



Class ReviewSM - Abbreviated

Dementia Class Update

August 2008

Products for Review:

donepezil (Aricept[®]) [Eisai/Pfizer]
rivastigmine (Exelon[®]) [Novartis]
memantine (Namenda[®]) [Novartis]

Dossier Provided by Manufacturer: No Dossier Evaluation: (NA)

- 1 - Dossier missing significant clinical trial(s).
- 2 - Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3 - Mfg. provided all relevant trials and information.

Executive Summary

- Dementia is a chronic progressive disease with no known cure.
- Disease progression confounds medication efficacy results in clinical trials and assessment of effectiveness in individual patients.
- There are no treatments that modify the underlying causes of dementia of Alzheimer's Disease (AD) or Parkinson's Disease (PD).
- Donepezil (Aricept), rivastigmine (Exelon), and galantamine (Razadyne, formerly known as Reminyl[®]) may help prevent some symptoms from becoming worse for a limited time in some patients with mild to moderate disease.^[9]
- Historically, donepezil (Aricept), rivastigmine (Exelon), and galantamine (Razadyne) have been Regence preferred/formulary products.
 - There are limited treatment options for dementia.
 - Regence members expect to have covered formulary treatment options for dementia.
- There is no reliable evidence of any difference in efficacy between rivastigmine (Exelon), donepezil (Aricept), and galantamine (Razadyne).^[5]
- Memantine (Namenda) was reviewed by the Pharmacy and Therapeutics Committee in 2004. It was maintained as non-preferred/non-formulary because there was inconclusive evidence to support its effectiveness.
- [Despite the shortcomings of individual dementia trials](#), there are statistically significant improvements demonstrated across a large number of trials. The clinical meaningfulness of these is inconsistent and modest at best.

- Without reliable evidence to guide decision making, issues considered in the formulary recommendation include:

Formulary Considerations for Dementia Medications	
Consideration	Impact
Incidence and Severity	Dementia is a severe disease with increased burden on families and society.
Other treatment options	There are no other proven effective therapies that slow the progression of Alzheimer's Disease.
Potential magnitude of clinical benefit	These medications have been used in many patients for many years, and there is a general public perception of marginal clinical benefit.
Safety	The adverse event profile of these medications is similar (with the exception of tacrine). These risks need to be considered when choosing to treat or not treat, and should be part of the risk versus benefit discussion between the provider, patient and their family. The available safety information is not helpful in making formulary determinations, aside from the hepatotoxicity of tacrine.
Member disruption	If these medications were to be removed from formulary there would be tremendous member impact.
Clinical Practice Guidelines	All of these medication are recommended in clinical practice guidelines

Evidence

- Individual studies were appraised as unreliable. The overall body of evidence for all agents suggests trending improvement and slowing rate of worsening disease, based on standardized tests.
- There is insufficient reliable evidence to draw conclusions about the comparative efficacy and safety of rivastigmine, donepezil, galantamine, tacrine or memantine for the treatment of dementia.
- Only tacrine appears to have an increased incidence of liver enzyme elevation compared to the other AD drugs.^[13]

Decision

- Memantine (Namenda) is non-preferred/non-formulary because it was evaluated and there is no new compelling evidence or considerations to change non-formulary status.
- Tacrine (Cognex) is non-preferred/non-formulary because liver toxicity is a major safety concern not seen with the other medications.
- Donepezil (Aricept), galantamine (Razadyne) and rivastigmine (Exelon) are preferred/formulary because:
 - Although there is uncertain evidence of effectiveness, there are no other treatment options, and these products offer a possibility of clinical improvement.
 - The safety concerns with these medications are well known and manageable.
- Rivastigmine patch (Exelon patch) is preferred/formulary because:

(SR5746)			neuropathy	
bapineuzumab	Wyeth and Elan	2012	Alzheimer's disease	Phase II

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