STEP THERAPY POLICY

POLICY: Alzheimer's Disease Step Therapy Policy

- Aricept®, Aricept® ODT (donepezil tablets and orally disintegrating tablets – Pfizer/Eisai, generics)
- Exelon® (rivastigmine capsules – Novartis, generics)
- 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)

REVIEW DATE: 11/11/2020

OVERVIEW

Therapeutic agents indicated for the treatment of Alzheimer's disease (AD) are the acetylcholinesterase inhibitors (ChIs) [donepezil, rivastigmine, galantamine], and the *N*-methyl-D-aspartate (NMDA) antagonist memantine.[1-6] 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)**. Namzaric is indicated for the **treatment of moderate to severe dementia of the Alzheimer's type in patients stabilized on donepezil 10 mg QD**.[7] Namzaric is a fixed-dose combination containing donepezil and memantine extended-release (ER). Donepezil, galantamine ER, and Namzaric can be dosed once daily (QD) while oral rivastigmine and galantamine immediate-release (IR) are dosed twice daily (BID). Rivastigmine transdermal is applied QD. 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.[1-4] Donepezil, galantamine, and rivastigmine are all second-generation ChIs. Persistent activation of central nervous system NMDA receptors by the excitatory amino acid glutamate has been hypothesized to contribute to Alzheimer's disease symptoms, and memantine is thought to exert its therapeutic effect as an uncompetitive NMDA receptor antagonist.[7]

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.[2-4,8] The clinical significance of these pharmacologic differences has yet to be established.

Donepezil and rivastigmine transdermal are the only ChIs indicated for severe AD.[1,4] Post-hoc analysis data for oral rivastigmine and galantamine also support the hypothesis that these ChIs may be effective in treating more advanced AD.[9]

Only rivastigmine (oral and transdermal) is indicated for the treatment of dementia associated with PD.[3,4] The indication for the rivastigmine transdermal preparation was based on data with the oral formulation. There are also data to support the use of donepezil for the treatment of dementia associated with PD.[10-13]

There is increasing evidence that the pathological processes associated with AD and vascular dementia interact to increase the incidence of clinically significant cognitive decline.[14-16] 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.[14] All ChIs have been studied in patients with mixed dementia or vascular dementia and the data suggest that these agents may be useful.[8]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 (A or B) 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 the **Aricept 23 mg strength products (brand or generic)**. All approvals are provided for 1 year in duration.

Automation: A patient with a history of one Step 1 (A or B) Product within the 130-day look-back period is 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 one Step 1A Product, approve a Step 2A Product.

2. No other exceptions are recommended.

Aricept 23 mg strength (brand or generic) rule

1. If the patient has tried one Step 1B Product, approve a Step 2B Product.

2. No other exceptions are recommended.

REFERENCES

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