Oscar Clinical Guideline: Memantine (Namenda) (PG213, Ver. 1)

Memantine (Namenda)

- Memantine Oral capsule, extended release
- Memantine Oral solution
- Memantine Oral tablet
- Memantine Hydrochloride 5mg & 10mg Tablet Titration Pak
- Namenda XR Titration Pak

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Memantine (Namenda) is an N-methyl-D-aspartate (NMDA) receptor antagonist used primarily for the treatment of moderate to severe Alzheimer's disease (AD). AD is a progressive neurodegenerative disorder characterized by cognitive decline, functional impairment, and behavioral changes. It is the most common cause of dementia, affecting millions of people worldwide.

- Current treatment options for AD are limited and focus on symptom management. Acetylcholinesterase inhibitors (AChEIs) such as donepezil, rivastigmine, and galantamine are first-line treatments for mild to moderate AD. Memantine is approved for moderate to severe AD and can be used alone or in combination with AChEIs.

- Memantine works by regulating glutamate activity, which is thought to play a role in the pathogenesis of AD. It has shown modest benefits in slowing cognitive decline and improving functional abilities in patients with moderate to severe AD. While not curative, memantine can help maintain quality of life and delay the need for full-time care in some patients.
- Memantine is available as immediate-release tablets and solution and extended-release capsules for once-daily dosing.

Off-label uses of memantine, supported by varying levels of evidence, include treatment of Parkinson's disease dementia, dementia with Lewy bodies, prevention of neurocognitive toxicity in patients undergoing whole brain radiation therapy, and management of trichotillomania and skin picking disorder.

Definitions

"**Activities of Daily Living (ADLs)**" refers to basic self-care tasks such as bathing, dressing, toileting, transferring, continence, and feeding.

"**Alzheimer's disease**" is a progressive neurodegenerative disorder characterized by cognitive decline, memory loss, and changes in behavior and personality.

"**Dementia with Lewy bodies**" is a type of progressive dementia characterized by the development of abnormal deposits of a protein called alpha-synuclein in the brain.

"**NMDA receptor**" refers to the N-methyl-D-aspartate receptor, an ionotropic glutamate receptor involved in synaptic transmission, plasticity, and excitotoxicity. Overstimulation of NMDA receptors may lead to neuronal cell death.

"**Parkinson's disease dementia**" refers to a decline in thinking and reasoning that develops in many people with Parkinson's disease at least a year after diagnosis.

"**Skin picking disorder**" (also known as excoriation disorder) is a mental health condition characterized by repeated picking at one's own skin.

"**Trichotillomania**" is a mental disorder characterized by recurrent, irresistible urges to pull out hair from the scalp, eyebrows, or other areas of the body.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Memantine (Namenda)** medically necessary when **ALL** of the following criteria are met:

1. The member is 18 years of age or older; ***AND***
2. The member has **ONE** of the following diagnoses or conditions:
    a. Moderate to severe Alzheimer's disease; ***or***
    b. Parkinson's disease dementia or dementia with Lewy bodies; ***or***
    c. Brain metastases requiring whole brain radiation therapy (for prevention of neurocognitive toxicity); ***or***
    d. Trichotillomania or skin picking disorder (excoriation disorder); ***AND***
3. Prescribed within the manufacturer's published dosing guidelines or falls within dosing guidelines found in a compendia of current literature (i.e., dose does not exceed 20 mg per day for immediate-release or 28 mg per day for extended-release formulations).

If the above prior authorization criteria are met, the requested product will be authorized for 12-months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if recent clinical documentation (within the last 3 months) indicates the member is responding positively to therapy as evidenced by at least one of the following, specific to their diagnosis:

1. Alzheimer's Disease:
    a. Slowing of cognitive decline compared to expected disease progression; ***or***
    b. Maintenance of ability to perform activities of daily living; ***or***
    c. Reduction in behavioral/psychiatric symptoms (if applicable); ***or***
2. Parkinson's Disease Dementia or Dementia with Lewy Bodies:
    a. Slowing of cognitive decline; ***or***
    b. Improvement in behavioral symptoms; ***or***
3. Prevention of Neurocognitive Toxicity:
    a. Maintenance of cognitive function as assessed by appropriate neurocognitive testing; ***or***
4. Trichotillomania and Skin Picking Disorder:
    a. Reduction in hair pulling or skin picking behaviors; ***or***
    b. Improvement in quality of life measures.

Experimental or Investigational / Not Medically Necessary

Memantine (Namenda) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Management of attention deficit hyperactivity disorder (ADHD).
- Management of autism spectrum disorders.
- Management of generalized anxiety disorder.
- Management of major depressive disorder.
- Treatment of bipolar disorder.
- Treatment of mild Alzheimer's disease.
- Treatment of obsessive-compulsive disorder (OCD).
- Treatment of post-traumatic stress disorder (PTSD).
- Treatment of schizophrenia.
- Treatment of vascular dementia without comorbid Alzheimer's disease.

References

1. Aman MG, Findling RL, Hardan AY, Hendren RL, Melmed RD, Kehinde-Nelson O, Hsu HA, Trugman JM, Palmer RH, Graham SM, Gage AT, Perhach JL, Katz E. Safety and Efficacy of Memantine in Children with Autism: Randomized, Placebo-Controlled Study and Open-Label Extension. J Child Adolesc Psychopharmacol. 2017 Jun;27(5):403-412. doi: 10.1089/cap.2015.0146. Epub 2016 Mar 15. PMID: 26978327; PMCID: PMC5510039.
2. Bago Rožanković P, Rožanković M, Badžak J, Stojić M, Šušak Sporiš I. Impact of Donepezil and Memantine on Behavioral and Psychological Symptoms of Alzheimer Disease: Six-month Open-label Study. Cogn Behav Neurol. 2021 Dec 2;34(4):288-294. doi: 10.1097/WNN.0000000000000285. PMID: 34851866.
3. Ballard C, Thomas A, Gerry S, Yu LM, Aarsland D, Merritt C, Corbett A, Davison C, Sharma N, Khan Z, Creese B, Loughlin P, Bannister C, Burns A, Win SN, Walker Z; MAIN-AD investigators. A double-blind randomized placebo-controlled withdrawal trial comparing memantine and antipsychotics for the long-term treatment of function and neuropsychiatric symptoms in people with Alzheimer's disease (MAIN-AD). J Am Med Dir Assoc. 2015 Apr;16(4):316-22. doi: 10.1016/j.jamda.2014.11.002. Epub 2014 Dec 15. PMID: 25523285.
4. Brown PD, Gondi V, Pugh S, Tome WA, Wefel JS, Armstrong TS, Bovi JA, Robinson C, Konski A, Khuntia D, Grosshans D, Benzinger TLS, Bruner D, Gilbert MR, Roberge D, Kundapur V, Devisetty K, Shah S, Usuki K, Anderson BM, Stea B, Yoon H, Li J, Laack NN, Kruser TJ, Chmura SJ, Shi W, Deshmukh S, Mehta MP, Kachnic LA; for NRG Oncology. Hippocampal Avoidance During Whole-Brain Radiotherapy Plus Memantine for Patients With Brain Metastases: Phase III Trial NRG Oncology CC001. J Clin Oncol. 2020 Apr 1;38(10):1019-1029. doi: 10.1200/JCO.19.02767. Epub 2020 Feb 14. PMID: 32058845; PMCID: PMC7106984.
5. Brown PD, Pugh S, Laack NN, Wefel JS, Khuntia D, Meyers C, Choucair A, Fox S, Suh JH, Roberge D, Kavadi V, Bentzen SM, Mehta MP, Watkins-Bruner D; Radiation Therapy Oncology Group (RTOG). Memantine for the prevention of cognitive dysfunction in patients receiving

whole-brain radiotherapy: a randomized, double-blind, placebo-controlled trial. Neuro Oncol. 2013 Oct;15(10):1429-37. doi: 10.1093/neuonc/not114. Epub 2013 Aug 16. PMID: 23956241; PMCID: PMC3779047.
6. Di Santo SG, Prinelli F, Adorni F, Caltagirone C, Musicco M. A meta-analysis of the efficacy of donepezil, rivastigmine, galantamine, and memantine in relation to severity of Alzheimer's disease. J Alzheimers Dis. 2013;35(2):349-61. doi: 10.3233/JAD-122140. PMID: 23411693.
7. Emre M, Tsolaki M, Bonuccelli U, Destée A, Tolosa E, Kutzelnigg A, Ceballos-Baumann A, Zdravkovic S, Bladström A, Jones R; 11018 Study Investigators. Memantine for patients with Parkinson's disease dementia or dementia with Lewy bodies: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2010 Oct;9(10):969-77. doi: 10.1016/S1474-4422(10)70194-0. Epub 2010 Aug 20. PMID: 20729148.
8. Grant JE, Chesivoir E, Valle S, Ehsan D, Chamberlain SR. Double-Blind Placebo-Controlled Study of Memantine in Trichotillomania and Skin-Picking Disorder. Am J Psychiatry. 2023 May 1;180(5):348-356. doi: 10.1176/appi.ajp.20220737. Epub 2023 Feb 22. PMID: 36856701.
9. Howard R, McShane R, Lindesay J, Ritchie C, Baldwin A, Barber R, Burns A, Dening T, Findlay D, Holmes C, Hughes A, Jacoby R, Jones R, Jones R, McKeith I, Macharouthu A, O'Brien J, Passmore P, Sheehan B, Juszczak E, Katona C, Hills R, Knapp M, Ballard C, Brown R, Banerjee S, Onions C, Griffin M, Adams J, Gray R, Johnson T, Bentham P, Phillips P. Donepezil and memantine for moderate-to-severe Alzheimer's disease. N Engl J Med. 2012 Mar 8;366(10):893-903. doi: 10.1056/NEJMoa1106668. PMID: 22397651.
10. Hyman SL, Levy SE, Myers SM; COUNCIL ON CHILDREN WITH DISABILITIES, SECTION ON DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS. Identification, Evaluation, and Management of Children With Autism Spectrum Disorder. Pediatrics. 2020 Jan;145(1):e20193447. doi: 10.1542/peds.2019-3447. Epub 2019 Dec 16. PMID: 31843864.
11. Isaac E, Ney D, Serruya M, Keith S, Lippa C, Sperling MR. Tolerability of memantine monotherapy versus adding memantine as combination therapy. J Natl Med Assoc. 2022 Jun;114(3):308-313. doi: 10.1016/j.jnma.2022.02.006. Epub 2022 Mar 7. PMID: 35272847.
12. Jones RW, Bayer A, Inglis F, Barker A, Phul R. Safety and tolerability of once-daily versus twice-daily memantine: a randomised, double-blind study in moderate to severe Alzheimer's disease. Int J Geriatr Psychiatry. 2007 Mar;22(3):258-62. doi: 10.1002/gps.1752. PMID: 17243195.
13. Kavirajan H, Schneider LS. Efficacy and adverse effects of cholinesterase inhibitors and memantine in vascular dementia: a meta-analysis of randomised controlled trials. Lancet Neurol. 2007 Sep;6(9):782-92. doi: 10.1016/S1474-4422(07)70195-3. PMID: 17689146.
14. Levin OS, Batukaeva LA, Smolentseva IG, Amosova NA. Efficacy and safety of memantine in Lewy body dementia. Neurosci Behav Physiol. 2009 Jul;39(6):597-604. doi: 10.1007/s11055-009-9167-x. PMID: 19517247.
15. McShane R, Westby MJ, Roberts E, Minakaran N, Schneider L, Farrimond LE, Maayan N, Ware J, Debarros J. Memantine for dementia. Cochrane Database Syst Rev. 2019 Mar 20;3(3):CD003154. doi: 10.1002/14651858.CD003154.pub6. PMID: 30891742; PMCID: PMC6425228.
16. Memantine Hydrochloride [prescribing information]. Wall, NJ: Seton Pharmaceuticals; February 2021.
17. Namenda (memantine) [prescribing information]. Madison, NJ: Allergan USA Inc; November 2018.
18. Namenda XR (memantine) [prescribing information]. Madison, NJ: Allergan USA Inc; November 2019.

19. Namenda XR Titration Pack (memantine) [prescribing information]. Irvine, CA: Allergan USA, Inc; October 2016.
20. National Institute for Health and Care Excellence (NICE). Dementia: assessment, management and support for people living with dementia and their carers. NICE guideline 97. https://www.nice.org.uk/guidance/ng97/evidence/full-guideline-pdf-4852695709.
21. National Institute for Health and Care Excellence (NICE). Parkinson's disease in adults. NICE guideline 71. https://www.nice.org.uk/guidance/ng71/resources/parkinsons-disease-in-adults-pdf-1837629189061.
22. O'Brien JT, Holmes C, Jones M, Jones R, Livingston G, McKeith I, Mittler P, Passmore P, Ritchie C, Robinson L, Sampson EL, Taylor JP, Thomas A, Burns A. Clinical practice with anti-dementia drugs: A revised (third) consensus statement from the British Association for Psychopharmacology. J Psychopharmacol. 2017 Feb;31(2):147-168. doi: 10.1177/0269881116680924. Epub 2017 Jan 20. PMID: 28103749.
23. Rabins PV, Rovner BW, Rummans T, Schneider LS, Tariot PN. Guideline Watch (October 2014): Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias. Focus (Am Psychiatr Publ). 2017 Jan;15(1):110-128. doi: 10.1176/appi.focus.15106. Epub 2017 Jan 11. PMID: 31997970; PMCID: PMC6519627.
24. Reeve E, Farrell B, Thompson W, Herrmann N, Sketris I, Magin PJ, Chenoweth L, Gorman M, Quirke L, Bethune G, Hilmer SN. Deprescribing cholinesterase inhibitors and memantine in dementia: guideline summary. Med J Aust. 2019 Mar;210(4):174-179. doi: 10.5694/mja2.50015. Epub 2019 Feb 16. PMID: 30771226.

Clinical Guideline Revision / History Information

Original Date: 07/31/2024
Reviewed/Revised: