

## Rivastigmine (Exelon)

- Rivastigmine Tartrate Oral capsule
- Rivastigmine Transdermal Patch - 24 Hour

### 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.*

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## Summary

Alzheimer's disease (AD) and Parkinson's disease (PD) are progressive neurodegenerative disorders that can lead to dementia. Alzheimer's dementia is characterized by cognitive decline, memory impairment, and functional disability, while Parkinson's disease dementia (PDD) typically presents with impairments in executive function, memory retrieval, and attention in the setting of an established PD diagnosis.

Treatment goals for both types of dementia involve improving cognitive function and overall quality of life. Alzheimer's dementia is often treated with acetylcholinesterase inhibitors (AChEIs), such as donepezil (Aricept), rivastigmine (Exelon), and galantamine (Razadyne), as first-line therapy for those with mild, moderate or severe dementia. Alternative therapies include N-methyl-D-aspartate (NMDA) receptor antagonists such as memantine (Namenda) for moderate-to-severe dementia - which can be used as monotherapy or combined with AChEIs.

Rivastigmine (Exelon) is a reversible acetylcholinesterase inhibitor (AChEI) indicated for the treatment of mild, moderate, or severe dementia of the Alzheimer's type and mild-to-moderate dementia associated with Parkinson's disease. It is available in oral capsules and one-daily transdermal patch formulations.

## 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 associated with Parkinson's disease" is defined as dementia that develops at least one year after an established diagnosis of Parkinson's disease, with cognitive deficits that are severe enough to impact daily functioning.

"Dementia of the Alzheimer's type" refers to dementia that meets diagnostic criteria for probable Alzheimer's disease, as established by the National Institute on Aging and the Alzheimer's Association.

"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.

"Mild cognitive impairment" refers to cognitive decline greater than expected for an individual's age and education level but that does not interfere notably with activities of daily life.

"[s]" indicates state mandates may apply.

## Clinical Indications

### Medical Necessity Criteria for Clinical Review

#### General Medical Necessity Criteria

The Plan considers rivastigmine (Exelon) medically necessary when ALL of the following criteria are met:

1. The member is 18 years of age or older; *AND*
2. Rivastigmine (Exelon) is being prescribed at a dose and frequency that is within FDA approved labeling (i.e., dose does not exceed 12 mg per day for oral formulations or 13.3 mg/24 hours for transdermal patch) OR is supported by compendia or evidence-based published dosing guidelines for the requested indication; *AND*
3. The member meets the applicable [Medical Necessity Criteria for Initial Clinical Review](#) or [Subsequent Clinical Review](#) listed below.

### Medical Necessity Criteria for Initial Clinical Review

#### Initial Indication-Specific Criteria

#### Dementia

The Plan considers rivastigmine (Exelon) medically necessary when ALL of the following criteria are met:

4. The member meets the above [General Medical Necessity Criteria](#); *AND*
5. The member has ONE (1) of the following diagnoses or conditions:
  - a. dementia of the Alzheimer's type (Alzheimer's disease); *or*
  - b. mild-to-moderate dementia associated with Parkinson's disease; *or*
  - c. dementia with Lewy bodies (DLB).

If the above prior authorization criteria are met, the requested product will be authorized for up to 12-months.<sup>[5]</sup>

#### *Continued Care*

### Medical Necessity Criteria for Subsequent Clinical Review

#### Subsequent Medical Necessity Criteria

#### Dementia

The Plan considers rivastigmine (Exelon) medically necessary when ALL of the following criteria are met:

1. The member meets the above applicable [General Medical Necessity Criteria](#) and/or [Initial Clinical Review](#); *AND*
2. The member has experienced a documented improvement in ONE of the following:
  - a. Improvement, slowing, or stabilization of cognitive function compared to expected disease progression or as assessed by a validated cognitive assessment tool; *or*
  - b. Maintenance of ability to perform activities of daily living; *or*

- c. Reduction in behavioral or psychiatric symptoms (if applicable); *or*
- d. Global improvement as reported by the member, caregiver, or healthcare provider.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.<sup>[5]</sup>

#### Experimental / Investigational, or unproven<sup>[5]</sup>

Rivastigmine (Exelon) for any other indication or use is considered Experimental / Investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Anxiety Disorders without a comorbid dementia diagnosis. There are no high quality large clinical trials to support the safety and efficacy of rivastigmine (Exelon) for the management of anxiety disorders, outside of the management of anxiety related to a dementia diagnosis
- Delirium. The use of rivastigmine (Exelon) for the management of delirium - either postoperative delirium, intensive care unit-related delirium, or stroke-related delirium, has not been supported by high quality, large, randomized clinical trials. While one study (n=100) found a significant reduction in day-one post-operative delirium compared to placebo, another study (n=104) was terminated early due to a higher rate of mortality amongst the rivastigmine versus placebo group. The unclear impact on mortality, and mixed results from smaller studies does not support the use of rivastigmine (Exelon) for the management of delirium.
- Depression without a comorbid dementia diagnosis. There are no high quality large clinical trials to support the safety and efficacy of rivastigmine (Exelon) for the management of depression, outside of the management of depression related to a dementia diagnosis.
- Mild cognitive impairment (MCI). In a double-blind, randomized controlled trial, rivastigmine (Exelon) did not significantly increase time to diagnosis of Alzheimer's disease compared to placebo over a 4 year period. In a small (n=28) randomized controlled trial, rivastigmine (exelon) did not significantly improve (but trended towards) AD global impression of change scores in those with PD and MCI. One study only recruited 1 participant and was terminated early (NCT01602198). There are no high quality large clinical trials to support the safety and efficacy of rivastigmine (Exelon) for the management of MCI.
- Psychosomatic Disorders. There are no high quality large clinical trials to support the safety and efficacy of rivastigmine (Exelon) for the management of psychosomatic disorders.
- Schizophrenia without comorbid dementia diagnosis.
- Traumatic Brain Injury (TBI). Clinical studies assessing the use of rivastigmine (Exelon) and other AChEIs have shown mixed results in improvement of TBI-related symptoms and cognitive impairment. Studies assessing rivastigmine (Exelon) for the management of TBI were small (n= 94-157), and generally found a weak trend (i.e., non-significant) towards improvements in TBI-related symptoms. There are no high quality large clinical trials to support the safety and efficacy of rivastigmine (Exelon) for the management of TBI.

## References

1. Ballard C, Lane R, Barone P, Ferrara R, Tekin S. Cardiac safety of rivastigmine in Lewy body and Parkinson's disease dementias. *Int J Clin Pract*. 2006;60(6):639-645. doi:10.1111/j.1368-5031.2006.00967.x
2. Ballard C, Sauter M, Scheltens P, et al. Efficacy, safety and tolerability of rivastigmine capsules in patients with probable vascular dementia: the VantagE study. *Curr Med Res Opin*. 2008;24(9):2561-2574. doi:10.1185/03007990802328142
3. Birks J, McGuinness B, Craig D. Rivastigmine for vascular cognitive impairment. *Cochrane Database Syst Rev*. 2013;(5):CD004744. doi: 10.1002/14651858.CD004744.pub3.
4. Brawman-Mintzer O, Tang XC, Bizien M, et al. Rivastigmine Transdermal Patch Treatment for Moderate to Severe Cognitive Impairment in Veterans with Traumatic Brain Injury (RiVET Study): A Randomized Clinical Trial. *J Neurotrauma*. 2021 Jul 15;38(14):1943-1952. doi: 10.1089/neu.2020.7146. Epub 2021 Mar 8.
5. Bullock R, Touchon J, Bergman H, et al. Rivastigmine and donepezil treatment in moderate to moderately-severe Alzheimer's disease over a 2-year period. *Curr Med Res Opin*. 2005 Aug;21(8):1317-27. doi: 10.1185/030079905X56565.
6. Burn D, Emre M, McKeith I, et al. Effects of rivastigmine in patients with and without visual hallucinations in dementia associated with Parkinson's disease. *Mov Disord*. 2006 Nov;21(11):1899-907. doi: 10.1002/mds.21077.
7. Emre M, Aarsland D, Albanese A, et al, "Rivastigmine for Dementia Associated with Parkinson's Disease," *N Engl J Med*, 2004, 351(24):2509-18.
8. Exelon Patch (rivastigmine) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2024.
9. Feldman HH, Ferris S, Winblad B, et al. Effect of rivastigmine on delay to diagnosis of Alzheimer's disease from mild cognitive impairment: the InDDEx study. *Lancet Neurol*. 2007 Jun;6(6):501-12. doi: 10.1016/S1474-4422(07)70109-6. Erratum in: *Lancet Neurol*. 2007 Oct;6(10):849.
10. Frederiksen KS, Cooper C, Frisoni GB, et al. A European Academy of Neurology guideline on medical management issues in dementia. *Eur J Neurol*. 2020 Oct;27(10):1805-1820. doi: 10.1111/ene.14412. Epub 2020 Jul 26.
11. Gamberini M, Bolliger D, Lurati Buse GA, et al. Rivastigmine for the prevention of postoperative delirium in elderly patients undergoing elective cardiac surgery--a randomized controlled trial. *Crit Care Med*. 2009 May;37(5):1762-8. doi: 10.1097/CCM.0b013e31819da780.
12. 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.
13. Grossberg G, Meng X, Olin JT. Impact of rivastigmine patch and capsules on activities of daily living in Alzheimer's disease. *Am J Alzheimers Dis Other Demen*. 2011 Feb;26(1):65-71. doi: 10.1177/1533317510391240.
14. Hansen RA, Gartlehner G, Webb AP, Morgan LC, Moore CG, Jonas DE. Efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer's disease: a systematic review and meta-analysis. *Clin Interv Aging*. 2008;3(2):211-225.
15. Hort J, O'Brien JT, Gainotti G, et al, "EFNS Guidelines for the Diagnosis and Management of Alzheimer's Disease," *Eur J Neurol*, 2010, 17(10):1236-48.
16. Mamikonyan E, Xie SX, Melvin E, Weintraub D. Rivastigmine for mild cognitive impairment in Parkinson disease: a placebo-controlled study. *Mov Disord*. 2015 Jun;30(7):912-8. doi: 10.1002/mds.26236. Epub 2015 Apr 25.
17. Massoudi N, Mohit B, Fathi M, Nooraei N, Hannani KK, ArianNik M. The impact of rivastigmine on post-surgical delirium and cognitive impairment; a randomized clinical trial. *Int J Geriatr Psychiatry*. 2023 Jul;38(7):e5970. doi: 10.1002/gps.5970.
18. McKeith I, Del Ser T, Spano P, et al, "Efficacy of Rivastigmine in Dementia With Lewy Bodies: A Randomised, Double-Blind, Placebo-Controlled International Study," *Lancet*, 2000, 356(9247):2031-6.

19. Meng YH, Wang PP, Song YX, Wang JH. Cholinesterase inhibitors and memantine for Parkinson's disease dementia and Lewy body dementia: A meta-analysis. *Exp Ther Med*. 2019 Mar;17(3):1611-1624. doi: 10.3892/etm.2018.7129. Epub 2018 Dec 24.
20. Miyasaki JM, Shannon K, Voon V, et al. Practice Parameter: Evaluation and Treatment of Depression, Psychosis, and Dementia in Parkinson Disease (An Evidence-Based Review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2006;66(7):996-1002.
21. Moretti R, Torre P, Antonello RM, Cazzato G, Pizzolato G. Different responses to rivastigmine in subcortical vascular dementia and multi-infarct dementia. *Am J Alzheimers Dis Other Demen*. 2008 Apr-May;23(2):167-76. doi: 10.1177/1533317507312558. Epub 2008 Jan 9.
22. 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>.
23. National Institute for Health and Care Excellence (NICE). Parkinson's disease in adults. NICE guideline 71. <https://www.nice.org.uk/guidance/ng71>
24. O'Brien JT, Holmes C, Jones M, et al. Clinical practice with anti-dementia drugs: a revised (third) consensus statement from the British Association for Psychopharmacology. *J Psychopharmacol*. 2017;31(2):147-168. doi: 10.1177/0269881116680924.
25. Oertel W, Poewe W, Wolters E, et al. Effects of rivastigmine on tremor and other motor symptoms in patients with Parkinson's disease dementia: a retrospective analysis of a double-blind trial and an open-label extension. *Drug Saf*. 2008;31(1):79-94. doi: 10.2165/00002018-200831010-00007.
26. Oldenbeuving AW, de Kort PL, Jansen BP, Kappelle LJ, Roks G. A pilot study of rivastigmine in the treatment of delirium after stroke: a safe alternative. *BMC Neurol*. 2008 Sep 20;8:34. doi: 10.1186/1471-2377-8-34.
27. Overshott R, Vernon M, Morris J, Burns A. Rivastigmine in the treatment of delirium in older people: a pilot study. *Int Psychogeriatr*. 2010 Aug;22(5):812-8. doi: 10.1017/S1041610209991359. Epub 2010 Mar 31.
28. 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.
29. Rabins PV, Blacker D, Rovner BW, et al, "American Psychiatric Association Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias. Second Edition," *Am J Psychiatry*, 2007, 164(12 Suppl):5-56.
30. Schmidt R, Hofer E, Bouwman FH, et al. EFNS-ENS/EAN Guideline on concomitant use of cholinesterase inhibitors and memantine in moderate to severe Alzheimer's disease. *Eur J Neurol*. 2015 Jun;22(6):889-98. doi: 10.1111/ene.12707. Epub 2015 Mar 25.
31. Silver JM, Koumaras B, Chen M, et al. Effects of rivastigmine on cognitive function in patients with traumatic brain injury. *Neurology*. 2006 Sep 12;67(5):748-55. doi: 10.1212/01.wnl.0000234062.98062.e9.
32. Stinton C, McKeith I, Taylor JP, et al. Pharmacological Management of Lewy Body Dementia: A Systematic Review and Meta-Analysis. *Am J Psychiatry*. 2015 Aug 1;172(8):731-42. doi: 10.1176/appi.ajp.2015.14121582. Epub 2015 Jun 18.
33. Tenovuo O. Central acetylcholinesterase inhibitors in the treatment of chronic traumatic brain injury-clinical experience in 111 patients. *Prog Neuropsychopharmacol Biol Psychiatry*. 2005 Jan;29(1):61-7. doi: 10.1016/j.pnpbp.2004.10.006. Epub 2004 Dec 8.
34. Tenovuo O, Alin J, Helenius H. A randomized controlled trial of rivastigmine for chronic sequels of traumatic brain injury-what it showed and taught? *Brain Inj*. 2009 Jun;23(6):548-58. doi: 10.1080/02699050902926275.
35. van Eijk MM, Roes KC, Honing ML, et al. Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial. *Lancet*. 2010 Nov 27;376(9755):1829-37. doi: 10.1016/S0140-6736(10)61855-7. Epub 2010 Nov 4.

36. Veroniki AA, Ashoor HM, Rios P, et al. Comparative safety and efficacy of cognitive enhancers for Alzheimer's dementia: a systematic review with individual patient data network meta-analysis. *BMJ Open*. 2022 Apr 26;12(4):e053012. doi: 10.1136/bmjopen-2021-053012.
37. Youn YC, Shin HW, Choi BS, Kim S, Lee JY, Ha YC. Rivastigmine patch reduces the incidence of postoperative delirium in older patients with cognitive impairment. *Int J Geriatr Psychiatry*. 2017 Oct;32(10):1079-1084. doi: 10.1002/gps.4569. Epub 2016 Aug 26.

#### Clinical Guideline Revision / History Information

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