DRUG FACTS BOX

ConsumerReports®

Razadyne (galantamine)

RAZADYNE tablets for mild-to-moderate dementia from Alzheimer's Disease

What is the purpose of this box?

To explain the benefits and side effects of RAZADYNE immediate release tablets to help you decide whether to use this drug.

What is this drug for?

To treat symptoms of dementia or mental decline due to mild-to-moderate Alzheimer's disease, which impairs people's ability to remember, learn, and reason. Like other dementia drugs, RAZADYNE may temporarily improve symptoms, but it is not a cure.

Who might consider taking it?

Adults with mild-to-moderate Alzheimer's Disease as indicated by a score of between 10 and 20 out of a possible 30 on the mini-mental status test of basic thinking skills (MMSE). An interactive version of the test is available at http://tinyurl.com/maghexp.

Precautions to take

Patients and caregivers need to ensure adequate fluid intake because the drug can cause **dehydration** from **not eating**, or prolonged **vomiting** or **diarrhea**. Be alert for weight loss, bleeding in the stomach and intestines, worsening of symptoms of asthma or obstructive lung disease and fainting from a slow heart rate. Routinely evaluate the ability to continue driving or operating machinery. **RAZADYNE CAN ALSO CAUSE OTHER UNCOMMON, LIFE-THREATENING OR SERIOUS SIDE EFFECTS**: A **very slow heart rate**, even in people with no prior heart problems, which could be potentially dangerous; **fainting** from too slow heart rate has been reported; **blockage** in the bladder making it difficult or impossible to urinate; **seizures**; **bleeding** in the stomach or intestines, especially people who have a history of ulcers or who are taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen (Advil, Motrin, and generic), or naproxen (Aleve and generic).

What other choices are there?

Donepezil (ARICEPT and generic) and rivastigimine (EXELON patch and capsules, generic capsules). Monitored exercise therapy, occupational therapy, and activities that stimulate the brain such as art and music may also be helpful.

BOTTOM LINE

RAZADYNE's benefit

Limited benefit in slowing deterioration of remembering, learning and reasoning—Studies have consistently shown that, for the typical patient, RAZADYNE slows deterioration in remembering, learning and reasoning **by only a modest amount**. The results reported in this Drug Facts Box™ are essentially the same as those reported in recent high-quality systematic reviews of all trials testing the drug for dementia. [Cochrane Collaboration (2012), UK Health Technology Assessment Programme (2012), American College of Physicians (2008) and Drug Effectiveness Review Project (2006)]

Never shown to improve quality of life, independent function or reduce institutionalization—No evidence that RAZADYNE improves quality of life for either patients or caregivers, prolongs people's ability to function independently, or reduces the need for institutionalization—all major goals of treating dementia. Here's how the FDA's Medical Reviewer described the benefit of RAZADYNE [Overall Conclusion in the Executive Summary]:

> *"It should be noted that the beneficial effects of Razadyne are small, and similar to those of other cholinesterase inhibitors, when compared with placebo; as with other cholinesterase inhibitors, only a small minority of patients actually improve in relation to baseline; the efficacy of galantamine beyond 6 months of treatment is uncertain, as randomized controlled studies longer than 6 months in duration have not been carried out."*

RAZADYNE's harm

Can cause bothersome and potentially serious side effects—RAZADYNE can cause fainting, slow heart rate, diarrhea, nausea, vomiting, decreased appetite and weight loss—all of which can be serious for older people with dementia.

Long track record means new, unexpected side effects are unlikely—The FDA approved RAZADYNE at these doses for mild to moderate dementia from Alzheimer's disease in **2001**. Because a large number of Alzheimer's patients have taken this drug for many years, new important side effects are unlikely to emerge.

Comparing doses

The FDA approved doses of 8 mg to 24 mg daily. The 16-mg dose may be the best choice as it works about as well as the 24-mg dose, but with fewer side effects. Do not use a 32-mg dose because the trials demonstrated no increased benefit, but substantially more side effects. Start with the 4-mg dose twice daily for a month before increasing to 8 mg twice daily. To reduce the risk of side effects, do not increase the dose faster than every four weeks.

Razadyne Study Findings

The FDA approved RAZADYNE immediate release tablets based on evidence from four randomized trials with similar results. The three longest trials included 1,686 people with mild-to-moderate Alzheimer's Disease (average MMSE of 19) who were an average of 76 years old; about two thirds were women. Researchers randomly assigned participants to take either RAZADYNE immediate release tablets or a placebo (inactive sugar pill) for **5 to 6 months**. Here's what happened:

	RAZADYNE 16 mg (8 mg twice daily)	RAZADYNE 24 mg (12 mg twice daily)	vs.	Placebo (No drug)
How did RAZADYNE help?*				
Doctor's rating of change in dementia				
Ratings were about the same for the 16-mg and 24-mg doses. For some people, RAZADYNE helped more than a placebo, but the improvement was minimal. The biggest differences were in how many people were unchanged or worse.				
Percent of people doctors rated as...				
Markedly or moderately **improved**	3%	4%	vs.	2%
Minimally **improved**	18%	18%	vs.	11%
Unchanged	46%	45%	vs.	37%
Minimally **worse**	24%	26%	vs.	33%
Markedly or moderately **worse**	8%	7%	vs.	17%
Remember, learn and reason				
The typical person taking RAZADYNE scored slightly higher on a **71-point test** than those taking a placebo—**3.6 points higher for those taking 16 mg** and **3.5 points higher for those taking 24 mg**.	1.5 points **better**	1.4 points **better**	vs.	2.1 points **worse**
17 percent of those taking a PLACEBO improved by the minimum noticeable amount (scores were better by 4 points or more). Compared to those taking a PLACEBO, **19 percent more of those taking RAZADYNE 16 mg and 17 percent more of those taking RAZADYNE 24 mg experienced this improvement.**	36%	34%	vs.	17%
Caregiver quality of life and use of healthcare resources				
RAZADYNE had no effect in the two trials that measured those factors.				
What were RAZADYNE's side effects?*				
Side effects based on 838 people where RAZADYNE dose was increased after 4 weeks.				
Compared to those taking a PLACEBO:				
1 to 2 percent more had a **slow heart beat**	2 to 3%	2-3%	vs.	<1%
0.6 percent more (16-mg dose) and 1.5 percent more (24-mg dose) **fainted**	2.2%	3.3%	vs.	0.7%
8 percent more (16-mg dose) and 12 percent more (24-mg dose) had **nausea**	13%	17%	vs.	5%
5 percent more (16-mg dose) and 9 percent more (24-mg dose) had **vomiting**	6%	10%	vs.	1%
4 percent more (16-mg dose) and 6 percent more (24-mg dose) had **less appetite**	7%	9%	vs.	3%
4 percent more (both 16-mg and 24-mg dose) had **weight loss**	5%	5%	vs.	1%
1 percent more (16-mg dose) and 3 percent more (24-mg dose) had **dizziness**	5%	7%	vs.	4%
1 percent more (16-mg dose) and 3 percent more (24-mg dose) had **sleepiness**	3%	5%	vs.	2%
4 percent more (16-mg dose) and 6 percent more (24-mg dose) had **fatigue**.	4%	5%	vs.	2%

* *Data from FDA Review Documents*

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