Oscar Clinical Guideline: Rivastigmine (Exelon) (PG212, Ver. 2)

Rivastigmine (Exelon)

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

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. Additionally, amyloid-targeting therapies, such as Leqembi (lecanemab) and Kisulna (donanemab), are indicated for initiation in those with mild cognitive impairment or mild dementia.

Rivastigmine (Exelon) is a reversible acetylcholinesterase inhibitor (AChEI) indicated for the treatment of mild, moderate orsevere 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.

Medical Necessity Criteria for Initial Authorization

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. 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); *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 12 mg per day for oral formulations or 13.3 mg/24 hours for transdermal patch).

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

Medical Necessity Criteria for Reauthorization

Reauthorization for up to 12 months will be granted if recent clinical documentation (within the last 6 months) indicates the member is responding positively to therapy as evidenced by at least one of the following:

1. Improvement, slowing, or stabilization of cognitive function compared to expected disease progression or as assessed by a validated cognitive assessment tool; *OR*
2. Maintenance of ability to perform activities of daily living; *OR*
3. Reduction in behavioral or psychiatric symptoms (if applicable); *OR*
4. Global improvement as reported by the member, caregiver, or healthcare provider.

Experimental or Investigational / Not Medically Necessary

Rivastigmine (Exelon) 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:

- 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.

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