ZUNVEYL®
(benzgalantamine)

A clear choice for Alzheimer's disease

With proven medication + purposefully designed delivery,
ZUNVEYL can help address treatment challenges
of Alzheimer's disease in older adults.

INDICATION AND USAGE

ZUNVEYL is a cholinesterase inhibitor indicated for the treatment of mild to moderate dementia of the Alzheimer's type in adults.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ZUNVEYL is contraindicated in patients with known hypersensitivity to benzgalantamine, galantamine, or to any inactive ingredients in ZUNVEYL. Serious skin reactions have occurred.

Please see additional Important Safety Information throughout and full Prescribing Information from your representative.

ZUNVEYL
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DELAYED RELEASE TABLETS
5 mg | 10 mg | 15 mg

ZUNVEYL: Purposefully Designed Delivery

ZUNVEYL is the first and only FDA-approved AChEI to utilize prodrug enteric-coated, delayed-release technology to minimize absorption in the stomach and overstimulation of neurons in the gastrointestinal (GI) nervous system[1,2]

Enteric-Coated

ZUNVEYL passes through the stomach inertly, limiting absorption[2]

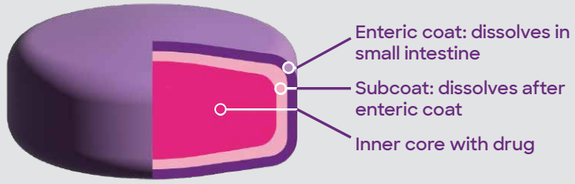
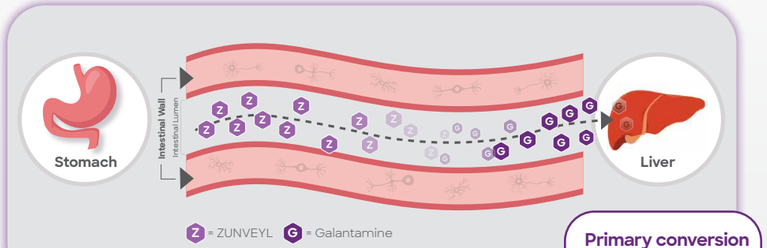


Image adapted from Components of Drug Product.

Prodrug Design

ZUNVEYL remains inactive until after first pass metabolism in the liver, and then converts to active galantamine[1-3]



Primary conversion of ZUNVEYL to galantamine occurs in the liver

ZUNVEYL provides dual protection

- Protects from peripheral and central cholinergic side effects[2]
  - Minimizes stomach absorption, enabling targeted delivery to the intestine
  - May minimize central emetic activation

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Serious Skin Reactions: Serious skin reactions (Stevens-Johnson syndrome and acute generalized exanthematous pustulosis) have been reported in patients receiving galantamine (the active metabolite of ZUNVEYL tablets). If signs or symptoms suggest a serious skin reaction, use of this drug should not be resumed, and alternative therapy should be considered.

Anesthesia: See Drug Interactions Section.

The Dual Acting Mechanism of Action of ZUNVEYL

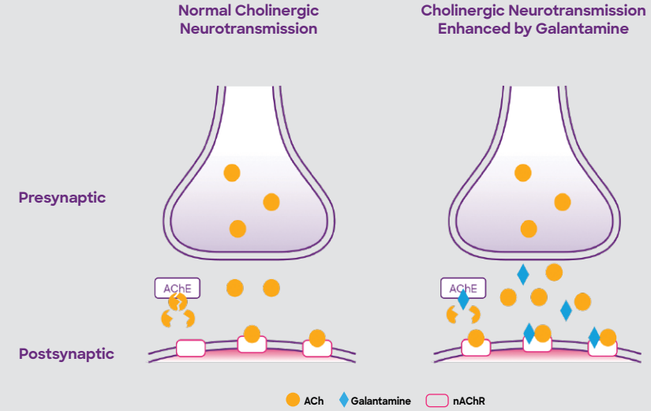
ZUNVEYL is believed to work in two ways*

Acetylcholinesterase Inhibitor

- Inhibits acetylcholinesterase, preventing the breakdown of acetylcholine and increasing its availability[1]

Nicotinic Receptor Modulator

- Modulates nicotinic acetylcholine receptors (nAChR) making acetylcholine pathways more responsive[4,5]
  - Stimulates the cholinergic pathway
  - Decreases inflammation
  - Buffers the effects of amyloid
  - Enhances release of other transmitters: glutamate, dopamine, GABA, serotonin, and norepinephrine



Adapted from Lilienfeld 2002.

*The mechanism of action of ZUNVEYL is not fully understood.

Acetylcholinesterase Inhibitor=AChEI; FDA=U.S. Food and Drug Administration; GABA=gamma-aminobutyric acid.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Cardiovascular Conditions: Cholinesterase inhibitors, including ZUNVEYL, have vagotonic effects on the sinoatrial and atrioventricular nodes, leading to bradycardia and AV block. Bradycardia and all types of heart block have been reported in patients taking cholinesterase inhibitors, both with and without known underlying cardiac conduction abnormalities. Therefore, all patients should be considered at risk for adverse effects on cardiac conduction.

Patients treated with galantamine up to 24 mg/day using the recommended dosing schedule showed a dose-related increase in risk of syncope.

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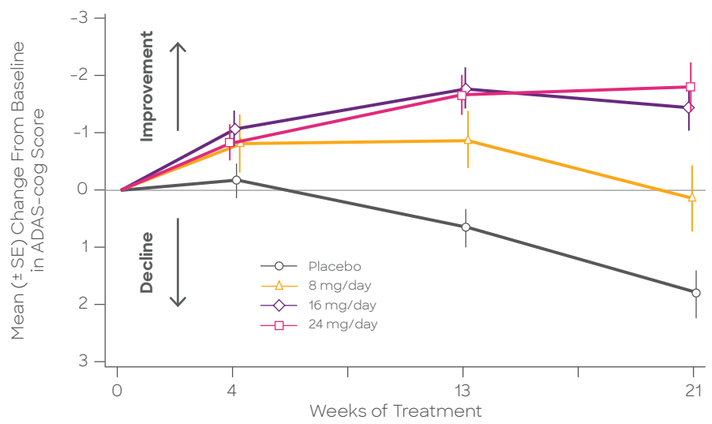
Clear Improvement in Cognitive Function

In a 21-week study of 978 patients with mild to moderate Alzheimer's disease, galantamine (the active ingredient of ZUNVEYL) showed sustained cognitive benefits through ADAS-cog scores.[1,6]

Co-Primary Clinical Endpoint: ADAS-cog

Time Course of the Change From Baseline in ADAS-cog Score for Patients Completing 21 Weeks of Treatment[1]



Improved ADAS-cog scores demonstrated delayed impairment in cognitive function, including memory, orientation, attention, language, reasoning, and praxis[1]

The mean difference versus placebo in ADAS-cog change scores was 3.3 points for 16 mg/day and 3.6 points for 24 mg/day[1]

Study design: A randomized, double-blind, placebo-controlled study of galantamine immediate-release tablets. Patients were randomized to doses of 8, 16, or 24 mg of galantamine per day, or to placebo, each given in 2 divided doses. Treatment was initiated at 8 mg/day for all patients randomized to galantamine and increased by 8 mg/day every 4 weeks. There was no statistically significant difference between the 16 mg and 24 mg treatments.[1]

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Neurological Conditions: Cholinesterase inhibitors are believed to have some potential to cause generalized convulsions. Seizure activity may also be a manifestation of Alzheimer's disease. Patients with Alzheimer's disease should be monitored closely for seizures while taking ZUNVEYL.

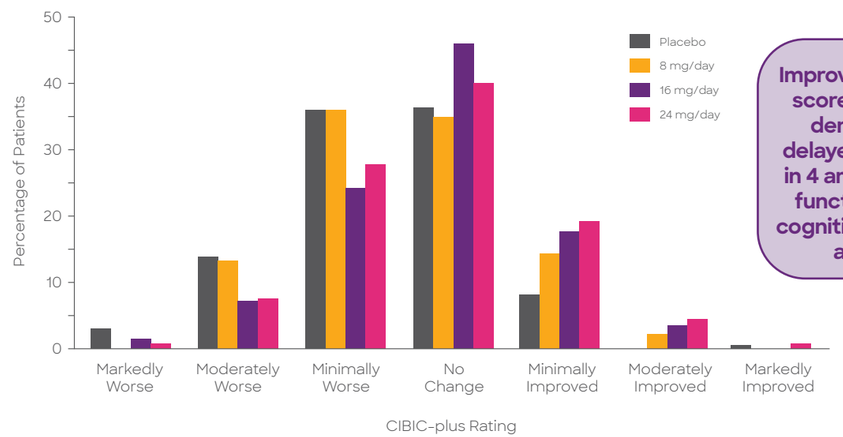
Pulmonary Conditions: Cholinesterase inhibitors, including ZUNVEYL, should be prescribed with care to patients with a history of severe asthma or obstructive pulmonary disease. Monitor for respiratory adverse reactions.

Improved Cognition, Behavior, and Daily Living

Patients treated with galantamine (the active ingredient of ZUNVEYL) showed significant gains or sustainment in CIBIC-plus scores, a measure of overall clinical response to therapy, demonstrating its impact across cognition, behavior, and daily living activities.[1]

Co-Primary Clinical Endpoint: CIBIC-plus

Mean Change from Baseline in CIBIC-plus Scores for Patients Completing 21 Weeks of Treatment[1]



Improved CIBIC-plus scores vs placebo demonstrated delayed impairment in 4 areas of patient function: general, cognitive, behavioral, and ADLs[1]

At 5 months, 64% to 68% of the 16 mg/day and 24 mg/day groups remained stable or improved compared with 47% of patients in the placebo group (observed cases analysis; $P<0.001$)[6]

- **The mean difference versus placebo in CIBIC-plus scores was 0.41 points for galantamine IR 16 mg/day and 0.44 points for galantamine IR 24 mg/day.**[1]

ADAS-cog=Alzheimer's Disease Assessment Scale-Subscale-Cognitive; ADLs=activities of daily living; CIBIC-plus=Clinician's Interview-Based Impression of Change Plus caregiver input; IR=immediate release; SE=standard error.

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

The most common adverse reactions with galantamine tablets (≥5%) were nausea, vomiting, diarrhea, dizziness, headache, and decreased appetite.

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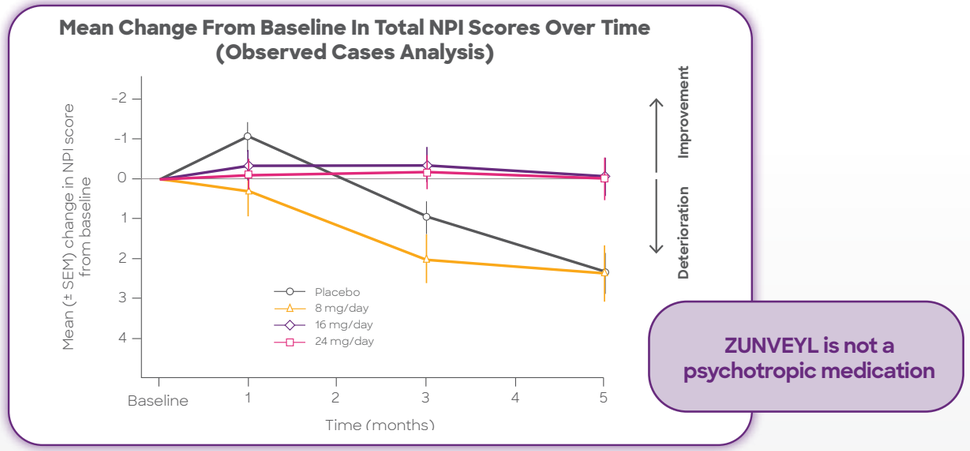
Improvement on Behavioral Symptoms

- Among patients treated with therapeutic doses of galantamine (the active ingredient of ZUNVEYL), the results of the NPI indicate a significant benefit of galantamine on behavioral symptoms compared to placebo[6]

Secondary Clinical Endpoint: Neuropsychiatric Inventory (NPI)



ZUNVEYL is not a psychotropic medication

SEM=Standard Error of the Mean

At 5 months, both the 16 mg/day and 24 mg/day groups had significantly better NPI total scores than placebo (observed cases analysis; $P<0.05$)[6]

- **The NPI assesses the frequency and severity of symptoms in 10 behavioral domains[6]**

NPI BEHAVIORAL DOMAINS[7]	DEFINITIONS
DELUSIONS	False beliefs about being harmed or in danger
HALLUCINATIONS	See, hear, or experience things not present
AGITATION/AGGRESSION	Resistant to care, aggressive behavior
DEPRESSION/DYSPHORIA	Persistent feelings of sadness and hopelessness
ANXIETY	Excessive worry or fear disproportionate to situation
ELATION/EUPHORIA	Excessive cheerfulness or inappropriate humor
APATHY/INDIFFERENCE	Lack of motivation, lack of interest in surroundings
DISINHIBITION	Socially inappropriate behavior or lack of restraint
IRRITABILITY/LABILITY	Quick to anger or displaying sudden mood changes
ABERRANT MOTOR BEHAVIOR	Repetitive, purposeless movements

IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS

Use with Anticholinergics: Galantamine has the potential to interfere with the activity of anticholinergic medications.

Established Safety Profile

- The safety profile of galantamine (the active ingredient of ZUNVEYL) has been established in 8 clinical trials[1]

Adverse Reactions Reported by ≥1% of Galantamine-Treated Patients in 8 Placebo-Controlled, Double-Blind Clinical Trials[1]

Adverse Reaction	Galantamine (n=3956) %	Placebo (n=2546) %
Metabolism and Nutrition Disorders		
Decreased appetite	7.4	2.1
Psychiatric Disorders		
Depression	3.6	2.3
Nervous System Disorders		
Dizziness	7.5	3.4
Headache	7.1	5.5
Tremor	1.6	0.7
Somnolence	1.5	0.8
Syncope	1.4	0.6
Lethargy	1.3	0.4
Cardiac Disorders		
Bradycardia	1.0	0.3
Gastrointestinal Disorders		
Nausea	20.7	5.5
Vomiting	10.5	2.3
Diarrhea	7.4	4.9
Abdominal pain	3.8	2.0
Abdominal discomfort	2.1	0.7
Dyspepsia	1.5	1.0
Musculoskeletal and Connective Tissue Disorders		
Muscle spasms	1.2	0.5
General Disorders and Administration Site Conditions		
Fatigue	3.5	1.8
Asthenia	2.0	1.5
Malaise	1.1	0.5
Investigations		
Decreased weight	4.7	1.5
Injury, Poisoning, and Procedural Complications		
Fall	3.9	3.0
Laceration	1.1	0.5

IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS (CONT'D)

Use with Cholinomimetics and Other Cholinesterase Inhibitors: A synergistic effect is expected when cholinesterase inhibitors are given concurrently with succinylcholine, other cholinesterase inhibitors, similar neuromuscular blocking agents or cholinergic agonists such as bethanechol.

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ZUNVEYL: A Clear Choice for Your Residents with AD

Purposefully Designed Delivery

- Enteric-coated, delayed-release prodrug technology designed to minimize absorption in the stomach and avoid overstimulation of the gastrointestinal nervous system.[1,2]
- Provides dual protection from peripheral and central cholinergic side effects.[2]

Dual Acting Mechanism of Action†

- Inhibits acetylcholinesterase, preventing the breakdown of acetylcholine and increasing its availability.[1]
- Modulates nicotinic acetylcholine receptors, making acetylcholine pathways more responsive.[4,5]

†The mechanism of action of ZUNVEYL is not fully understood.

Proven Medication for Cognition, Behaviors and Daily Function

- Galantamine (the active ingredient of ZUNVEYL) showed significant and sustained improvement in cognition, behaviors, and functional performance.[1,6]

No Significant Impact on Sleep

- No incidence of insomnia in the ZUNVEYL label.[1]

Scan the QR code to visit Zunveyl.com for access support and additional resources

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on animal data may cause fetal harm.

Hepatic Impairment: In patients with moderate hepatic impairment, a decrease in clearance of galantamine was observed; therefore, a dosage adjustment is recommended. Use of ZUNVEYL in patients with severe hepatic impairment is not recommended.

Renal Impairment: In patients with a creatinine clearance of 9 to 59 mL/min, an increase in exposure of galantamine was observed; therefore, a dosage adjustment is recommended. Use of ZUNVEYL in patients with creatinine clearance less than 9 mL/min is not recommended.

REFERENCES: **1.** ZUNVEYL (benzgalantamine) delayed-release tablets [Prescribing Information]. Grapevine, TX. Alpha Cognition Inc. 2024. **2.** Data on File, Alpha Cognition; Grapevine, TX (ZUNVEYL IND Components of the Drug Product). **3.** Liederer BM, Borchardt RT. *J Pharm Sci.* 2006;95(6):1177-1195. **4.** Lilienfeld S. *CNS Drug Rev.* 2002;8(2):159-176. **5.** Ago Y, et al. J *Pharmacol Sci.* 2011;116(1):6-17. **6.** Tariot PN, et al; Galantamine USA-10 Study Group. *Neurology*. 2000;54(12):2269-2276. **7.** Cummings JL. Neuropsychiatric Inventory (NPI): instructions for use and administration. Mary S. Easton Center for Alzheimer's Disease Research at UCLA; 2009.

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Alpha Cognition