Iowa PDL New Drug Review

Proprietary Name: Zunveyl®
Common Name: benzgalantamine delayed-release tablets
PDL Category: Alzheimer – Cholinomimetics

Pharmacology/Usage: Benzgalantamine, the active ingredient of Zunveyl®, is a prodrug of galantamine, an acetylcholinesterase inhibitor. Galantamine, a tertiary alkaloid, is a competitive and reversible inhibitor of acetylcholinesterase. While the exact mechanism of action is not known, it is thought to exert its therapeutic effect by enhancing cholinergic function. This is done by increasing the concentration of acetylcholine through reversible inhibition of its hydrolysis by cholinesterase. If this mechanism is correct, galantamine's effect may lessen as the disease process advances and fewer cholinergic neurons remain functionally intact. There is no evidence that galantamine alters the course of the underlying dementing process.

While the etiology of cognitive impairment in Alzheimer's disease (AD) is not fully understood, it has been reported that acetylcholine-producing neurons degenerate in the brains of patients with AD. The degree of this cholinergic loss has been correlated with degree of cognitive impairment and density of amyloid plaques (a neuropathological hallmark of AD).

Indication: For the treatment of mild to moderate dementia of the Alzheimer's type in adults.

There is no pregnancy category for this medication; however, the risk summary indicates that there are no adequate data on the developmental risk associated with Zunveyl® or galantamine use in pregnant women. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Enteric-coated, delayed-release tablets: 5mg, 10mg, and 15mg.

Swallow tablets whole; do not split, crush, or chew.

Recommended Dosage: The recommended starting dosage is 5mg PO BID (10mg/day). Increase to initial maintenance dosage of 10mg BID (20mg/day) after a minimum of 4 weeks, based on clinical response and tolerability. Dosage may be increased to the maximum recommended dosage of 15mg BID (30mg/day) after a minimum of 4 weeks at 10mg BID.

Take with or without food and ensure adequate fluid intake during treatment. Should not be taken with alcohol.

If therapy has been interrupted for more than 3 days, the patient should be restarted at the lowest dosage and the dosage escalated to the current dose.

Dosage adjustment is not recommended for patients with mild hepatic impairment. With moderate hepatic impairment, the dosage should generally not exceed 10mg BID. The use of Zunveyl® with severe hepatic impairment is not recommended. In patients with creatinine clearance of 9 to 59ml/min, the dosage should generally not exceed 10mg BID. In patients with creatinine clearance less than 9ml/min, the use of Zunveyl® is not recommended.

Drug Interactions: Galantamine has the potential to interfere with the activity of anticholinergic medications.

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.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (galantamine) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included decreased appetite (5.3%), depression (1.3%), dizziness (4.1%), headache (1.6%), tremor (0.9%), somnolence (0.7%), syncope (0.8%), lethargy (0.9%), bradycardia (0.7%), nausea (15.2%), vomiting (8.2%), diarrhea (2.5%), abdominal pain (1.8%), abdominal discomfort (1.4%), dyspepsia (0.5%), muscle spasms (0.7%), fatigue (1.7%), asthenia (0.5%), malaise (0.6%), decreased weight (3.2%), fall (0.9%), and laceration (0.6%).

Serious skin reactions (e.g., Stevens-Johnson syndrome and acute generalized exanthematous pustulosis) have been reported in patients receiving galantamine tablets (the active metabolite of Zunveyl®). Zunveyl® should be discontinued at the first appearance of a skin rash, unless the rash is clearly not drug-related. If signs or symptoms suggest a serious skin reaction, use of this drug should not be resumed and alternative treatment should be considered.

Zunveyl®, as a cholinesterase inhibitor, is likely to increase the neuromuscular blocking effects of succinylcholine-type and similar neuromuscular blocking agents during anesthesia.

Because of their pharmacological action, 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. Thus, all patients should be considered at risk for adverse effects on cardiac conduction.

Through their primary action, cholinomimetics, including Zunveyl®, may be expected to increase gastric acid secretion because of increased cholinergic activity. Thus, patients should be monitored closely for symptoms of active or occult gastrointestinal bleeding, especially those with an increased risk for developing ulcers. Clinical studies of galantamine have shown no increase, relative to placebo, in the incidence of either peptic ulcer disease or gastrointestinal bleeding. Galantamine, as a predictable consequence of its pharmacological properties, has been shown to produce nausea, vomiting, diarrhea, anorexia, and weight loss. Monitor the patient's weight during therapy.

While this was not observed in clinical trials with galantamine, cholinomimetics, including Zunveyl®, may cause bladder outflow obstruction.

Cholinesterase inhibitors are believed to have some potential to cause generalized convulsions. Seizure activity may also be a manifestation of AD. Patients with AD should be monitored closely for seizures while taking Zunveyl®.

Because of its cholinomimetic action, Zunveyl® should be prescribed with care to patients with a history of severe asthma or obstructive pulmonary disease. Respiratory function should be closely monitored for the occurrence of respiratory adverse reactions.

Contraindications: In patients with known hypersensitivity to benzgalantamine, galantamine, or to any inactive ingredient in the product.

Manufacturer: Alpha Cognition, Inc.

Analysis: The efficacy of Zunveyl® is based upon 3 bioavailability studies in healthy adults comparing galantamine immediate-release (IR) tablets and galantamine extended-release (ER) capsules to Zunveyl®. The efficacy of galantamine as a treatment for AD is demonstrated by the results of 5 randomized, double-blind, placebo-controlled clinical investigations in patients with probable AD, 4 with the IR tablet and 1 with the ER capsule. Galantamine IR

tablets and ER capsules have been available for many years; a solution is also available. No new clinical studies were found in the Zunveyl® prescribing information.

Place in Therapy: Zunveyl® is a cholinesterase inhibitor indicated for the treatment of mild to moderate dementia of the Alzheimer's type in adults. It is prodrug of galantamine, which has been available in various dosage forms for many years. The efficacy of Zunveyl® is based upon 3 bioavailability studies in healthy adults comparing galantamine IR tablets and galantamine ER capsules to Zunveyl®. Zunveyl® is available as a delayed-release tablet, with the potential to be better tolerated due to minimal absorption in the stomach. A cholinesterase inhibitor agent (donepezil, galantamine, or rivastigmine) is suggested for patients with newly diagnosed mild to moderate AD dementia.[2]

Summary

There is no evidence to suggest that Zunveyl® is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Zunveyl® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Zunveyl [package insert]. Grapevine, TX: Alpha Cognition, Inc; 2024.
[2] UpToDate online. Treatment of Alzheimer disease. Accessed August 2025.