Neurodegenerative Disease

OBJECTIVE

The objective of this Clinical Practice Guideline (CPG) is to provide evidence-based practice recommendations for the treatment and management of Neurodegenerative Diseases (NDs). This includes the most common types of NDs – Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), and Huntington's disease. The CPG outlines Measureable Health Outcomes, discusses behavioral health implications, and outlines organizations that WellCare aligns with regarding NDs.

OVERVIEW

Neurodegenerative diseases occur when nerve cells in the brain or peripheral nervous system lose function over time and deteriorate. Treatments can relieve some of the physical and/or mental symptoms however there is no cure. The risk of being diagnosed with a ND increases with age. Genetics also play a role as well as one's environment (e.g., toxins, chemicals, viruses).[1] These types of disease can impact a patient's balance, movement, talking, breathing, and heart function. While many NDs are genetic, other causes may include a medical condition such as alcoholism, a tumor, or a stroke. The cause is not known in some cases.[2] Concerns surround the aging population in the United States as diagnosis is often made in mid- to late-life. By 2030, as many as 1 in 5 Americans will be over the age of 65. If left untreated, estimates show that over 12 million people will suffer from a ND in 30 years. The emphasis must be on treatment as well as research for treatments and cures.[3] The most common types of NDs are Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), and Huntington's disease. Approximately 5 million Americans suffer from Alzheimer's, 1 million from Parkinson's, 30,000 from ALS, and 30,000 from Huntington's.[3] The common types of ND are outlined below.

Alzheimer's Disease

Dementia refers to any disease that causes a change in memory and/or thinking skills that is severe enough to impair a person's daily functioning. The most common type is Alzheimer's disease. Most dementias are caused by a gradual worsening of symptoms over the course of years due to progressive damage to nerve cells in the brain. Symptoms vary from among individuals and include: memory problems, mood changes, difficulty walking or speaking, or getting lost).[4]

Alzheimer's disease (AD) is an age-related, non-reversible brain disorder that develops over a period of years. It is the most common cause of dementia among people age 65 and older. Symptoms gradually lead to behavior and personality changes, a decline in cognitive abilities such as decision-making and language skills, and problems recognizing family and friends; the late stages of Alzheimer's leads to a severe loss of mental function. Diagnosis in one's 30s, 40s, and 50s is rare (early onset) – over 90 percent of Alzheimer's diagnosis are in people over the age of 65 (late onset). The course of disease varies, as does the rate of decline. In most cases, symptoms initially appear after age 65. Risk factors include age, genetic, environmental, and lifestyle factors. Memory loss does not always equate to having dementia – Providers should rule out any other potential causes of memory loss such as systemic abnormalities (metabolic syndrome), in which the combination of high blood pressure, high cholesterol, and diabetes causes confusion and memory.[5]

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As the population in the United States of those over age 65 continues to rise, the number of diagnoses of Alzheimer's or other dementias will also rise. The population of Americans in this cohort is expected to nearly double from 48 million to 88 million by 2050. This is a result of the Baby Boom generation living past age 65 – the age range of greatest risk of being diagnosed. For perspective, the initial members of generation turned 70 in 2016. The following states estimate an increase in prevalence of 35% or more of Alzheimer's dementia between 2017 and 2025: Alaska, Arizona, Florida, Idaho, Nevada, New Mexico, South Carolina, Utah, Vermont, and Wyoming. Another 20 states expect an increased prevalence of over 20%.[6]

- Of the 10 leading causes of deaths in the United States, Alzheimer's is the only one that cannot be prevented, slowed or cured.
- 1 in 10 people over age 65 has Alzheimer's. Millions of Americans have Alzheimer's or other dementias.
- Risk increases with age. Diagnosis of Alzheimer's dementia is 3% among people age 65-74, 17% among people age 75-84, and 32% are among those over the age of 85.
- Of people who have Alzheimer's dementia, 82% are age 75 or older.
- Based on data for Medicare beneficiaries over age 65, dementia had been diagnosed in 7% of Whites, 9.4% of African-Americans and 11.5% of Hispanics.
- Between 2000 and 2014 there was an 89% increase in deaths due to Alzheimer's. Deaths nearly doubled during this period while deaths from heart disease (the leading cause of death) have declined.

While more non-Hispanic whites are living with the disease than any other racial/ethnic group in the United States, older African-Americans and Hispanics are more likely than older Whites to have the disease (per capita). Older African-Americans are about twice as likely to have the disease as older Whites; Hispanics are about one and one-half times as likely to have dementia as older Whites. Varying lifestyle and socioeconomic risk factors across racial/ethnic groups likely account for most of differences related to risk by race, especially among African-American and Hispanics. This includes lower levels of education, higher rates of poverty, and greater exposure to early life adversity and discrimination. Genetics do not appear to play as large of a role among racial and ethnic groups as health conditions do. Cardiovascular disease and diabetes are associated with an increased risk for dementias – they account for these differences as they are more prevalent in African-American and Hispanic people. Vascular dementia accounts for a larger proportion of dementia in African-Americans than in whites.[6]

The costs of health care and long-term care for those with Alzheimer's or other dementias are high. Payment for care related to dementia is estimated to be $259 billion in 2017. Medicare and Medicaid are expected to cover $175 billion (67%) of the total health care and long-term care payments. Out-of-pocket expenses are estimated to total $56 billion (22%). Looking forward, annual payments for health care, long-term care and hospice care is estimated to increase from $259 billion in 2017 to more than $1.1 trillion in 2050. This represents a more than four-fold increase in both government spending (Medicare and Medicaid) and in out-of-pocket spending.[6]

In terms of hospital stays, those with Alzheimer's or other dementias are twice as much as other older people. Utilization of health care services by people with other serious medical conditions is strongly affected by the presence or absence of dementia. Of note, individuals with coronary artery disease, diabetes, chronic kidney disease, chronic obstructive pulmonary disease (COPD), stroke or cancer who also have dementias have higher utilization (and costs) compared to individuals with these medical conditions but no coexisting dementia. Skilled nursing facility stays and home health care visits among older people are also higher than those without dementia.[6]

To review additional information from the Alzheimer's Association's annual report, click here.[6]

Parkinson's Disease

Parkinson's disease (PD) is caused by a loss of dopamine-producing brain cells. The disease is characterized by four primary symptoms: tremor (or trembling in hands, arms, legs, jaw, face); rigidity (or stiffness of the limbs and trunk); bradykinesia (slowness of movement); and postural instability (impaired balance and coordination). Age of onset is typically over the age of 60. Initial symptoms are subtle and gradually occur and ultimately interfere with activities of daily living (ADLs). Progression of the disease varies by individual. Diagnosis is made based on medical history and a neurological examination; brain scans or laboratory tests may be requested to rule out other diseases. Additional symptoms include:[7]

- Depression and other emotional changes
- Difficulty in swallowing, chewing, and speaking
- Urinary problems or constipation
- Skin problems
- Sleep disruptions

As many as one million Americans live with Parkinson's disease and approximately 60,000 Americans are diagnosed annually. Worldwide, over 10 million people have Parkinson's. Risk for the disease increases with age however 4% are diagnosed before the age of 50. Men are one and a half times more likely to have Parkinson's than women.[8] The combined direct and indirect cost of Parkinson's (including treatment, social security, lost income) is estimated to be nearly $25 billion per year in the United States alone. Medication costs $2,500 a year alone; therapeutic surgery can cost nearly $100,000 per patient.[7]

PD is a chronic disease as well as a progressive disease as symptoms grow worse over time. Some individuals become severely disabled while others experience minor motor disruptions. Tremors may also be a common symptom for some yet others report it as a minor complaint while other symptoms can cause more concern. Currently there is no cure for PD however there are medications that can provide dramatic relief. Surgery may be needed when the disease is not responsive to medication. Deep brain stimulation (DBS) is an FDA approved treatment where electrodes are implanted into the brain and connected to a small electrical device called a pulse generator that can be externally programmed. DBS may also decrease the need for levodopa and related drugs – this in turn decreases dyskinesias (involuntary movements), a common side effect of levodopa. DBS also may alleviate variation in symptoms as well as a reduction in tremors, slowness of movements, and gait problems.[7]

Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's Disease)

Amyotrophic lateral sclerosis (ALS) is a rapidly progressive that can be fatal. It affects the nerve cells (neurons) in the brain and spinal cord that control voluntary muscle movement (e.g., walking, breathing, chewing, talking). Motor neurons that connect from the brain and spinal cord to the rest of the body degenerate and die, thus messages are not sent to muscles. The progression of ALS includes a gradually weakening of muscles that can waste away and twitch; the brain cannot start and control voluntary movement. Initial symptoms are noticed in the arms and hands, legs, or swallowing muscles. Those with the disease will see a decrease in strength and become unable to move their arms and legs, and to hold the body upright. Breathing issues and cognitive issues may also be present. The cause of ALS has no known cause but is believed to be inherited in a small number of cases.[9]

Progression of ALS varies in individuals however, muscle weakness and atrophy spread throughout the body as ALS progresses. Increased problems with moving, swallowing, and speaking/forming words are signs of progression. In the later stages, those with ALS will be unable to stand or walk, get in and out of bed, or use their hands and arms; breathing difficulties also develop as the respiratory system muscles weaken. Ventilation support can ease symptoms and prolong life however it does not impact the progression of disease. Respiratory failure is a common cause of death – typically within 3 to 5 years from the onset of symptoms. Ten percent of individuals survive for 10 or more years.[9]

Huntington's Disease

Huntington's disease (HD) is the result of the degeneration of brain cells in motor control regions of the brain; the disease can impact other areas as well. Symptoms get progressively worse and can include uncontrolled movements, abnormal body postures, and changes in behavior, emotion, judgment, and cognition. Impaired coordination, slurred speech, and difficulties with feeding and swallowing are also common. The disease is common between ages 30 and 50 however juvenile HD can occur in those under age 20. Juvenile HD has some differences including unsteadiness, rigidity, difficulty at school, and seizures. The disease impacts more than 30,000 Americans and is caused by a mutation in the gene for a protein called huntingtin. This results in the cytosine, adenine, and guanine (CAG) building blocks of DNA to repeat many more times than is normal. A person who inherits the HD gene will eventually develop the disease; genetic testing is one tool to help in the diagnosis of HD. Huntington's disease causes disability that worsens over time and the individuals with HD die within 15 to 20 years after diagnosis.[10]

Other Types of Neurodegenerative Diseases

For additional information on the diagnosis, treatment, and prognosis of other common NDs, access the links below:[11]

- Creutzfeldt-Jakob Disease
- Corticobasal Degeneration
- Frontotemporal Dementia
- Lewy Body Dementias
- Primary Progressive Aphasia
- Progressive Supranuclear Palsy
- Spinal Muscular Atrophy (SMA)

Additional Resources

Please see the Addendum at the end of this guideline for additional information on NDs as well as a comparison chart of the common types of dementia and links to Provider Resources. For additional information on the types of dementia, the University of California San Francisco (UCSF) provides an overview of the types of dementia here.[4]

Hierarchy of Support

GUIDELINE HIERARCHY

CPGs are updated annually or as necessary due to updates made to guidelines or recommendations by the American Psychiatric Association (APA), American Academy of Family Physicians (AAFP), National Institute for Health and Care Excellence (NICE), and the American Academy of Neurology (AAN). When there are differing opinions noted by national organizations, WellCare will default to the member's benefit structure as deemed by state contracts and Medicaid / Medicare regulations. If there is no specific language pertaining to Neurodegenerative Disease, WellCare will default (in order) to the following:

- National Committee for Quality Assurance (NCQA);
- United States Preventive Services Task Force (USPSTF), National Quality Strategy (NQS), Agency for Healthcare Research and Quality (AHRQ);
- Specialty associations, colleges, societies, etc. (e.g., American Academy of Family Physicians, American Congress of Obstetricians and Gynecologists, American Cancer Society, etc.).

Links to websites within the CPGs are provided for the convenience of Providers. Listings do not imply endorsement by WellCare of the information contained on these websites. NOTE: All links are current and accessible at the time of MPC approval.

WellCare aligns with the APA, AAFP, NICE, and the AAN on the topic of Neurodegenerative Disease. Highlights from their respective publications are noted below.

ALZHEIMER'S DISEASE

AMERICAN PSYCHIATRIC ASSOCIATION (APA)

The American Psychiatric Association (APA) published the *Practice Guideline for the Treatment of Patients with Alzheimer's Disease and Other Dementias* in 2007. The aim of the guideline is to serve as a tool for psychiatrists in caring for people diagnosed with dementia. Components of the APA's guideline are listed below:[12]

- *Formulation and Implementation of a Treatment Plan.* Includes determining site of treatment and frequency of visits as well as components of psychiatric management. The APA outlines diagnostic and evaluation options such as neuropsychological testing, neuroimaging, biomarkers, and genetic testing. Items related to patient safety and monitoring are also explored (e.g., suicidal ideation, aggravation/aggression, supervision, falls, abuse and neglect, wandering, driving). The section also focuses on how to provide education to the patient and those that care for them, including referral to services.
- *Specific Clinical Features Influencing the Treatment Plan.* Includes demographic and social factors (age, gender, cultural) as well as co-occurring conditions / other dementias. Site-specific issues are also discussed (e.g., home care, day care, long term care, medical and behavioral inpatient).
- *Review of Evidence.* Includes disease definition, natural history, and epidemiology with a look at specific dementias. The APA also explores specific psychotherapies and psychosocial treatments. Somatic treatments are also included for treatment for cognitive and functional losses, psychosis and agitation, sleep disturbance and depression (and related symptoms).
- *Future Research Needs.* The APA notes that more research is needed on models of care delivery including potential impact of changes in payment for health services. Attention is also noted for research on alternative

living environments that may provide a better quality of life for the patient and are less expensive. Research is also needed on caregivers and how to decrease adverse outcomes.

A *Guideline Watch* was published in 2014 and includes developments since the 2007 publication. Highlights include:[13]

- Pharmacological Treatments for cognitive and behavioral symptoms, including use for depression and apathy
- Psychosocial Interventions including the value of psychosocial interventions to improve or maintain cognition, function, adaptive behavior, and quality of life. Support programs for caregivers and patients are also explored as a way to decrease the odds of institutionalization and improved caregiver well-being.

The original guideline published in 2007 is located here; the 2014 *Guideline Watch* can be accessed here.[12,13]

AMERICAN ACADEMY OF FAMILY PHYSICIANS (AAFP)

The American Academy of Family Physicians (AAFP) publication *Treatment of Alzheimer's Disease* features key recommendations for practice as well as a review of therapies. To read the document, please click here.[14]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE)

The National Institute for Health and Care Excellence (NICE) published guidance on *Dementia, Disability and Frailty in Later Life – Mid-Life Approaches to Delay or Prevent Onset.* Highlights include recommendations for promoting health lifestyles as well as delivery of health care to those impacted by dementia. The document can be found here.[15]

PARKINSON'S DISEASE

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE)

The National Institute for Health and Care Excellence (NICE) published guidance on *Parkinson's Disease in Adults.* The aim of the guideline is to improve care from the time of diagnosis, including monitoring and managing symptoms, providing information and support, and palliative care among those diagnosed with PD. To review the guidance in its entirety, click here.[16]

AMYOTROPHIC LATERAL SCLEROSIS (ALS)

AMERICAN ACADEMY OF NEUROLOGY

The American Academy of Neurology (AAN) published two guidelines for the care of individuals with ALS:

- Drug, Nutritional, and Respiratory Therapies – available here[17]
- Multidisciplinary Care, Symptom Management, and Cognitive/Behavioral Impairment – available here[18]

HUNTINGTON'S DISEASE

AMERICAN ACADEMY OF NEUROLOGY

The American Academy of Neurology published an evidence-based guideline on *Pharmacologic Treatment of Chorea in Huntington Disease.* The guideline can be found here.[19]

Evidence Based Practice

AGENCY FOR HEALTHCARE RESEARCH AND QUALITY (AHRQ)

The Agency for Healthcare Research and Quality (AHRQ) has not published reports on this topic.

MEASUREMENT OF COMPLIANCE

WellCare is committed to adhering to the measures and standards published by the Centers for Medicare and Medicaid Services (CMS) and the National Committee for Quality Assurance (NCQA). Please reference WellCare's Clinical Policy Guiding Document titled *Measures of Compliance.*

NOTE: To access Clinical Policy Guiding Documents visit www.wellcare.com – select the Provider tab, then "Tools" and "Clinical Guidelines".

Care Management

The goals for Care Management are to support the member's ability to self-manage their disease, minimize risks associated with Neurodegenerative Disease, and remove barriers preventing them from achieving those goals.
Integrated Care Management:

- Ensure member has a specialist who can provide timely follow ups to monitor and/or manage symptoms
- Ensure member has adequate support from caregiver, community, family, etc.
- Ensure member/caregiver understanding of medication dosing and adherence to medications, refilling timely
- Provide assistance with functional status and ADLs (e.g. DME, therapies)
- Provide education on ways to manage their disease (e.g. non-pharmacological strategies, ways to combat fatigue and reduction of fall risks)
- Completing Fall Risk Assessments to reduce risk of injuries related to falls
- Assess for risk of depression and share with appropriate provider(s) if risks are identified

MEASURABLE HEALTH OUTCOMES

Targeted Health Outcomes (Extended Program Goals) result from successful member self-management (see Case Management Objectives).

1. The Member experiences a reduction in falls with adherence to medication regimen, DME and therapies at 6-12 months post engagement. In absence of documentation, Provider and/or Member narrative/HRA data may be used
2. The Member experiences an increase in ability to complete ADLs at 6-12 months post engagement.
3. Adherence to medication regimen, when appropriate, as evidenced by pharmacy claims pre and post engagement at 6-12 months. In absence of documentation, Provider and/Member narrative/HRA data may be used
4. The member experiences a slowing of the progression of the disease with adherence to medication regimen and therapies 12 months post-engagement. In absence of documentation, Provider and/or Member narrative/HRA data may be used

CASE MANAGEMENT GOALS

Case Goals should target specific care gaps and/or adherence issues, and measure the member's progress towards self-management and adherence which will lead to the targeted health outcomes above. Examples:

- Member will obtain and attend Neurology (or PCP) and other specialist appointments as scheduled by provider within 60 days
- Member will be adherent to medication regimen as evidenced by pharmacy claims over last 30 days
- Member will be able to increase functional activity levels by 5 minutes each week over the next 30 days
- Member will be able to complete specific ADLs with the assistance of caregiver and/or DME within 60 days
- Specific for Members requiring hospitalization: The Member participates in provider follow-up visit within 7 days of hospital discharge

CASE MANAGEMENT OBJECTIVES

Case Management Objectives should focus on improving the Member's self-management skills up to and including:

- Addressing barriers to medication adherence
- Assisting with scheduling provider appointments or obtaining specialist referrals
- Providing education on therapies to slow progression or increase functional status
- Providing education on disease process
- Assisting with coordination of needed DME
- Conduct screening for anxiety/depression as appropriate

MEDICAL BEHAVIORAL INTEGRATION

It is common to have social and emotional changes and disruptions with Neurodegenerative Disease such as; anxiety, dysphoric/euphoric mood, apathy and loss of inhibition. While there can be variations in behaviors, the behavior changes can be predictable due to the disease progression in the brain. It is important to look at the environment and

find out what may be triggering behavioral outbursts to minimize environmental stressors. Co-occurring underlying psychological diagnoses such as depression and anxiety are often underdiagnosed in this population. For Huntington's Disease, social interaction and activities outside the home may ward off some behavioral problems. Psychotropic medications may be prescribed to manage behavioral symptoms.[20] However, the FDA has issued Black Box Warnings on all First and Second Generation Antipsychotic medications as they can increase the likelihood of death among the elderly with dementia.[21]

MEMBER EDUCATIONAL RESOURCES

Currently there are no Krames/StayWell Member educational materials utilized by WellCare Case Managers.

PHARMACOLOGY

ALZHEIMER'S DISEASE

Currently there are no medications that slow the progression of Alzheimer's however, there are five FDA-approved medications are used to treat AD symptoms. Donepezil (Aricept), rivastigmine (Exelon), galantamine (Razadyne), and memantine HCl / donepezil HCl (Namzaric) are prescribed to treat mild to moderate AD symptoms. Donepezil was recently approved to treat severe AD as well. The newest AD medication is memantine (Namenda), which is prescribed to treat moderate to severe AD symptoms. The medications may improve one's ability to carry out activities of daily living (ADLs) by maintaining thinking, memory, or speaking skills. Behavioral and personality changes may also improve with medication – research shows that the medication may help an individual for only a few months to a few years.

Medications for Alzheimer's Disease [22]

	Namenda® (memantine)	**Razadyne® (galantamine)**	**Exelon® (rivastigmine)**	**Aricept® (donepezil)**
Drug Type and Use	N-methyl D-aspartate (NMDA) antagonist prescribed to treat symptoms of moderate to severe Alzheimer's	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate Alzheimer's	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate Alzheimer's	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate, and moderate to severe Alzheimer's
How It Works	Blocks the toxic effects associated with excess glutamate and regulates glutamate activation	Prevents the breakdown of acetylcholine and stimulates nicotinic receptors to release more acetylcholine in the brain	Prevents the breakdown of acetylcholine and butyrylcholine (a brain chemical similar to acetylcholine) in the brain	Prevents the breakdown of acetylcholine in the brain
Common Side Effects	Dizziness, headache, constipation, confusion	Nausea, vomiting, diarrhea, weight loss, loss of appetite	Nausea, vomiting, diarrhea, weight loss, loss of appetite, muscle weakness	Nausea, vomiting, diarrhea
Manufacturer's Recommended Dosage	• Tablet: Initial dose of 5 mg once a day • May increase dose to 10 mg/day (5 mg twice a day), 15 mg/day (5 mg and 10 mg as separate doses), and 20 mg/day (10 mg twice a day) at minimum 1-week intervals if well tolerated • Oral solution: same dosage as above • Extended-release tablet: Initial dose of 7 mg once a day; may increase dose to 14 mg/day, 21mg/day, and 28	• Tablet*: Initial dose of 8 mg/day (4 mg twice a day) • May increase dose to 16 mg/day (8 mg twice a day) and 24 mg/day (12 mg twice a day) at minimum 4-week intervals if well tolerated • Oral solution*: same dosage as above • Extended-release capsule*: same dosage as above but taken once a day	• Capsule*: Initial dose of 3 mg/day (1.5 mg twice a day) • May increase dose to 6 mg/day (3 mg twice a day), 9 mg (4.5 mg twice a day), and 12 mg/day (6 mg twice a day) at minimum 2-week intervals if well tolerated • Patch: Initial dose of 4.6 mg once a day; may increase to 9.5 mg once a day after minimum of 4 weeks if well tolerated • Oral solution: same dosage as capsule	• Tablet*: Initial dose of 5 mg once a day • May increase dose to 10 mg/day after 4-6 weeks if well tolerated, then to 23 mg/day after at least 3 months • Orally disintegrating tablet*: same dosage as above • 23-mg dose available as brand-name tablet only

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	mg/day at minimum 1 wk intervals if tolerated			
For More Information	Visit *www.namenda.com*. Click on "Prescribing Information" to see the drug label.	Visit *www.razadyneer.com*. Click on "Important Safety Information" to see links to prescribing information.	Visit *www.fda.gov/cder*. Click on "Drugs@FDA," search for Exelon, and click on drug-name links to see "Label Information."	Visit *www.fda.gov/cder*. Click on "Drugs@FDA," search for Aricept, and click on drug-name links to see "Label Information."

Educate members about clinical trials – volunteers are needed. For more information, go to the ADEAR Center's listing of clinical trials www.nia.nih.gov/alzheimers/clinical-trials. More information is also available at www.ClinicalTrials.gov.

PARKINSON'S DISEASE

Medications are available to provide relief for patients. Initial therapy includes levodopa combined with carbidopa. Carbidopa delays the conversion of levodopa into dopamine until it reaches the brain. Nerve cells can use levodopa to make dopamine and replenish the brain's dwindling supply. The drug, while effective, not all symptoms respond equally to the drug. Bradykinesia and rigidity respond most favorably, while tremor may be only slightly reduced; balance and other symptoms may see minimal improvement. Anticholinergics may be prescribed to control tremor and rigidity. Bromocriptine, pramipexole, and ropinirole, mimic the role of dopamine in the brain, causing the neurons to react as they would to dopamine. Amantadine (antiviral) also may reduce symptoms. Rasagiline is prescribed with levodopa for those with advanced PD or as a single-drug treatment for early PD. In March 2017, safinamide tablets were approved by the FDA as an add-on treatment for those with PD and are currently taking levodopa/carbisopa and experiencing 'off' episodes (periods when the medications are not effective and cause an increase in symptoms).[7]

AMYOTROPHIC LATERAL SCLEROSIS (ALS)

A cure for ALS has not been discovered. The Food and Drug Administration (FDA) has approved riluzole and edaravone for the treatment of ALS. Riluzole can prolong life by 2-3 months however it does not alleviate symptoms. Edaravone can slow the clinical decline in daily functioning of those with ALS. The NeuRx Diaphragm Pacing System has also been approved by the FDA. The system uses implanted electrodes and a battery pack to cause the diaphragm (breathing muscle) to contract and may benefit individuals who have ALS before the onset of severe respiratory failure. Drugs may be prescribed to help control spasticity, pain, panic attacks, and depression. Physical therapy, occupational therapy, and rehabilitation may prevent joint immobility and decrease muscle weakness and atrophy. The use of mechanical ventilation (respirators) may also be needed.[9]

HUNTINGTON'S DISEASE

Currently there is no treatment that can stop or reverse the course of HD. Those with HD may experience side effects from drugs used to treat symptoms – these may include fatigue, sedation, decreased concentration, restlessness, or hyperexcitability. Prescribing should occur only when symptoms interfere with the individual's quality of life. Common drugs used to treat symptoms include:[10]

- Tetrabenazine and deuterabenazine are prescribed for treating chorea.
- Antipsychotic drugs may alleviate chorea and control hallucinations, delusions, and violent outbursts.
- Drugs may be prescribed to treat depression and anxiety.

Related WellCare Guidelines

In addition to the information contained in this document, please reference the following CPGs: *Anxiety Disorders: HS-1057, Behavioral Health Screening in Primary Care Settings: HS-1036, Depressive Disorders Adults, Children & Adolescents: HS-1022, Fall Risk Assessment: HS-1033, Frailty and Special Populations: HS-1071, Long Term Services and Support (LTSS): HS-1052 , Palliative Care: HS-1043, Suicidal Behavior: HS-1027,* and *Traumatic Brain Injury (TBI): HS-1066.*

NOTE: Clinical Policies can be accessed by going to www.wellcare.com – select the Provider tab, then "Tools" and "Clinical Guidelines".

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Disclaimer

Medical Policy Committee Approval History

Date	History and Revisions by the Medical Policy Committee
4/18/2018	• Approved by MPC. Inclusion of Namzaric (combination drug).
10/5/2017	• Approved by MPC. Expanded scope of CPG to include all neurodegenerative diseases.
11/6/2014	• Approved by MPC.
11/1/2012	• Approved by MPC. New.

Addendum

GENERAL INFORMATION ON NDs

Types of Dementia [23]

	Characteristics &Symptoms	Brain Changes
Alzheimer's disease (AD)	• Most common type; 60 to 80 percent of cases. • Early symptoms: Difficulty remembering names and recent events, apathy and depression. • Later symptoms: Impaired judgment, disorientation, confusion, behavior changes and difficulty speaking, swallowing and walking.	• Hallmark abnormalities are deposits of the protein fragment beta-amyloid (plaques) and twisted strands of the protein tau (tangles) as well as evidence of nerve cell damage and death in brain. • Should be considered a disease with three stages.
Vascular dementia Previously known as multi-infarct or post-stroke dementia	• Second most common cause of dementia. • Initial symptom: Impaired judgment or ability to plan steps needed to complete a task (opposed to memory loss often associated with onset of AD). • Often caused by brain injury (e.g., microscopic bleeding, blood vessel blockage); location of injury determines impact of thinking, physical functioning.	• Brain imaging can detect blood vessel problems implicated in VD. Previously, evidence for VD was used to exclude a diagnosis of AD (and vice versa). This is no longer consistent with pathologic evidence, which shows brain changes of several dementias can be present simultaneously. • Mixed Dementia = 2+ types of dementia are present.
Dementia with Lewy bodies (DLB)	• Symptoms are similar to AD, but are more likely to have early symptoms such as sleep disturbances, well-formed visual hallucinations, and muscle rigidity or other parkinsonian movement features. • Brain changes alone cause dementia or they can be present at the same time as the brain changes of AD and/or vascular dementia; each abnormality contributing to the development of dementia (mixed).	• Lewy bodies are abnormal aggregations (or clumps) of the protein alpha-synuclein. When they develop in the cortex, dementia can result. Alpha-synuclein also aggregates in the brains of people with Parkinson's disease, but aggregates may appear in a pattern different from DLB.
Mixed dementia	• Abnormalities linked to more than one type of dementia occur simultaneously in the brain. • Mixed dementia is more common than thought.	• Hallmark abnormalities of more than one type of dementia, most commonly AD and vascular dementia as well as Lewy body.
Parkinson's disease	• Often results in a progressive dementia similar to dementia with Lewy bodies or AD. • Problems with movement are an early symptom. If dementia develops, symptoms are often similar to dementia with Lewy bodies.	• Alpha-synuclein clumps are likely to begin in the substantia nigra. These clumps are thought to cause degeneration of the nerve cells that produce dopamine.
Frontotemporal dementia	• Includes behavioral variant FTD (bvFTD), primary progressive aphasia, Pick's disease and progressive supranuclear palsy. • Symptoms: Changes in personality and behavior and difficulty with language. Nerve cells in the front and side regions of the brain are especially affected.	• No distinguishing microscopic abnormality is linked to all cases. People with FTD generally develop symptoms at a younger age (at about age 60) and survive for fewer years than those with AD.
Creutzfeldt-Jakob disease (CJD)	• The most common human form of a group of rare, fatal brain disorders affecting people and certain mammals. • Variant CJD (mad cow disease) occurs in cattle; has been transmitted to people. • Rapidly fatal disorder; impairs memory and coordination and causes behavior changes.	• Results from misfolded prion protein that causes a "domino effect" in which prion protein throughout the brain misfolds and thus malfunctions.
Normal pressure hydrocephalus	• Symptoms include difficulty walking, memory loss and inability to control urination.	• Caused by the buildup of fluid in the brain. Can sometimes be corrected with surgical installation of a shunt in the brain to drain excess fluid.
Huntington's disease	• A progressive brain disorder caused by a single defective gene on chromosome 4. • Symptoms: Abnormal involuntary movements, a severe decline in thinking and reasoning skills, and irritability, depression, other mood changes.	• The gene defect causes abnormalities in a brain protein that, over time, lead to worsening symptoms.
Wernicke-Korsakoff syndrome	• A chronic memory disorder caused by severe deficiency of thiamine (vitamin B1). • Most common cause is alcohol misuse. • Memory problems may be severe while other thinking / social skills seem relatively unaffected.	• Thiamine helps brain cells produce energy from sugar. When thiamine levels fall too low, brain cells cannot generate enough energy to function properly.

ALZHEIMER'S DISEASE

Diagnostic Criteria

In April 2011, diagnostic criteria were updated from the original criteria established in 1984. Key differences:[24,25]

- Recognition that Alzheimer's disease progresses on a spectrum with three stages - an early, preclinical stage with no symptoms; a middle stage of mild cognitive impairment; and a final stage marked by symptoms of dementia. The 1984 criteria addressed only one stage of disease—the final stage of dementia.
- Criteria expands beyond memory loss as the first or only major symptom. Aspects such as word-finding ability or judgment, may become impaired first; previously memory loss was the central emerging characteristic.
- A better understanding is reflected of the distinctions and associations between Alzheimer's and non-Alzheimer's dementias, as well as between Alzheimer's and disorders that may influence its development, such as vascular disease. In 1984, these relationships were not well recognized or understood.
- Recognition of the potential use of biomarkers (indicators of underlying brain disease) to diagnose. However, the biomarkers are almost exclusively to be used in research rather than clinically. Biomarkers did not exist when the 1984 criteria were developed; diagnosis confirmation was possible only through autopsy after death.

In summary, the updated diagnostic guidelines describe three stages of Alzheimer's disease:

- ***Preclinical*:** Brain changes, including amyloid buildup and other nerve cell changes, may already be in progress, but significant clinical symptoms are not yet evident.
- ***Mild cognitive impairment (MCI):*** A stage marked by symptoms of memory and/or other thinking problems that are greater than normal for a person's age and education, but that do not interfere with his or her independence. People with MCI may or may not progress to Alzheimer's dementia.
- ***Alzheimer's dementia*:** The final stage of the disease in which symptoms such as memory loss, word-finding difficulties, and visual/spatial problems, are significant enough to impair one's ability to function independently.

MCI refers to the symptomatic, pre-dementia phase of the disease. It should be noted, however, that MCI may be due to causes other than Alzheimer's disease. A diagnosis of MCI requires all of the following:

- Concern about a change in cognition relative to previous functioning;
- Impairment of one or more cognitive functions (e.g., memory and problem solving) that is greater than expected for the person's age and education.
- Preserved ability to function independently in daily life, - some complex tasks may be more difficult than before;
- No dementia.

Clinicians should obtain long-term assessments of cognition whenever possible to gain evidence of progressive decline. To determine that MCI is due to Alzheimer's disease, a doctor must rule out other brain diseases or other causes--such as medications, depression, or major life changes--that could account for cognitive decline.

Clinicians should continue to use the many validated neuropsychological tests currently available. These include formal tests that assess various cognitive functions (e.g., episodic memory, executive function, language, visual and spatial skills, and attention). Interviews with the person as well as a family member, friend, or caregiver about changes in the person's thinking skills are also helpful.

Summary Table: Criteria and Guidelines for Alzheimer's Disease [24]

Clinical Use Research Use

	Stage of Alzheimer's Disease	*Test/Criteria*	*Clinical or Research Use*
	Introduction (Jack et al, 2011)	Notable differences from 1984 NINCDS-ADRDA criteria include formulation of 3 AD stages and inclusion of biomarkers.	Broad consensus that use of biomarkers must be validated and standardized before routine clinical application.
Dementia due to AD	**Dementia due to Alzheimer's Disease** (McKhann et al, 2011) Includes 3 sets of criteria: 1. Probable AD dementia 2. Possible AD dementia	1. Probable AD dementia (core clinical criteria) – includes meeting the clinical criteria for all-cause dementia along with insidious onset; clear history of worsening of cognition by report or observation; and initial and most prominent cognitive deficits include amnestic presentation and/or deficits in language presentation, visuospatial presentation and executive function. 2. Possible AD dementia – diagnosis for patients who meet core clinical criteria but exhibit an atypical course of cognitive decline or mixed etiological presentation.	1. Probable AD dementia criteria retained the framework of the 1984 NINCDS-ADRDA criteria and can be used in the clinical setting. 2. Possible AD dementia criteria can be used in the clinical setting. Any patient with previous possible AD dementia per the 1984 NINCDS-ADRDA criteria should be reevaluated with the updated criteria.
	3. Probable AD dementia with evidence of AD pathophysiology	3. Probable AD dementia with evidence of AD pathophysiology – diagnosis for patients who meet the core clinical criteria and incorporate biomarkers, advanced imaging and evaluation of biochemical changes.	3. It is not recommended to use biomarker tests for routine AD diagnosis. If undertaken, biomarker evidence may increase the certainty that clinically assessed dementia is due to the AD pathological process.
MCI due to AD	**Mild Cognitive Impairment due to Alzheimer's Disease** (Albert et al, 2011) Includes 2 sets of criteria: 1. Core clinical criteria	1. Core clinical criteria – clinical and cognitive assessments that establish concern of change in cognition over time; impairment in 1 or more cognitive domain; preservation of independence in functional abilities; not demented, and etiology of MCI consistent with AD, including where relevant, AD genetic factors.	1. Core clinical criteria can be used in clinical settings.
	2. Research criteria	2. Research criteria – incorporates biomarkers, advanced imaging and evaluation of biochemical changes with probabilistic framework for levels of certainty for MCI due to AD.	2. Research criteria established solely for the purpose of research. Workgroup noted that prior to use in community settings, validation of biomarker criteria and standardization of biomarker analyses must occur.
Preclinical	**Preclinical** (Sperling et al, 2011) A new conceptual phase to encompass individuals with pathophysiological changes in the brain but are cognitively normal (no evidence of dementia or MCI).	Preclinical criteria incorporates biomarkers / advanced imaging. Measure of Aβ accumulation (CSF Aβ42 and PET imaging with amyloid tracer). Measure of neuronal injury (CSF tau/p-tau, FDG-PET/fMRI, and sMRI).	Preclinical criteria established solely for the purpose of research. This is a conceptual model and is not meant to imply that all individuals with early AD pathology will progress to clinical AD dementia.

Abbreviations: Aβ = amyloid beta; AD = Alzheimer's disease; CSF = cerebral spinal fluid; FDG = fluorodeoxyglucose; fMRI = functional magnetic resonance imaging; MCI = mild cognitive impairment; MRI = magnetic resonance imaging; PET = positron emission tomography; NINCDS-ADRDA = criteria for the clinical diagnosis of AD published in 1984 by the National Institutes of Neurologic and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association workgroup; sMRI = structural magnetic resonance imaging

Caregiver Education [26]

	What to Expect	Role of a Caregiver	Tips
Early-Stage	• Loved one may still be active, work, able to drive and part of normal activities. • Mild changes in thinking, learning. • There will be good days and bad. • Tell others about the diagnosis.	• Prepare for the future. • Provide support. • Keep appointments. • Remember words and names. • Manage money. • Keep track of medications.	• Encourage loved one to share feelings; ask how you can be supportive. • Encourage independence; remain active in the things they enjoy. • Locate a support group.
Middle-Stage	• Importance of a daily routine. • Changes in behavior. • Communication difficulty. • Assist with daily care needs. • Inability to continue to drive. • Wandering. • Not leaving a loved one alone. • Respond to the emotion vs. the specific question; reassure your loved one.	• Making safety modifications to the home (e.g., alarms to prohibit wandering, railing). • Oversee medication use. • Contact the provider of any changes in behavior. • Ensure end of life decisions have been established (e.g., living will, power of attorney, health care surrogacy). In addition, prepare legal matters (e.g., wills, estate). • Resolve family conflicts, if able.	• Speaking slowly, in a gentle tone • Provide activities that give meaning (e.g., making dinner together, gardening, listening to music, go for a walk). • Find support in caregiver groups • Use simple written reminders if the loved one can still read. • Take care of yourself; seek respite care or adult day care for your loved one.
Late-Stage	• May last several weeks or years. • Difficulty eating and swallowing. • May need assistance walking; may eventually be unable to walk. • Bowel and bladder function. • Full-time care needed. • Susceptible to infections. • Loses ability to communicate. • World is primarily experienced through senses.	• Prepare for home health care into the home or transitioning loved one to a care facility. • As disease progresses, Hospice care may be initiated. • Due to difficulty communicating, look for physical signs of discomfort and pay attention to nonverbal signs and changes in behavior.	• Play his or her favorite music or read to them. • Look at old photos together. • Rub lotion with their favorite scent • Brush their hair. • Sit outside together. • Maintain your stress level through support from family, friends or support groups.

NOTE: Direct members and their caregiver(s) to http://www.alz.org/care/alzheimers-early-mild-stage-caregiving.asp for more information.

Providers may find the following websites useful for additional information on Alzheimer's disease:

- http://www.alz.org/health-care-professionals/clinical-guidelines-information-tools.asp
- https://www.nia.nih.gov/health/alzheimers-disease-diagnostic-guidelines
- https://www.nia.nih.gov/health/alzheimers-dementia-resources-for-professionals