



Drug used in Alzheimer's Disease

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Dementia of the Alzheimer type has three distinguishing features:

1. Accumulation of senile plaques (β -amyloid accumulations)
2. Formation of numerous neurofibrillary tangles
3. Loss of cortical neurons, particularly cholinergic neurons.

Overstimulation of glutamate receptors, particularly of the NMDA type, may result in excitotoxic effects on neurons, neurodegenerative or apoptotic (programmed cell death processes)

Aim of therapies to either:

- Improve cholinergic transmission within the CNS

Or

- Prevent excitotoxic actions resulting from overstimulation of NMDA-glutamate receptors in selected areas of the brain.

Note: Pharmacologic intervention for Alzheimer's disease is only palliative and provides modest short-term benefit. ¬ alter the neurodegenerative process

Pharmacokinetic properties of dopamine agonists pramipexole, ropinirole, and rotigotine. V_d = volume of distribution. ¹Increases to 12 hours in patients older than 65 years; ²Less than 10% excreted unchanged; ³Administered as a once-daily transdermal patch

Characteristic	<i>Pramipexole</i>	<i>Ropinirole</i>	<i>Rotigotine</i>
Bioavailability	>90%	55%	45%
V_d	7 L/kg	7.5 L/kg	84 L/kg
Half-life	8 hours ¹	6 hours	7 hours ³
Metabolism	Negligible	Extensive	Extensive
Elimination	Renal	Renal ²	Renal ²

Acetylcholinesterase inhibitors

Donepezil , Galantamine and Rivastigmine

- Mild to moderate Alzheimer's disease
- Selectivity for acetylcholinesterase in the CNS as compared to the periphery
- The inhibition of acetylcholinesterase within the CNS will improve cholinergic transmission
- Galantamine may also augment the action of acetylcholine at nicotinic receptors in the CNS

Adverse Effects of Acetylcholinesterase Inhibitors

- Nausea, diarrhea, vomiting, anorexia
- Tremors
- Bradycardia
- Muscle cramps

NMDA receptor antagonist

Memantine

- It is an NMDA receptor antagonist indicated for moderate to severe Alzheimer's disease
- It is often given in combination with an acetylcholinesterase inhibitors
- It acts by blocking the NMDA receptor and limiting Ca^{2+} influx into the neuron

Adverse Effect of Memantine

It is well tolerated, with few dose-dependent adverse effect.

- Confusion, agitation, and restlessness (are indistinguishable from the symptoms of Alzheimer's disease).