AD: Quality-of-Life Results from a Randomized, Double-Blind Phase 3 Trial in Early Alzheimer's Disease. Cohen S, et al. September 29, 2023, *Journal of Prevention of Alzheimer's Disease*, Vol 10, pp 771-777.
15. Clinical Aspects of Alzheimer's Disease, Zvěřová M, et al, *Clinical Biochemistry*, Oct. 2019 Vol 72 pp 3 - 6
16. Conceptual Evolution in Alzheimer's Disease: Implications for Understanding the Clinical Phenotype of Progressive Neurodegenerative Disease, Jicha, GA, Carr, SA, *Journal of Alzheimer's Disease*, 2010, Vol 19, Is. 1, pp 253-272
17. Practical Principles for the Management of Alzheimer's Disease. Christensen, D., *The Primary Care Companion to the Journal of Clinical Psychiatry*, April 2, 2022, Vol 4, pp 63-69.
18. Alzheimer's Association. Medical Tests for Diagnosing Alzheimer's. Alzheimer's Association. [Online] 06 28, 2022. [Cited: 10 24, 2023.] https://www.alz.org/alzheimers-dementia/diagnosis/medical_tests.
19. High-Precision Plasma-Amyloid 42/40 Predicts Current and Future Brain Amyloidosis. Schindler, S et al. 17, October 22, 2019, *Neurology*, Vol 93, pp e1647-e1659.

20. NIA-AA Research Framework: Toward a Biological Definition of Alzheimer's Disease. Jack CR Jr, et al. April 2018, *Alzheimer's Dement*, Vol 14, pp 535-562.
21. Tracking Pathophysiological Processes in Alzheimer's Disease: An Updated Hypothetical Model of Dynamic Biomarkers. Jack, CR, et al. 2, Feb 2013, *The Lancet Neurology*, Vol 12, pp 207-216.
22. Cognitive Assessment & Care Plan Services, U.S. Department of Health & Human Services Guidance Portal, Published 7/28/2021, <https://www.hhs.gov/guidance/document/cognitive-assessment-care-plan-services-0>)
23. Dr. Scott McGinnis, Assistant Professor of Neurology at Harvard Medical School and Alzheimer's disease expert at Brigham and Women's Hospital, Start of New Era for Alzheimer's Treatment, Harvard Gazette interview, June 5, 2023, <https://news.harvard.edu/gazette/story/2023/06/start-of-new-era-for-alzheimers-treatment/>
24. Biogen to Realign Resources for Alzheimer's Disease Franchise, Biogen.com website, news release, January 31, 2024, <https://investors.biogen.com/news-releases/news-release-details/biogen-realign-resources-alzheimers-disease-franchise>
25. FDA Grants Traditional Approval for lecanemab-irmb for the Treatment of Alzheimer's Disease, Eisai.com website, news release July 7, 2023, <https://www.eisai.com/news/2023/news202349.html>
26. Results from Lilly's Landmark Phase 3 Trial of Donanemab Presented at Alzheimer's Association Conference and Published in JAMA, Lilly News Release July 17, 2023, <https://investor.lilly.com/news-releases/news-release-details/results-lillys-landmark-phase-3-trial-donanemab-presented>
27. Eisai Presents New LEQEMBI[®] (lecanemab-irmb) Investigational Subcutaneous Formulation Interim Study Results and Clinical Improvement Data in Earlier Stages of Early Alzheimer's Disease from Additional Analyses of Clarity AD at the Clinical Trials on Alzheimer's Disease (CTAD) Conference, Eisai press release, Oct. 26, 2023, <https://www.eisai.com/news/2023/news202368.html>
28. Treatment Combinations for Alzheimer's Disease: Current and Future Pharmacotherapy options, Cummings, J, et al., *Journal of Alzheimer's Disease* , 2019 Vol 67 Issue 3, pp 779-794, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6398562/>
29. CAG-00431R National Coverage Analysis Decision Memo, October 13, 2023, Center for Medicare & Medicaid Services, <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=308>
30. Medicare Rolls Out Alzheimer Patient Registry After FDA Approval[®], Castronuovo, C, Phengsitthy, N, Bloomberg Law News, July 6, 2023, <https://news.bloomberglaw.com/health-law-and-business/medicare-rolls-out-alzheimer-patient-registry-after-fda-approval>
31. CMS Alzheimer's Disease Sample Form and Data Dictionary, Center for Medicare & Medicaid Services Quality Net Website: Alzheimer's CED Registry Resources, <https://qualitynet.cms.gov/alzheimers-ced-registry/resources> and <https://qualitynet.cms.gov/files/64a7185c749e52001c0e6cdf?filename=Alzheimers%20Disease%20Treatment%20-%20CED%20Study%20Registry%20Form%20Resources.pdf>
32. Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD), Centers for Medicare & Medicaid Services, January 31, 2024, <https://www.cms.gov/medicare/coverage/coverage-evidence-development/monoclonal-antibodies-directed-against-amyloid-treatment-alzheimers-disease-ad>
33. More Than Half of Commercial Payers Are Denying Coverage for Lecanemab, Shaw, G., *Neurology Today*, December 7, 2023, https://journals.lww.com/neurotodayonline/fulltext/2023/12070/more_than_half_of_commercial_payers_are_denying.8.aspx#:~:text=The%20remaining%2015%20health%20plans,%2C%20Humana%2C%20and%20United%20Healthcare.
34. Amyloid-Related Imaging Abnormalities: An Update, Roytman, M. et al., *American Journal of Roentgenology*, Vol 220, Iss 4, Nov. 2, 2022, [https://ajronline.org/doi/full/10.2214/AJR.22.28461#:~:text=Amyloid%2Drelated%20imaging%20abnormalities%20\(ARIA,for%20Alzheimer%20disease%20\(AD\)](https://ajronline.org/doi/full/10.2214/AJR.22.28461#:~:text=Amyloid%2Drelated%20imaging%20abnormalities%20(ARIA,for%20Alzheimer%20disease%20(AD)).
35. Amyloid-Related Imaging Abnormalities in Alzheimer Disease Treated with Anti-Amyloid-Therapy, Agarwal, A., et al., *RadioGraphics*, Vol. 43 No 9, <https://pubs.rsna.org/doi/10.1148/rg.230009#:~:text=Routine%20surveillance%20MRI%20should%20be,can%20help%20detect%20ARIA%20early>.
36. Advancing Early Detection, Centers for Disease Control Healthy Brain Initiative, January 2019, <https://www.cdc.gov/aging/healthybrain/pdf/Issue-Map-Early-Detection-508.pdf>
37. NAMCP Medical Director's Spotlight Guide: An Intervention for Early Alzheimer's Disease, National Association of Managed Care Physicians *Journal of Managed Care Medicine*, 2023
38. Medical Policy:Lecanemab-irmb RX501.152. HCSC Health Care Service Corporation. [Online] 08 15, 2023. [Cited: 10 24, 2023.] https://medicalpolicy.hcsc.com/activePolicyPage?path=rx/RX501.152_2023-08-15&corpEntCode=HCSC&corpEntCd=HCSC.
39. Medical Policy: Prescription Drugs: Central Nervous System Drugs: Leqembi. BlueCross BlueShield Federal Employee Program. [Online] 3 10, 2023. [Cited: 10 24, 2023.] <https://www.fepblue.org/-/media/FEPBlue-Sitecore-10-Media/PDFs/04-01-2023/Phar%20Policy%20New%20Add/560056%20Leqembi%20lecanemabirmb.pdf>.
40. CMS announces new details of plan to cover new Alzheimer's drugs, CMS, June 22, 2023, <https://www.cms.gov/newsroom/fact-sheets/cms-announces-new-details-plan-cover-new-alzheimers-drugs>
41. Barakos, J. et al, Detection and Management of Amyloid-Related Imaging Abnormalities I Patients with Alzheimer's Disease Treated with Anti-amyloid beta therapy, *Journal Prevention Alzheimer's Disease*, 2022 Feb. 2, p 1-10
42. Cogswell PM et al, Amyloid-Related Imaging Abnormalities with Emerging Alzheimer Disease Therapeutics Detection and Reporting Recommendations for Clinical Practice, *American Journal Neuroradiol* Sept. 1, 2022, Vol 43 Iss 9, pp E19-E35

