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Pharmacists' Guide to Recommending Prevacen®

DECLINES IN COGNITIVE FUNCTION OFTEN occur as adults age and can include memory loss.¹ Pharmacists can support the brain health and well-being of older adults in the community setting by understanding age-related cognitive function changes and the dietary supplement options available that can promote healthy brain activity.

Prevagen® is an OTC brain health supplement clinically shown to be safe and to improve memory and support brain function, such as mild memory loss associated with aging.*

APOAEQUORIN, THE UNIQUE INGREDIENT OF PREVAGEN

Neuronal calcium dysregulation is an established contributor to age-related deficits in learning and memory.^{2,3} Apoaequorin is a calcium-binding protein found in luminescent jellyfish (*Aequorea victoria*) and is the unique ingredient of Prevacen. Calcium-binding proteins play an important role in the regulation of intracellular calcium homeostasis integral to neuronal cell function.²⁻⁴ It has been proposed that age-related declines in the expression and concentration of intracellular calcium-binding proteins and their altered distribution throughout the central nervous system may contribute to

cognitive decline, as well as enhance susceptibility to neuronal cell damage and death.²⁻⁴ Given the role of calcium-binding proteins in the pathophysiology of age-related neurocognitive decline, there may be benefits to the administration of the exogenous form of apoaequorin.

Results from several animal studies support the hypothesis that apoaequorin treatment may be neuroprotective.⁵⁻⁹ In a study of aged canines, apoaequorin treatment improved memory- and performance-related behaviors, including measures of learning and attention.¹⁰ As apoaequorin treatment modified markers of cognitive decline in pre-clinical studies, Prevacen was further investigated in an in-human clinical trial.

CLINICAL EFFICACY

The Madison Memory Study was a randomized, double-blinded, placebo-controlled trial that investigated the effects of Prevacen on cognitive performance in adults with self-reported memory and cognitive concerns.^{11,12} The trial enrolled a generally healthy population of 218 adults aged 40 to 91 years, without a history of neurologic or cognitive illness. Participants were randomized (3:2) to

TABLE. Key Efficacy Results from the Madison Memory Study^{11,12}

Cognitive measurement test	Percent change in test score from Day 0 to Day 90		
	Placebo	Prevagen®	Between-group P value
Population with AD8 scores of 0-1 (n=61) ^a			
Groton Maze Learning: delayed recall ^b	-4.3%	-30.9%	P = .011
Detection ^c	-0.53%	2.17%	P = .015
One Card Learning ^d	3.16%	0.25%	P = .010
Population with AD8 scores of 0-2 (n=100) ^a			
Groton Maze Learning ^b	-17.1%	-20.7%	P = .040
Identification ^e	0.22%	-0.15%	P = .037
One Card Learning ^d	2.78%	1.27%	P = .02

AD8 indicates Ascertain Dementia 8.

^aAD8 scores 0-1 indicate no cognitive impairment. AD8 scores 0-2 indicate no or minimal cognitive impairment.

^bMeasures executive function and visual or spatial memory. A grid is presented on the computer screen, and participants must find the hidden pathway by clicking tiles within the grid, starting at the top left-hand corner and working toward the bottom right-hand corner. Participants are guided by visual and audio clues after clicking on a tile. The total number of errors is the outcome measure for both tests, and lower scores indicate better performance (fewer moves to complete the maze).

^cMeasures psychomotor speed (reaction time). Participants must click a button as soon as they see a card presented in the center of the screen turn faceup. The mean speed of performance for correct responses is the outcome measure, and lower scores represent better performance (faster reaction times).

^dMeasures visual attention and recognition memory (learning). A playing card is presented faceup and the participant must indicate whether they have seen the card before in the sequence. Accuracy is the outcome measure, and a higher score indicates better performance.

^eMeasures visual attention. A playing card is presented on the screen, and the participant must identify it as red or black as quickly as possible. The mean speed of performance for correct responses is the outcome measure, and lower scores represent better performance (faster reaction times).

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receive one 10-mg capsule of Prevagen or placebo daily for 90 days. A total of 211 participants completed the study.^{11,12}

At baseline, participants were stratified into distinct cohorts based on their level of self-reported cognitive impairment as measured via the Ascertain Dementia 8 (AD8) screening tool. The AD8 is a validated, interview-based, 8-question screening tool that differentiates those with cognitive changes attributed to normal aging from those with early signs of dementia.¹³ An AD8 score of 2 was used as a cutoff value to identify the populations with normal cognitive function (AD8 0-1) and very mildly impaired cognitive function (AD8 0-2) from those with higher levels of impairment (AD8 3-8). Because Prevagen is a dietary supplement intended for healthy, nondemented individuals, results from participants in the AD8 0-1 and AD8 0-2 cohorts are most relevant to the efficacy of the product.¹¹⁻¹³

To assess the effect of Prevagen compared with placebo, changes in cognitive function were quantitatively assessed at baseline and at 8-, 30-, and 90-day time points using tests from the Cogstate Research battery, a widely used and validated tool to assess verbal and visual learning, memory and working memory, executive functioning, and psychomotor function and attention via computer-based maze learning and recall tasks.^{11,12} Although no statistically significant results were observed over the entire study population, the Prevagen-treated participants in the AD8 0-1 and AD8 0-2 cohorts achieved statistically significant improvement in the Cogstate mean test scores measuring aspects of cognitive function compared with the placebo treatment group (TABLE).^{11,12}

As a result of the findings, it was concluded that dietary supplementation with Prevagen enhances cognitive function among healthy adults with normal cognitive aging or very mild impairment.

SAFETY

The unique ingredient in Prevagen, apoaequorin, has undergone extensive safety testing for toxicity and allergenicity. In human clinical trials, apoaequorin was well tolerated for up to 90 days.¹¹ In animal safety studies, apoaequorin was found to be safely consumed in doses much higher than the recommended dosage (4000 to 16,000 times the recommended daily amount of Prevagen Regular Strength) and without adverse effects when taken orally.^{14,15} Apoaequorin is not a known allergen and is not likely to be cross-reactive with any known allergens. In a separate safety study, apoaequorin exhibited a digestibility profile similar to those of other nonallergic dietary proteins, without any significant risk of allergic reactivity when ingested orally.¹⁶

ROLE OF THE PHARMACIST

According to the 2021-2022 *Pharmacy Times*® OTC national survey, Prevagen is the number-1 pharmacist-recommended memory support brand among pharmacists who recommend memory

support products. If asked for a recommendation, pharmacists can provide information about Prevagen's safety, efficacy, and clinically tested ingredient. In a clinical trial, a subgroup of adults with mild, age-related cognitive impairment taking just 1 Prevagen a day, over 90 days, achieved improvements in measurements related to memory.^{11,12,*}

As with any new dietary supplement, pharmacists can be a helpful resource for information and can answer questions regarding the use of Prevagen. Prevagen is available in Regular Strength (10 mg) and Extra Strength (20 mg) dosages as a once-daily oral capsule or chewable tablet. Note that it is recommended to take Prevagen for 90 days to fully gauge its effectiveness. In addition to recommending Prevagen, pharmacists can provide education on lifestyle choices that can promote cognitive health, such as regular physical and social activity.¹ ■

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