

New & Off-Label Treatments for Agitation in Dementia

A Guide for Patients, Families & Caregivers

Agitation may look like pacing, repeated calling out, resistance to care, distress, or verbal or physical aggression. It is often a sign of an unmet need—not intentional misbehavior. Treatment aims to reduce distress and improve safety while preserving alertness, movement, and quality of life.

First: Look for Treatable Causes

- Sudden change? Ask about delirium, infection, dehydration, medication effects, or another acute illness.
- Look for pain, constipation, urinary retention, hunger, poor sleep, fear, overstimulation, and hearing or vision problems.
- Try reassurance, predictable routines, personalized activities, caregiver coaching, and a quieter environment.

What Does “Off-Label” Mean?

FDA-approved (on-label) means the FDA has authorized a medication for a specific condition. Off-label means a clinician prescribes an approved medication for a different condition, symptom, age group, or regimen. Off-label prescribing is legal and sometimes appropriate, but it does NOT mean the FDA has approved the drug for dementia agitation. “Investigational” means a treatment is still being studied or lacks adequate evidence for routine use.

FDA-Approved for Agitation in Alzheimer’s Dementia (U.S., October 2026)

Medication	Status and possible benefit	Important cautions
Brexpiprazole (Rexulti)	FDA-APPROVED for agitation associated with dementia due to Alzheimer’s disease; a daily antipsychotic, not a PRN rescue medication.	Boxed warning: increased death risk in older adults with dementia-related psychosis; possible stroke, sedation, falls, movement effects, weight/metabolic changes.
Dextromethorphan/bupropion (Auvelity)	FDA-APPROVED in April 2026 for agitation associated with dementia due to Alzheimer’s disease; non-antipsychotic oral medication.	Dizziness, nausea, sleepiness, blood pressure elevation, seizure risk, medication interactions; antidepressant suicidality warning in younger patients.

These approvals are for Alzheimer’s-related agitation—not every type of dementia or every cause of restlessness. Neither treatment cures dementia. Medication choice requires individualized assessment.

When Is Medication Considered?

Medication may be considered when agitation causes significant distress, threatens safety, or persists despite addressing triggers and using supportive approaches. The care team should agree on a specific target symptom and how improvement will be measured.

Other Medications Sometimes Used — OFF-LABEL for Dementia Agitation

The medications below are FDA-approved for other conditions, but NOT specifically for agitation in dementia. Research support varies considerably; some options have little high-quality evidence.

Option — ALL OFF-LABEL	Why it may be considered	Main concerns / evidence
Citalopram, escitalopram, sertraline (SSRIs)	Persistent distress, anxiety or mood symptoms; citalopram has some agitation trial evidence.	Benefits are not guaranteed; nausea, low sodium, bleeding and falls; citalopram can prolong QT and worsen cognition at higher studied doses.
Trazodone	Sleep disruption or evening distress when sedation might be useful.	Limited evidence for agitation itself; dizziness, low blood pressure, falls, daytime sedation.
Risperidone, aripiprazole, quetiapine, olanzapine; haloperidol	Severe dangerous aggression, psychosis or intense distress in selected situations.	Increased mortality/stroke warnings; sedation, falls, movement effects; quetiapine has weaker agitation evidence. Haloperidol generally avoided for routine long-term use.
Gabapentin / pregabalin	Sometimes considered if pain, anxiety or neuropathic discomfort may contribute.	Only weak evidence for agitation; sleepiness, unsteadiness, edema; kidney-dose considerations.
Prazosin	Occasionally considered for persistent agitation; small preliminary studies.	Limited evidence; low blood pressure, dizziness and falls.
Carbamazepine	Rarely considered by specialists in difficult cases.	Limited evidence; low sodium, blood-count/liver effects, drug interactions.
Propranolol	Occasionally explored for severe motor restlessness/aggression.	Very limited evidence; slow pulse, low blood pressure, fatigue, bronchospasm.
Dextromethorphan/quinidine (Nuedexta)	Small agitation trial; approved for pseudobulbar affect, NOT dementia agitation.	QT/interaction concerns, dizziness, falls; quinidine raises interaction burden.

Important: medicines that generally should NOT be used routinely for agitation

- Valproate/divalproex: trials do not support routine use for dementia agitation, and adverse effects can be significant (sedation, falls, thrombocytopenia).
- Benzodiazepines (such as lorazepam): sometimes used briefly in exceptional circumstances, but may worsen confusion, disinhibition, falls, breathing problems and dependence.
- Anticholinergic sedatives and “just make them sleep” approaches may increase confusion without treating the underlying distress.

Novel, Emerging & Non-Drug Approaches

Approach	Current role
Personalized music, meaningful activities, caregiver training, pain treatment Cholinesterase inhibitors or memantine	FIRST-LINE supportive approaches; adjust to the person's preferences and triggers. Used for selected cognitive symptoms; may help some behavioral symptoms over time, but NOT reliable rapid treatment for severe agitation.
Cannabinoids (e.g., nabilone, dronabinol)	INVESTIGATIONAL / OFF-LABEL for agitation; small studies, mixed evidence, potential sedation, confusion, falls and cardiovascular effects.
Electroconvulsive therapy (ECT)	OFF-LABEL for dementia-related agitation; specialist option for exceptional, severe treatment-resistant situations. Evidence is limited and anesthesia/cognitive risks require careful review.
Neuromodulation (e.g., TMS), light-based or other experimental therapies	INVESTIGATIONAL for dementia agitation; evidence insufficient for routine use.

Special Safety Considerations

- Lewy body dementia and Parkinson's disease dementia: people may have severe sensitivity to dopamine-blocking antipsychotics; involve a knowledgeable specialist.
- Vascular dementia, prior stroke, heart disease, frailty and falls: risks may change the medication decision.
- Polypharmacy: ask the team to review all prescription, over-the-counter and herbal products for interactions.
- Never stop a regularly taken psychiatric medication abruptly without discussing a safe plan.

What Families Should Monitor

Target benefit	Watch for harm
Less distress; fewer or shorter episodes of aggression; improved ability to accept care; better quality of life	Excessive sleepiness, reduced eating or drinking, falls, fainting, new stiffness/tremor, worsening confusion, abnormal movements, or new difficulty swallowing

Seek urgent medical assessment for sudden severe confusion, fever with rigidity, seizure, fainting, new one-sided weakness, chest pain, or trouble breathing.

Questions to Ask the Prescriber

- Is this medication FDA-approved for my loved one's diagnosis and symptom, or is its use OFF-LABEL?
- What specific behavior are we trying to improve, and how will we measure benefit?
- What are the alternatives, especially non-drug options?
- What side effects and interactions are most important for this person?
- When will we reassess, and what is the plan to reduce or stop it if it does not help?

A Simple Family Tracking Worksheet

Date / time	What happened just before?	What helped?	Medication change or side effect?

Reliable Educational Resources

- Alzheimer's Association — Treatments for Behavior: alz.org/alzheimers-dementia/treatments/treatments-for-behavior
- Alzheimer's Association 24/7 Helpline: 800-272-3900
- U.S. Food and Drug Administration — FDA medication approvals and safety: fda.gov
- National Institute on Aging — Alzheimer's and dementia information: nia.nih.gov
- American Psychiatric Association — Dementia guideline and patient/family materials: psychiatry.org
- International Psychogeriatric Association — Agitation reduction and prevention algorithm (clinical resource): ipa-online.org

Key Takeaways

- Start by identifying causes of distress and using personalized non-drug support.
- For Alzheimer's-related agitation, Rexulti and Auvelity are FDA-approved options as of October 2026.
- Many other medications are used OFF-LABEL; their evidence and risks differ, and "new" does not necessarily mean safer or more effective.
- Aim for meaningful comfort and function—not simply sedation. Revisit the need for medication regularly.

Educational information only; not a substitute for individualized medical advice. Drug approvals, availability and safety information can change. Last reviewed: October 2026.