Clinical Policy: Memantine ER (Namenda XR), galantamine (Razadyne, Razadyne ER)

Reference Number: CP.CPA.102
Effective Date: 11.16.16
Last Review Date: 11.17 Revision Log
Line of Business: Medicaid – Medi-Cal

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The following are antidementia agents requiring prior authorization: memantine extended release (Namenda XR®), galantamine (Razadyne®), galantamine (Razadyne® ER).

FDA approved indication
Galantamine (Razadyne, Razadyne ER) is indicated for the treatment of mild to moderate dementia of the Alzheimer's type.

Memantine extended release (Namenda XR) is indicated for the treatment of moderate to severe dementia Alzheimer's type.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Namenda XR, Razadyne, Razadyne ER are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Mild dementia (must meet all)**:**
1. Diagnosis of mild dementia;
2. Request is for Razadyne or Razadyne ER;
3. Failure to a trial of donepezil or Exelon unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 24 mg/day.

Approval Duration: Length of Benefit

B. Moderate dementia (must meet all):
1. Diagnosis of mild dementia;
2. Failure to a trial of donepezil or Exelon unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed: Razadyne/Razadyne ER - 24 mg/day, Namenda XR – 28 mg/day.

Approval Duration: Length of Benefit

C. Severe Dementia (must meet all)**:**
1. Diagnosis of severe dementia;
2. Request is for Namenda XR;
3. Failure to a trial of donepezil unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 28 mg/day.

Approval duration: Length of Benefit

D. Other diagnoses/indications
1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Dose does not exceed: Razadyne/Razadyne ER - 24 mg/day, Namenda XR – 28 mg/day.

Approval duration: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
N/A

Appendix B: General Information
- In a randomized double blind placebo controlled trial in 434 patients with chronic fatigue syndrome, there was no significant difference between Razadyne® (galantamine) and placebo for Clinician Global Impression Scale or any of the secondary outcome measures.
- Per the American Psychiatric Association practice guidelines for the treatment of Alzheimer`s, there is modest data that the combination of Namenda® and Aricept® is

better than Aricept® alone, and there is no evidence that the combination is better than monotherapy with Namenda®.

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
donepezil (Aricept®/Aricept ODT®)	Alzheimer's dementia, mild to moderate: 5 mg PO QD at bedtime. If no response after 4 - 6 weeks, titrate dose to 10 mg QD. If no improvements after 4-8 weeks, consider discontinuation of therapy. Alzheimer's dementia, moderate to severe: 5 mg PO QD at bedtime. If no response after 4 - 6 weeks, titrate dose to 10 mg daily at bedtime for three months then may increase to 23 mg at bedtime.	10 mg/day 23 mg/day
Exelon® (rivastigmine)	Oral: 1.5 mg PO BID initially. Then titrate as tolerated with a minimum of 2 weeks between dose increases (4 weeks for dementia associated with Parkinson's Disease) to 3 mg BID, 4.5 mg BID, or 6 mg BID. Transdermal: initiate with 4.6 mg TD QD; after a minimum of 4 weeks, increase to 9.5 mg QD, which is the minimum effective dose.	Oral: 12 mg/day Transdermal: 13.3 mg/24 hours

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Memantine ER (Namenda XR)	Moderate to severe dementia of the Alzheimer's type	I Initial dose 7 mg PO QD. Increase by 7 mg per day at one-week intervals to a maximum of 28 mg QD.	28 mg QD
Galantamine (Razadyne)	Mild to moderate dementia of the Alzheimer's type	4 mg PO BID initially. Then titrate as tolerated with a minimum of 4 weeks between dose increases to 8 mg BID and 12 mg BID. Take with food.	12 mg BID

Galantamine (Razadyne ER)	Mild to moderate dementia of the Alzheimer's type	8 mg PO QAM initially. Then titrate as tolerated with a minimum of 4 weeks between dose increases to 16 mg daily and 24 mg daily. Take with food.	24 mg QD

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

VI. Product Availability

Namenda XR® Capsule: 7 mg, 14 mg, 21 mg, 28 mg
Namenda XR® titration pack: 7 x 7 mg, 7 x 14 mg, 7 x 21 mg, 7 x 28 mg
Razadyne® Tablet: 4 mg, 8 mg, 12 mg
Razadyne ER® Capsule: 8 mg, 16 mg, 24 mg
Razadyne® Oral Solution: 4 mg/mL

VII. References

1. Namenda XR® [Prescribing Information] St. Louis, MO: Forest Pharmaceuticals Inc; September 2014.
2. Razadyne/Razadyne ER® [Prescribing Information] Titusville, NJ: Ortho-McNeil-Janssen Pharmaceuticals, Inc; September 2016.
3. Aricept® [Prescribing Information] Woodcliff Lake, NJ:Eisai Inc; September 2013.
4. Exelon® [Prescribing Information] East Hanover, NJ: Novartis Pharmaceuticals; September 2013.
5. Trinh NH, Hoblyn J, Mohanty S and Yaffe K. Efficacy of cholinesterase inhibitors in the treatment of neuropsychiatric symptoms and functional impairment in Alzheimer Disease. *JAMA* 2003;289: 2: 210-216.
6. Blacker CV, Greenwood DT, Wesnes KA, et al. Effect of galantamine hydrobromide in chronic fatigue syndrome: a randomized, controlled trial. *JAMA* 2004;292(10):1195-204.
7. Tariot PN, Farlow MR, Grossberg GT, et al for the Memantine Study Group. Memantine treatment in patients with moderate to severe Alzheimer Disease already receiving donepezil; A Randomized controlled trial. *JAMA* 2004;201:3:317-324.
8. Rabins PV (2007). Guideline watch: Practice guideline for the treatment of patients with Alzheimer's disease and other dementias, Second Edition. Arlington, VA: American Psychiatric Association. Available online at: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/alzheimers.pdf. Accessed January 26, 2016.
9. Peskind ER, Potkin SG, Pomara N, et al. Memantine treatment in mild to moderate Alzheimer disease: a 24-week randomized, controlled trial. *Am J Geri Psych*. 2006; 14(8):704-15.

10. The American Geriatrics Society. A Guide to Dementia Diagnosis & Treatment. Available at: http://www.americangeriatrics.org/. Accessed June 19, 2015.
11. AHFS Drug Information Updates. Available at http://www.ahfsdruginformation.com. Accessed January 112, 2017.
12. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January12, 2017.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	1.12.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible

for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.