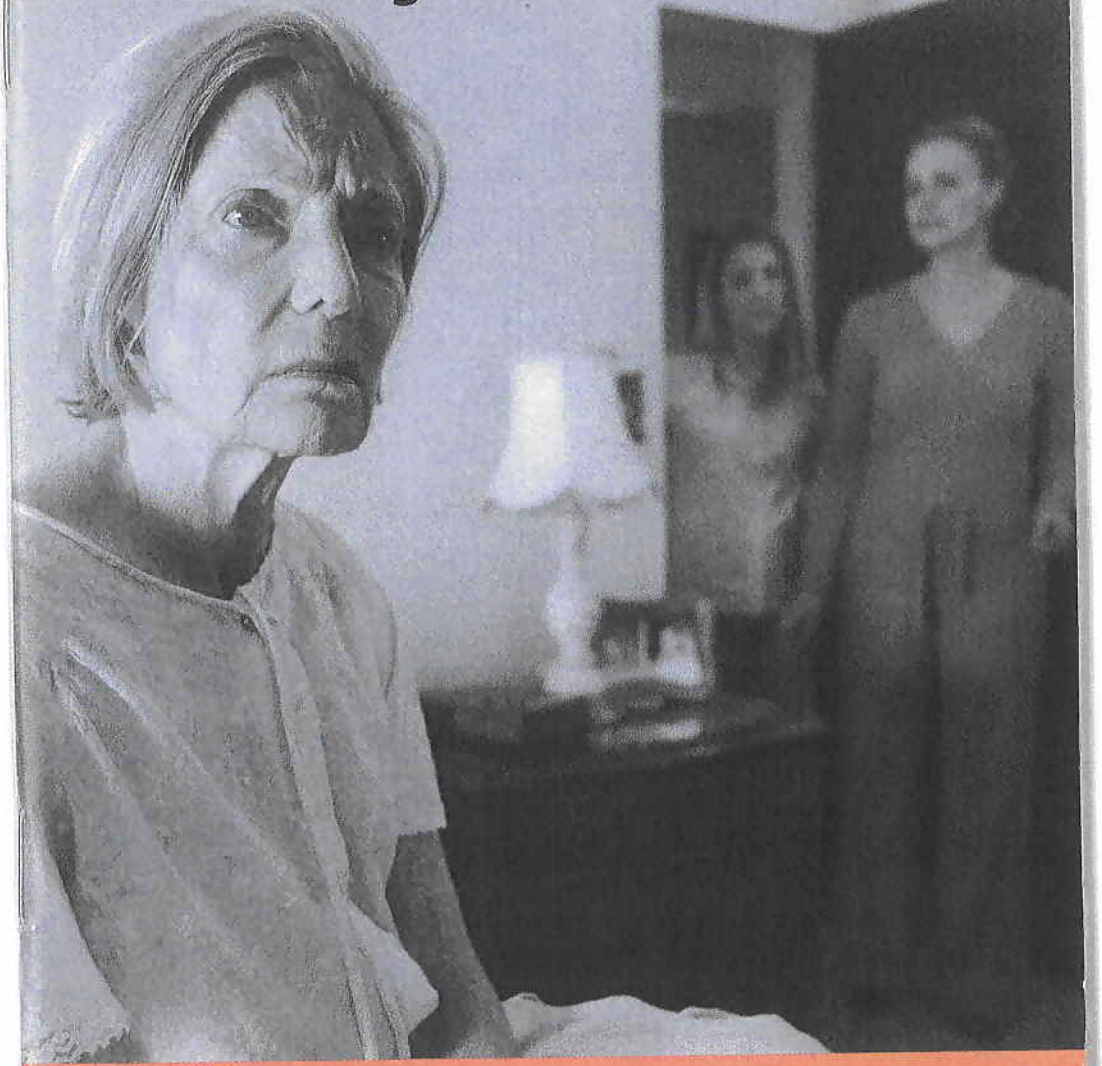
When Alzheimer's disease starts to turn loved ones into strangers...



Please see enclosed complete prescribing information.

It's time to turn to EXELON

Please see enclosed complete prescribing information

Turn to EXELON for efficacy

- Improved cognition versus placebo in controlled clinical trials[1]
- A majority of patients not responding to donepezil responded to EXELON in open-label studies[2,3]
- Helps maintain activities of daily living (ADLs) and aspects of behavior[4,5]
- Inhibits both acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE)[6]
  - The clinical significance of BuChE inhibition has not been established

Turn to EXELON for a favorable safety profile

- No known pharmacokinetic drug-drug interactions (DDIs)[1]
  - Cholinesterase inhibition not affected by Namenda® (memantine HCl)[1]*
- No increased incidence in cardiac adverse events as measured by electrocardiogram (ECG)[7]

Turn to EXELON — An effective choice in Alzheimer's disease therapy

EXELON is indicated for the treatment of mild to moderate Alzheimer's disease (AD)

*Based on in vitro and in vivo studies.

Namenda is a registered trademark of Forest Laboratories, Inc.

For mild to moderate Alzheimer's disease

EXELON®

(rivastigmine tartrate)

1.5, 3, 4.5, 6 mg Capsules

2 mg/ml Oral Solution

Efficacy matters most

In an open-label study, the majority of donepezil nonresponders responded to EXELON

- Primary end point: Effects of EXELON on global functioning in donepezil nonresponders[2]
  - Measured by Clinician's Global Impression of Change (CGIC)[2]

DONEPEZIL NONRESPONDERS MET 1 OF THE FOLLOWING CRITERIA[2]

- ≥2 point Mini-Mental State Examination (MMSE) decline within previous 6 months

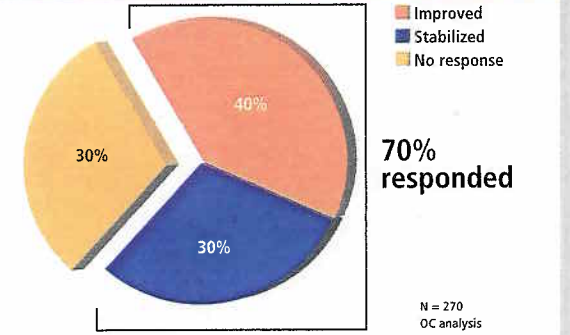
or

- Investigator-determined clinical decline in ≥1 of the following:
  - ADLs
  - Behavioral aspects
  - Global functioning

or

- Caregiver dissatisfaction with patient's response to treatment
  - Lack of efficacy or benefits

RESULTS ON PRIMARY END POINT[2]

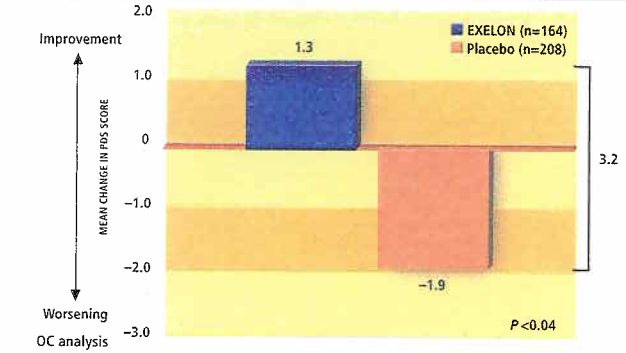


Results of a 26-week, open-label, single-arm, prospective, US multicenter study (N=270) during which patients received EXELON 1.5 mg/day BID within 1 week after last dose of donepezil after a minimum of 3 months of poor response to donepezil 10 mg/day (mean duration = 2 years). A majority initiated the next day (average 1.6 days).[2] Percent response based on mean CGIC scores at end point. OC refers to observed case.[2]

- 70% of donepezil nonresponders responded to EXELON in this open-label study[2]
  - Response defined as no change or improvement in CGIC[2]
- The most common adverse events (AEs) reported in the study were nausea (32%), vomiting (23%), dizziness (10%), and weight loss (10%)—with a discontinuation rate of 8% due to gastrointestinal (GI) AEs[2]

Turn to EXELON to help maintain functionality

EXELON HELPED SUSTAIN ADLs AT 26 WEEKS[4]



Results from a randomized, double-blind, parallel-group trial involving 725 patients with AD and MMSE scores of 10 to 26. After a 12-week dose escalation phase, patients received 6 to 12 mg/day based on maximum tolerated dose [4]

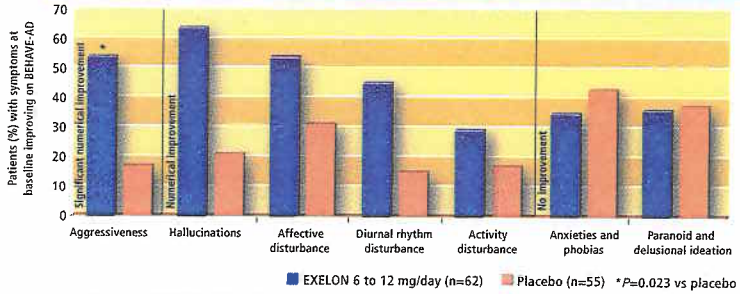
- Progressive Deterioration Scale (PDS) domains included[4]:
  - Social interaction
  - Housework
  - Hobbies
  - Awareness of time
  - Handling financial matters
  - Dressing, eating abilities

For the primary end points:

- **Patients taking EXELON had a 3.93 Clinician's Interview–Based Impression of Change Scale with Caregiver Input (CIBIC-plus)** score versus 4.34 with placebo ($P<0.05$)[4]
  - CIBIC-plus globally assesses cognition, behavior, functioning, and ADLs[4]
- **EXELON improved Alzheimer's Disease Assessment Scale Cognitive Subscale** (ADAS-Cog) by 1.17 points versus a 1.41-point decline with placebo ($P<0.001$)[4]
  - ADAS-Cog measures cognition, including aspects of memory, language, orientation, and praxis[4]

EXELON may help manage some aspects of behavior

A RETROSPECTIVE SUBSET ANALYSIS IN POOLED STUDIES OF MODERATE AD PATIENTS[5]



Pooled results from 3, 26-week trials involving patients with MMSE scores of 10 to 26 taking either EXELON 6-12 mg/day or placebo. Only patients with the behavioral symptoms present at baseline were included in the analysis. Therefore, only the OC analysis is presented, and the baseline frequency of behavioral symptoms varies.[5]

The analysis is based on the Behavioral Pathology in Alzheimer's disease (BEHAVE-AD) scale, a 2-part scale based on caregiver's evaluation of impact of symptoms on the patient and caregiver. In the original studies, BEHAVE-AD was reported as part of the CIBIC-Plus.[5] Affective disturbance signifies affective or mood disturbance. Diurnal rhythm disturbance is a disorder of the sleep-wake cycle.

- Significantly reduced aggression at 26 weeks[5]
  - Numerically reduced hallucinations and affective disturbance, diurnal rhythm, and activity disturbances after 26 weeks with daily dosages of 6 to 12 mg/day. Statistical significance was not shown[5]
- No improvement versus placebo was seen in anxieties and phobias as well as paranoid and delusional ideation[5]

Weight loss (7% of baseline weight) associated with EXELON occurred more commonly among women (26%) versus men (18%) receiving high doses (>9 mg/day) in clinical trials.

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Turn to EXELON with confidence

EXELON HAS A SAFETY PROFILE THAT PROVIDES CONFIDENCE[1]

	EXELON
No known pharmacokinetic DDIs	✓
Plasma protein binding	Low (approx. 40%)
No hepatic metabolism	✓
Inactive metabolite elimination	✓
No required dose adjustments for renal/hepatic impairment	✓
No increased incidence of ECG abnormality	✓

- **No known pharmacokinetic interactions** with many commonly prescribed medications (eg, fluoxetine, warfarin, digoxin)[1]

MEAN CHANGE FROM BASELINE TO END POINT IN QTc INTERVAL[7]

	≥6 mg/day group (n=1188)	<6 mg/day group (n=702)	Placebo (n=858)
Heart rate (bpm)	–1.7	–0.2	0.6
QTc interval (msec)*	–2.3	–1.4	0.0

Pooled results from an ECG analysis of 4 26–week phase III double–blind trials involving patients with mild to moderate AD. QT corrected using Bazett formula.

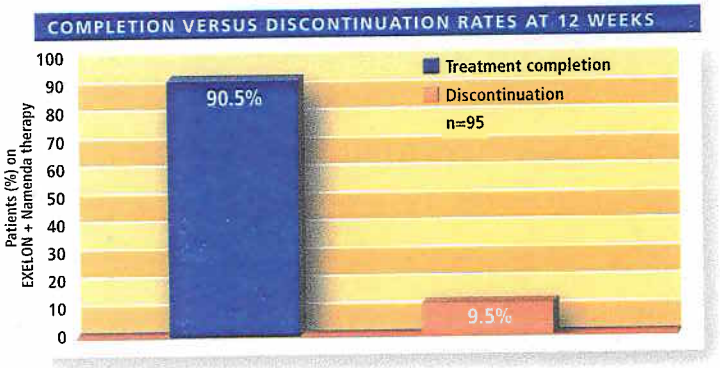
- No increased incidence of cardiac AEs per ECG[7]
  - No clinically meaningful differences were apparent between EXELON and placebo in heart rate and corrected QT (QTc) intervals[7]

Due to increased cholinergic activity, cholinesterase inhibitors may be expected to increase gastric acid secretion and/or have vagotonic effects on heart rate. Therefore, EXELON should be used with caution in patients with peptic ulcers, gastrointestinal bleeding, "sick sinus syndrome" or other supraventricular cardiac conduction conditions, and in those who use nonsteroidal anti-inflammatory drugs (NSAIDS). (Please see important WARNINGS in complete prescribing information.)

*QTc is the QT corrected for heart rate (QT decreases as heart rate increases). QT corrected in this study was calculated by the Bazett formula. $QTc=QT/RR^{0.5}$

Please see enclosed complete prescribing information.

Results of an open-label noncomparative study of EXELON + Namenda® (memantine HCl)[6]



Results of a 12-week, open-label, single-arm, historically-controlled pilot study in which patients used EXELON for a maximum of 24 weeks prior to initiating Namenda. Efficacy baseline defined as patients established on EXELON.[6]

- **9.5% of patients discontinued when Namenda was added to EXELON[6]**
  - Overall, AEs affected 31.6% of patients; AEs >5% were nervous system (10.5%), GI (8.4%), and psychiatric (6.3%)[6]
  - Discontinuation rate due to AEs was 4.2%[6]
- Mean change in ADAS-Cog score was –1.73 (n=90)[6]
  - Mean daily EXELON dose was 6.8 mg/day; mean Namenda dose was 19.0 mg/day[6]
- Both EXELON and Namenda are dosed BID, making administration convenient for patients and caregivers
- The inhibition of cholinesterase by EXELON is not affected during the concomitant administration of Namenda[1*]

*Based on in vitro and in vivo studies

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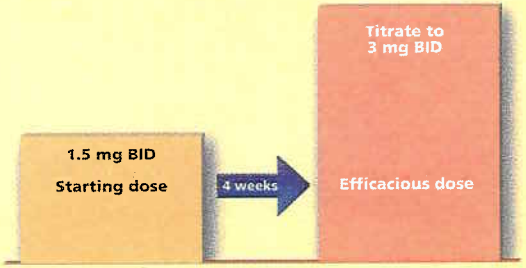
Efficacy matters most

One step to a therapeutic dose



- Patients should take EXELON with a full meal to help manage potential GI AEs[1]
- Linear dose response[8]
- Titrate based on individual patient needs:
  - 4.5 mg and 6 mg capsules available; also 2 mg/mL oral solution
  - Higher doses may lead to increased incidence of AEs, especially during dose titration
- 4-week titration intervals are suggested for all doses

EXELON has shown no significant increase, relative to placebo, in the incidence of either peptic ulcer disease or gastrointestinal bleeding in clinical trials. However, because of their pharmacological action, cholinesterase inhibitors may be expected to increase gastric acid secretion due to increased cholinergic activity. Therefore, EXELON should be used with caution in patients with peptic ulcer disease or gastrointestinal bleeding and in those who use nonsteroidal anti-inflammatory drugs.

- Low discontinuation rate (1%) due to nausea and vomiting during maintenance[1]
  - 8% and 4% discontinuation rate due to nausea and vomiting during titration[1]
- Incidence of GI AEs during the maintenance phase of the pivotal trials (6 to 12 mg/day) was 17% for nausea, and 14% for vomiting[1]
- When vomiting and nausea occur, they are generally transient and may be manageable[1,6]
  - Last a median of 1 and 3 days, respectively[6*]
  - Incidence of nausea and vomiting during the forced-dose titration was 43% and 24%, respectively[1†]

EXELON has been associated with significant gastrointestinal adverse reactions, including nausea and vomiting (47% and 31%), anorexia, and weight loss. If therapy is interrupted for longer than several days, treatment should be reinitiated with the lowest daily dose in order to avoid the possibility of severe vomiting and its potentially serious sequelae.

*EXELON dosage was 6 mg/day.
† Pivotal trial design required 1- to 2-week forced-dose titration during the dose-titration phase.

References:

1. EXELON [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp; October 2004.
2. Figiel G, et al. Poster presented at: 57th Annual Scientific Meeting of the Gerontological Society of America; November 17-23, 2004; Washington, DC.
3. Auriacombe S, et al. *Curr Med Res Opin*. 2002;18:129-138.
4. Rösler M, et al. *BMJ*. 1999;313:633-638.
5. Burns A, et al. *Int J Geriatr Psychiatry*. 2004;19:243-249.
6. Data on file. Novartis Pharmaceuticals Corp.
7. Morganroth J, et al. *J Clin Pharmacol*. 2002;42:1-11.
8. Anand R, et al. *Int J Geriatr Psychopharmacol*. 2002;2:68-72.

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Turn to EXELON—An effective choice in AD therapy

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(1-888-82 PART D)

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NOVARTIS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936

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