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PRACTICE GUIDELINES FOR Alzheimer's Disease Treatment

TREATING NEUROPSYCHIATRIC FEATURES

A critical part of managing Alzheimer's Disease (AD) is the treatment of neuropsychiatric features. Antidepressants and antipsychotics are often prescribed to treat behavioral and psychiatric changes in patients with AD.[1]

>90% of AD patients develop behavioral/psychiatric changes.[2]

PHARMACOLOGY KEY

- Anti-Dep — **Antidepressants**
- ChEI — **ChEI:** Cholinesterase inhibitor
- NMDA — **NMDA receptor antagonists:** N-methyl-D-aspartate receptor antagonists[3]
- SGA — **Second-Generation Antipsychotic (SGA):** Serotonin-dopamine antagonist, also known as atypical antipsychotic[4]

	EAN Guidelines European Academy of Neurology	APA Guidelines American Psychiatric Association	CCCDTD4 & 5 4th & 5th Canadian Consensus Conferences on the Diagnosis & Treatment of Dementia
Mild To Moderate AD	**Cognitive Therapy:** Preliminary studies suggest a beneficial effect of cognitive stimulation (ie. Reality Orientation).[5] ChEI **ChEIs:** Consider when diagnosed, bearing in mind therapeutic benefits and possible safety issues.[5]	ChEI **ChEIs:** Modest evidence supports efficacy for mild–moderate AD.[1] **ChEI Transdermal Patch:** Higher doses possibly associated with greater benefit.[1]	**Nonpharmacologic measures (Nonpharm):** Encourage proper nutrition and sleep, physical exercise, hearing screening, cognitive training, and social engagement.[8] **Hypertension Treatment:** May reduce dementia risk.[8] ChEI **ChEIs:** Consider, weighing benefits and risks.[1]
Moderate To Severe AD	NMDA + ChEI **NMDA receptor antagonist & ChEI Combination Therapy:** Suggested rather than ChEI alone in patients with moderate to severe AD.[6]	NMDA and/or ChEI **ChEIs or NMDA receptor antagonists:** Modest evidence supports efficacy for moderate–severe AD.[1] **NMDA receptor antagonist & ChEI Combination Therapy:** Slight/unclear clinical significance.[1]	NMDA and/or ChEI **ChEIs or NMDA receptor antagonists:** May be considered for the treatment of vascular cognitive impairment in selected patients.[8] **NMDA receptor antagonist & ChEI Combination Therapy:** Insufficient evidence for or against.[1]
Depression	Anti-Dep **Antidepressants:** Use selective serotonin reuptake inhibitors (SSRIs) rather than tricyclic antidepressants.[5]	Anti-Dep **Antidepressants:** Mixed evidence for efficacy.[1]	Anti-Dep **Antidepressants:** Trial could be considered.[1]
Agitation/ Psychosis	**Nonpharm:** Management of Behavioral and Psychological Symptoms of Dementia (BPSD) should begin with a careful search for triggers and causative factors (i.e. physical illness). Where possible, initial treatment should be non-pharmacological. ChEIs may be considered.[5] SGA **Antipsychotics:** If patient does not respond to above measures, consider for moderate–severe behavioral and psychological symptoms that cause notable distress, or when other treatments are not appropriate.[5]	**Nonpharm:** Review clinical response to nonpharm. interventions prior to non-emergency use of an antipsychotic medication.[7] SGA **Nonemergency Antipsychotics:** Consider for agitation/psychosis with severe, dangerous, and/or significantly distressing symptoms. Assess and discuss potential risks and benefits with patient and caregiver(s).[7] Anti-Dep **Antidepressants:** Benefits shown in SSRI single trial. Treatment constrained by cardiac adverse events (AEs).[1]	**Nonpharm:** Exercise, group cognitive therapy, psychoeducational and psychosocial interventions for caregivers, & dementia-friendly organizational design.[8] SGA **Antipsychotics:** Recommended for severe agitation, aggression, and psychosis symptoms with risk of harm to the patient and/or others. Weigh potential benefits against significant risks.[1] **NMDA receptor antagonists and/or ChEIs:** Insufficient evidence for or against use for treating neuropsychiatric symptoms as a primary indication.[8]
Not Recommended	**Aspirin:** Do not use to treat AD.[5] **Vitamin E:** Do not use to treat AD.[5] **Insufficient evidence to support the use of:** anti-inflammatory drugs, a specific monoamine oxidase (MAO) inhibitor, estrogens, pentoxifylline, statins, and porcine brain-derived proteolytic peptide fraction.[5]	**Alternative Agents:** Uncertain efficacy and safety, and generally not recommended (e.g., statins, anti-inflammatory drugs, vitamin E, and estrogens).[1]	**Certain Anticonvulsants:** Do not use for treating agitation and aggression.[1] **Aspirin:** Do not use for patients with Mild Cognitive Impairment (MCI) or dementia with covert white matter lesions of vascular origin without stroke history or brain infarcts.[8]

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