Alzheimer's Disease Step Therapy Program

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Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for brand name Alzheimer's Disease medication when the following criteria are met. The brand name medications affected are:

- Aricept®, Aricept® ODT (donepezil tablets and orally disintegrating tablets – Pfizer/Eisai, generics)
- Exelon® (rivastigmine capsules and oral solution [oral solution discontinued 4/2014] – Novartis, generics [capsules only])
- Exelon® Patch (rivastigmine transdermal system – Novartis, generics)
- Namzaric™ (memantine extended-release and donepezil capsules – Forest)
- Razadyne® (galantamine tablets and oral solution – Janssen, generics)
- Razadyne® ER (galantamine extended-release capsules – Janssen, generics)

When Policy Topic is covered
A step therapy program has been developed to encourage the use of one Step 1 (A or B) ChI product prior to the use of a Step 2 (A or B) product. If the step therapy rule is not met for the Step 2 (A or B) product at the point of service, then coverage will be determined by the step therapy criteria below. The program has two separate components: one for Generic ChI products first (does NOT include donepezil 23 mg tablets) and one for Aricept 23 mg strength (brand or generic). All approvals are provided for 1 year in duration.

Automation: Patients with a history of one Step 1 (A or B) drug within the 130-day look-back period are excluded from step therapy.

Generic first

**Step 1A:**
- Generic galantamine tablets or oral solution, generic galantamine extended-release capsules, generic rivastigmine capsules, generic donepezil tablets and orally disintegrating tablets (does NOT include donepezil 23 mg tablets), generic rivastigmine transdermal system

**Step 2A:**
- Aricept 5 and 10 mg tablets, Aricept ODT, Exelon, Exelon Patch, Namzaric, Razadyne, Razadyne ER

Aricept 23 mg strength (brand or generic)

**Step 1B:**
- Aricept 10 mg tablets (brand or generic) or Aricept ODT 10 mg (brand or generic)

**Step 2B:**
- Aricept 23 mg tablets (brand or generic)

Criteria

Generic first rule

1. If the patient has tried a Step 1A agent, then authorization for a Step 2A agent may be given.
2. No other exceptions are recommended.

**Aricept 23 mg strength (brand or generic) rule**

1. If the patient has tried a Step 1B agent, then authorization for a Step 2B agent may be given.

2. Patients who have taken Exelon Patch or Cognex at any time in the past and discontinued their use may receive authorization to restart the agent they used in the past.

3. Authorization may be given for Exelon Patch or Cognex if the patient has been established on therapy for \( \geq 60 \) days. (In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion.)

4. If the patient has difficulty swallowing or cannot swallow, authorization may be given for Exelon Patch.

5. No other exceptions are recommended.

**When Policy Topic is not covered**

The use of Alzheimer's Disease medication is considered *investigational* for all other indications.

**Considerations**

Alzheimer's Disease medications require prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

**Description of Procedure or Service**

Therapeutic agents indicated for the treatment of Alzheimer's disease (AD) are the acetylcholinesterase inhibitors (ChIs) [donepezil, rivastigmine, galantamine, tacrine], and the N-methyl-D-aspartate (NMDA) antagonist memantine (Namenda® and Namenda XR™). Donepezil and rivastigmine transdermal are the only agents approved for all degrees of AD [mild, moderate, and severe]. Galantamine/galantamine ER and oral rivastigmine are approved for mild to moderate AD. Oral and transdermal rivastigmine are also indicated for the treatment of mild to moderate dementia associated with Parkinson's disease (PD). Donepezil, galantamine extended-release (ER), and memantine ER can be dosed once daily (QD) while oral rivastigmine, galantamine, and memantine immediate-release (IR) are dosed twice daily (BID). Rivastigmine transdermal is applied QD. Namzaric is a fixed-dose combination containing donepezil and memantine ER. This policy does not further detail the single-agent NMDA antagonists.

ChIs enhance the secretion or prolong the half-life of acetylcholine by inhibiting its degradation within the synapse. Donepezil, galantamine, and rivastigmine are all second-generation ChIs. Tacrine, a first-generation ChI, was rarely used in clinical practice due to its hepatotoxic effects and frequent lab monitoring requirements, a property not observed with the second generation ChIs. Its use has been discontinued and it is no longer available.

The ChIs differ pharmacologically regarding the inhibition of acetylcholinesterase. All of these agents inhibit acetylcholinesterase; in addition, rivastigmine also inhibits butyrylcholinesterase (a cholinesterase enzyme that constitutes about 10% of the total cholinesterase in the brain).
Galantamine also has nicotinic agonist properties.\textsuperscript{2-4,8} The clinical significance of these pharmacologic differences has yet to be established.\textsuperscript{9}

Donepezil and rivastigmine transdermal are the only ChIs indicated for severe AD.\textsuperscript{1,10} Post-hoc analysis data for oral rivastigmine and galantamine also support the hypothesis that these ChIs may be effective in treating more advanced AD.\textsuperscript{11}

Only rivastigmine (oral and transdermal)\textsuperscript{3-4} is indicated for the treatment of dementia associated with PD.\textsuperscript{12-15} The indication for the rivastigmine transdermal preparation was based on data with the oral formulation.\textsuperscript{3-4} There are also data to support the use of donepezil for the treatment of dementia associated with PD.\textsuperscript{16-19}

There is increasing evidence that the pathological processes associated with AD and vascular dementia interact to increase the incidence of clinically significant cognitive decline.\textsuperscript{20-21} This coexistence of AD and vascular dementia pathology is referred to as mixed dementia. The coexistence of AD and vascular dementia are reported to occur in approximately one-fourth of all AD cases.\textsuperscript{20} All ChIs have been studied in patients with mixed dementia or vascular dementia and the data suggest that these agents may be useful.\textsuperscript{20-23}

Namzaric is indicated for the treatment of moderate to severe dementia of the Alzheimer’s type in patients stabilized on donepezil 10 mg QD and memantine IR (5 mg or 10 mg BID) or ER (14 mg or 28 mg QD).\textsuperscript{24}

**Rationale**

**References**

1. Aricept\textsuperscript{®} tablets/Aricept\textsuperscript{®} ODT (orally disintegrating tablets) [prescribing information]. New York, NY and Teaneck, NJ: Pfizer Inc. and Eisai Co., Ltd.; July 2015.
2. Razadyne\textsuperscript{®} tablets and oral solution and Razadyne™ ER extended-release capsules [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; February 2015.
3. Exelon\textsuperscript{®} capsules and oral solution [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; January 2015.
4. Exelon\textsuperscript{®} patch [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2015.
5. Namenda\textsuperscript{®} tablets and oral solution [prescribing information]. St. Louis, MO: Forest Laboratories, Inc.; October 2013.
7. Namenda XR\textsuperscript{®} extended-release capsules [prescribing information]. St. Louis, MO: Forest Laboratories, Inc.; April 20September 201413.


**Billing Coding/Physician Documentation Information**

N/A The Alzheimer’s Disease medications are considered a pharmacy benefit.

**Additional Policy Key Words**

Policy Number: 5.01.578

**Policy Implementation/Update Information**

07/2014 New Policy titled Alzheimer’s Disease Step Therapy Program
07/2015 Annual Review – no changes made
07/2016 Annual Review – no changes made to policy statement
07/2017 Annual Review – no changes made to policy statement

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.